# Canine and Feline Dermatology Drug Handbook

**Sandra N. Koch** DVM, MS, DACVD
Assistant Clinical Professor
College of Veterinary Medicine
University of Minnesota
Saint Paul, Minnesota, USA

**Sheila M.F. Torres** DVM, MS, PhD, DACVD
Associate Clinical Professor
College of Veterinary Medicine
University of Minnesota
Saint Paul, Minnesota, USA

**Donald C. Plumb** PharmD
Stockholm, Wisconsin, USA

WILEY-BLACKWELL
A John Wiley & Sons, Ltd., Publication

This edition first published 2012


Wiley-Blackwell is an imprint of John Wiley & Sons, formed by the merger of Wiley's global Scientific, Technical and Medical business with Blackwell Publishing.

*Editorial Offices*
2121 State Avenue, Ames, Iowa 50014–8300, USA
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
9600 Garsington Road, Oxford, OX4 2DQ, UK

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com/wiley-blackwell.



*Library of Congress Cataloging-in-Publication Data*

Koch, Sandra N.
Canine and feline dermatology drug handbook / Sandra N. Koch, Sheila M.F. Torres, Donald C. Plumb.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-4051-9896-7 (pbk. : alk. paper)
I. Torres, Sheila M.F. II. Plumb, Donald C. III. Title.
[DNLM: 1. Skin Diseases–drug therapy–Handbooks. 2. Skin Diseases–veterinary–Handbooks.
3. Cat Diseases–drug therapy–Handbooks. 4. Dermatologic Agents–therapeutic use–Handbooks.
5. Dog Diseases–drug therapy–Handbooks. SF 992.S55]
636.089'65–dc23
2011038035

A catalogue record for this book is available from the U.S. Library of Congress.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Set in 8.5/10.5pt Frutiger-Light by SPi Publisher Services, Pondicherry, India

1 2012

To my husband, Robert, for his love and support; my son, Kaio, for the inspiration and my parents, Sebastião and Mara, for the encouragement and education.

*Sandra Koch*

To my husband, Maurilio, for his patience and continuous support during the production of this book.

*Sheila Torres*

# Disclaimer

While a sincere effort has been made to ensure that the dosages and information included in this book are correct, errors may occur, and it is suggested that the reader refer to the original reference or the approved labeling information of the product for additional information. The authors and publisher assume no responsibility for and make no warranty with respect to results that may be obtained from the uses, procedures, or dosages listed, and do not necessarily endorse such uses, procedures, or dosages. The authors and publisher shall not be liable to any person whatsoever for any damages, or equivalencies, or by reason of any mis-statement or error, negligent or otherwise, contained in this work. Should the purchaser not wish to be bound by the above, he/she may return the book to the publisher for a full refund.

**A note about trade names and proprietary names**

The notation used to signify trade names or proprietary names is an italicized, capitalized name followed by ® (e.g., *Soriatane*®). This notation may not accurately represent the drug's official registered copyright trade mark or licensed status.

# Contents

## Antibacterials, Tetracyclines



## Antibacterials, Miscellaneous



## Antifungals



## Antihistamines



## Anti-inflammatory Agents

## Anti-inflammatory Agents, Glucocorticoids



## Antineoplastic/chemotherapeutic Agents



## Antiparasitic Agents



## Antivirals



## Behavior Modifying Drugs, Opioid Antagonists

## Immunomodulatory Agents



## Retinoids



## Antiparasitic Agents



## Miscellaneous



## Otic Preparations

# Preface

The idea to write this book came from the need to have a concise yet complete and easy-to-use reference focusing on drugs especially used for dermatological conditions of dogs and cats. What makes this work different from other available drug references is the inclusion of dermatological drugs not listed in those other drug references, and the compilation of compounded medications for ear diseases. In addition, we are providing detailed drug information applicable to veterinary dermatology that includes indications and dosages for drugs used for many dermatological diseases, and specific details on adverse effects (e.g., ototoxicity). Lastly, this work contains the unique addition of a brief discussion of the common dermatological diseases of dogs and cats, with an associated list of drugs that can be considered for their treatment.

The information contained in this book is derived from an extensive literature search that included important veterinary peer-reviewed journals and textbooks, and reliable online sources, in addition to the authors' clinical experience. The book is divided into four sections encompassing systemic drugs, topical agents, allergen-specific immunotherapy, and common dermatological diseases with a list of drugs that can be used for their treatment. Both veterinary and human-labeled drugs applicable to veterinary dermatology are included. When available, manufacturers' recommended indications and dosages for veterinary-labeled drugs are listed, but extra-label and anecdotal indications and dosages are also mentioned when appropriate. Drug interactions reported are mostly extrapolated from humans, as there is limited information available in dogs and cats, and we hope this will bring awareness to veterinarians when using drug combinations. We have included drugs available in the United States, Canada and the United Kingdom, and additionally some drugs not available in the United States that have been used by veterinarians in other countries.

We believe the information presented in this work valuably complements other available references for veterinary dermatology and drug information. This work is written primarily for general practice veterinarians, veterinary students, veterinary dermatology residents and dermatologists, and overall, for everyone passionate about veterinary dermatology. We believe it will be useful not only for clinical practice, but also as a teaching tool for veterinary students and residents. We hope that this work will help veterinarians improve patient care by having broad information in a single dermatological drug reference.

As clinical experience and research in veterinary dermatological therapeutics expand, and as new information becomes available, the authors welcome any feedback from readers by e-mail (dermdrughandbook@wiley.com), including clinical experience, adverse effects and drug interactions, omissions and errors, to help us improve the quality of this book.

*Sandra N. Koch*
*Sheila M.F. Torres*
*Donald C. Plumb*

# Acknowledgments

The authors would like to sincerely thank Dr. Alisa Craig, PharmD, director of pharmacy services, and Dr. Antonella Borgatti, board-certified veterinary oncologist, both from the University of Minnesota, for providing valuable information for the elaboration of this work. A special thank you to our dermatology team at the University of Minnesota, and to our families, friends, and colleagues, for supporting us and being excited by the development of this book, and to our special patients and their owners for allowing us to gain clinical experience over the years.

# Abbreviations and Conversions

## Abbreviations

| | |
|---|---|
| CA | Canada |
| EU | Europe |
| UK | United Kingdom |
| US | United States |
| CDC | Centers for Disease Control and Prevention |
| EPA | Environmental Protection Agency |
| FDA | Food and Drug Administration |
| USDA | United States Department of Agriculture |
| WHO | World Health Organization |
| OTC | over-the-counter |
| Rx | prescription |
| IM | intramuscular |
| IV | intravenous |
| PO | by mouth |
| SC | subcutaneous |
| h | hour |
| q6h | every 6 hours |
| q8h | every 8 hours |
| q12h | every 12 hours |
| q24h | every 24 hours |
| q48h | every 48 hours |
| kg | kilogram |
| g | gram |
| mg | milligram |
| mcg | microgram |
| ng | nanogram |
| lb | pound |
| oz | ounce |
| L | liter |
| mL | milliliter |
| dL | deciliter |
| mcL | microliter |
| gal | gallon |
| qt | quart |
| pt | pint |
| $m^2$ | square meter |

| | |
|---|---|
| $mm^3$ | cubic millimeter |
| IU | international unit |
| MU | million units |
| PNU | protein nitrogen unit |
| nmol | nanomole |
| ppm | parts per million |

| | |
|---|---|
| btl | bottle |
| pkt | packet |
| tb | tube |

| | |
|---|---|
| ABCB1 | ATP-binding cassette B1 |
| AD | atopic dermatitis |
| ACTH | adrenocorticotropic hormone |
| ALP | alkaline phosphatase |
| ALT | alanine aminotransferase |
| ASIT | allergen-specific immunotherapy |
| AST | aspartate aminotransferase |
| ATP | adenosine triphosphate |
| BUN | blood urea nitrogen |
| CBC | complete blood cell count |
| CD | cluster of differentiation |
| CNS | central nervous system |
| CYP | cytochrome P450 |
| DNA | deoxyribonucleic acid |
| ECG | electrocardiogram |
| EDTA | ethylene diamine tetra-acetic acid |
| ELISA | enzyme-linked immunosorbent assay |
| FeLV | feline leukemia virus |
| FHV | feline herpes virus |
| FIV | feline immunodeficiency virus |
| fT4 | free thyroxine 4 |
| GABA | gamma-aminobutyric acid |
| hIVIG | human intravenous immunoglobulin |
| Ig | immunoglobulin |
| IL | interleukin |
| MDR1 | multi-drug resistant-1 |
| NF-kB | nuclear factor kappa B |
| NSAID | non-steroidal anti-inflammatory drug |
| RNA | ribonucleic acid |
| Th | T helper |
| TNF | tumor necrosis factor |
| TRH | thyrotropin-releasing hormone |
| TSH | thyroid-stimulating hormone |
| tT3 | total thyroxine 3 |
| tT4 | total thyroxine 4 |
| UV | ultraviolet |
| UVA | ultraviolet A |
| UVB | ultraviolet B |

## Conversions

### WEIGHT

1 pound (lb) = 0.454 kilogram = 454 grams = 16 ounces
1 ounce (oz) = 28.4 grams
1 kilogram (kg) = 2.2 pounds = 1000 grams
1 gram (g) = 1000 milligrams
1 milligram (mg) = 1000 micrograms
1 microgram (mcg) = 1000 nanograms
Note: For weight to body surface area conversion, refer to Table 9 in *The Merck Veterinary Manual*, 10th edn. Whitehouse Station, NJ: Merck, 2010; p. 2829.

### LIQUID MEASURE

1 gallon (gal) = 4 quarts = 8 pints = 128 ounces = 3.785 liters = 3784 milliliters
1 liter (L) = 1000 milliliters = 10 deciliters
1 deciliter (dL) = 100 milliliters
1 milliliter (mL) = 1000 microliters
1 milliliter (mL) = 20 drops (1 drop = 0.05 milliliters)

# Section 1
# Systemic Drugs

## Acitretin

**Trade/brand name**: *Soriatane*® (US, CA), *Neotigason*® (UK), generic: 13-cis-acitretin; etretin; isoetretin (Rx)
**Classification:** Synthetic retinoid (second-generation)

### INDICATIONS

Acitretin is indicated for several keratinization, follicular and sebaceous gland abnormalities.

**Dogs:** Primary or idiopathic seborrhea of cocker and springer spaniels, golden retrievers, Irish setters and mixed-breed dogs, vitamin-A responsive dermatosis, sebaceous adenitis, sebaceous gland hyperplasia and adenoma, solar dermatosis, actinic keratosis, squamous cell carcinoma, infundibular keratinizing acanthoma (i.e., keratoacanthomas or intracutaneous cornifying epitheliomas), ichthyosis, schnauzer comedo syndrome, follicular dysplasias (e.g., color dilution alopecia), inflammatory linear verrucous epidermal nevus, idiopathic nasodigital hyperkeratosis, ear margin seborrhea/dermatosis, epitheliotropic lymphoma. A recent study showed a potential benefit of retinoic acids (particularly 9-cis retinoic acid or alitretinoin at 2 mg/kg/day PO) for the treatment of canine pituitary-dependent hyperadrenocorticism (Castillo *et al*. 2006); however, investigations have not been performed with acitretin.

**Cats:** Actinic keratosis, solar-induced squamous cell carcinoma, Bowenoid in-situ carcinoma (multicentric squamous cell carcinoma in situ), sebaceous adenitis, acne.

**Note:** This medication may be difficult to obtain, and treatment cost can be prohibitive.

### CONTRAINDICATIONS

Patients with hypersensitivity to acitretin or other retinoids, severe renal or hepatic disease, cardiovascular disease, hypertriglyceridemia or other lipid abnormalities. Because of its known teratogenic effect, it should not be used in unspayed or pregnant females and breeding males, or in households with pregnant women or women planning to become pregnant (drug should not be handled by pregnant women).

*Canine and Feline Dermatology Drug Handbook*, First Edition.
Sandra N. Koch, Sheila M.F. Torres and Donald C. Plumb.

Published 2012 by Blackwell Publishing Ltd.

## MECHANISM OF ACTION

The exact mechanism of action of acitretin (active metabolite of etretinate) is unknown. It is believed to alter gene expression through nuclear retinoic acid receptors and bind to DNA to cause transcription or transrepression changes in protein synthesis leading to cellular differentiation and variable antiproliferative, anti-inflammatory, and immunomodulatory effects.

## DOSAGES

Acitretin must be given with food to optimize absorption.

### Dogs

- General dose: 0.5–3 mg/kg PO q24h
- Primary seborrhea, vitamin-A responsive dermatosis: 1–2 mg/kg PO q24h
- Sebaceous adenitis: 1–3 mg/kg PO q24–48h
- Color dilution alopecia: 0.5–1 mg/kg PO q24h
- Ichthyosis: 1–2 mg/kg PO q12h
- Bowenoid carcinoma: 3 mg/kg PO q24h
- Epitheliotropic lymphoma: 2.5 mg/kg PO q24h (palliative treatment)

### Cats

- General dose: 0.5–3 mg/kg PO q24h
- Actinic keratosis, squamous cell carcinoma and Bowenoid in-situ carcinoma, sebaceous adenitis and acne: 3 mg/kg or 10 mg per cat PO q24h

**Note:** Dose may be tapered to every other day after clinical remission is achieved.

## FORMULATIONS

**Veterinary-labeled products:** None

### Human-labeled products

- Oral capsules: 10 mg, 25 mg; *Soriatane*®, *Neotigason*®, generic

## SIDE EFFECTS

There is limited experience in veterinary medicine.

### Dogs

- Rare: anorexia, vomiting, diarrhea, polydipsia, lethargy, joint pain/stiffness, eyelid abnormalities, keratoconjunctivitis sicca, behavioral changes, musculoskeletal abnormalities, hepatotoxicity, increased transaminases, increased triglycerides and cholesterol, swollen tongue, cracking/fissures of footpads, ventral abdominal erythema, increased ceruminous gland hyperplasia and secretion, cheilitis, exfoliative dermatitis

### Cats

- Rare: anorexia with resultant weight loss

## DRUG INTERACTIONS

**Cyclosporine:** increase in serum levels of cyclosporine

**Methotrexate or other hepatotoxic drugs:** increased risk of hepatotoxicity

**Other retinoids (e.g., isotretinoin, tretinoin) or vitamin A, tetracycline, azole antifungals, macrolides:** increase in serum levels of acitretin

**Phenytoin:** reduction of protein binding of phenytoin

### MONITORING

- Efficacy and adverse effects
- Liver function tests, Schirmer tear tests (baseline, 1–2 months after treatment, and if symptoms appear)
- Avoid excessive exposure to sunlight, as the effects of UV lights are enhanced by retinoids
- Avoid concurrent intake of other vitamin A supplements to reduce the possibility of additive toxic effects

## Acyclovir

**Trade/brand name:** *Zovirax®* (US, CA, UK), generic: acyclovir; aciclovirum; acycloguanosine (Rx)
**Classification:** Antiviral

### INDICATIONS

There is limited experience in veterinary medicine. True efficacy is unknown.

**Dogs:** Herpes-virus-induced erythema multiforme.

**Cats:** Feline herpes virus 1 (FHV-1) ulcerative facial and nasal dermatitis and stomatitis (herpetic dermatitis); FHV-1 rhinotracheitis associated with oral and cutaneous ulcers; FHV-1 keratoconjunctivitis; herpes-virus-induced exfoliative erythema multiforme.

**Note:** FHV-1 has been shown to be resistant to acyclovir.

### CONTRAINDICATIONS

Hypersensitivity to acyclovir or other antivirals, dehydrated states, renal dysfunction, neurologic deficits. Use with caution in nursing patients.

### MECHANISM OF ACTION

Acyclovir is a synthetic purine analog (acyclic nucleoside analog) that inhibits DNA replication of herpes virus.

### DOSAGES

Doses are anecdotal and extrapolated from humans. Acyclovir appears to have poor absorption in cats.

**Dogs and cats**

- 3–10 mg/kg PO 5 times daily for 10 days
- 10–20 mg/kg IV q8h (slow infusion for 1 hour)
- Feline FHV-1 infections: 10–25 mg/kg PO q12h or 200 mg per cat PO q4h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 400 mg, 800 mg; *Zovirax®*, generic
- Oral capsules: 200 mg; *Zovirax®*, generic
- Oral suspension: 200 mg/5 mL in 473 mL; *Zovirax®*, generic

- Powder for injection (for IV infusion only): 500 mg/vial in 10 mL vials; 1 g/vial in 20 mL vials; *Zovirax®*, generic

### SIDE EFFECTS

There is limited experience in veterinary medicine; therefore, acyclovir should be used with caution. Potential adverse effects with parenteral therapy include thrombophlebitis, acute renal failure, and encephalopathologic changes (rare). Gastrointestinal side effects may occur with either oral or parenteral therapy. May be fetotoxic at high doses.

**Dogs**
- Common: vomiting, diarrhea, anorexia, and lethargy
- Rare: polyuria and polydipsia

**Cats**
- Common: vomiting, diarrhea, anorexia, and lethargy
- Rare: leukopenia and anemia (likely reversible with discontinuation of therapy)

### DRUG INTERACTIONS

**Amphotericin B:** increases antiviral effect of acyclovir

**Other nephrotoxic medications:** increase risk of nephrotoxicity

**Zidovudine:** CNS depression

### MONITORING

- Efficacy and adverse effects
- Renal function tests (BUN, serum creatinine) mainly with parenteral therapy
- CBC: baseline and every 2–3 weeks (cats)

## Allopurinol

**Trade/brand name:** *Zyloprim®* (US, CA), *Lopurin®* (US), *Novo-Purol®* (CA), *Allopur®* (UK), *Zyloric®* (UK), generic (Rx)
**Classification:** Anti-inflammatory

### INDICATIONS

**Dogs:** Allopurinol is often administered with pentavalent antimonial compounds such as meglumine antimoniate or sodium stibogluconate to treat leishmaniasis.

**Cats:** Use of allopurinol is not well investigated in cats. It may be used for leishmaniasis.

### CONTRAINDICATIONS

Hypersensitivity to allopurinol. Caution in patients with impaired hepatic or renal function. Caution in nursing dams as allopurinol can be excreted into milk. Safety in breeding or pregnant animals has not been established.

### MECHANISM OF ACTION

Allopurinol is a purine analog that inhibits the enzyme xanthine oxidase with consequent inhibition of uric acid synthesis and inhibition of formation of superoxide anion radical. Allopurinol is metabolized by *Leishmania* organisms into an inactive analog of inosine, which is incorporated into leishmanial RNA causing faulty protein translation and inhibition of parasite multiplication. Allopurinol may also inhibit hepatic microsomal enzymes.

### DOSAGES

**Dogs:** Dosage schedules vary widely and the optimal dosage has not been established. Dose adjustments are based on clinical signs. Administer 1 hour after meals.

- Induction (with or without antimony drugs): 15–30 mg/kg PO q12h for 1–8 months (until clinical remission is achieved)
- Maintenance: 15–20 mg/kg PO q24h for 1 week per month indefinitely

**Note:** Patients with renal insufficiency or hepatic dysfunction: reduce the dose to 5 mg/kg PO q12h, increase interval of administration or avoid use.

**Cats:** 20 mg/kg PO q24h for up to 15 months

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 100 mg, 300 mg; *Zyloprim®*, *Lopurin®*, *Allopur®*, *Zyloric®*, generic

### SIDE EFFECTS

**Dogs:** Side effects are reported mostly with low purine diets. If used for long-term therapy may need to reduce dose and purine precursors in the diet.

- Uncommon (mostly reported in humans): vomiting, diarrhea, nausea, dermatologic eruption (pruritus and rash), myelosuppression, xanthine urolith formation, hepatitis, vasculitis
- Rare: hemolytic anemia, trigeminal neuropathy

**Cats:** No information available

### DRUG INTERACTIONS

**Aminophylline or theophylline, oral anticoagulants (e.g., warfarin):** reduces metabolism of these drugs

**Amoxicillin:** cutaneous hypersensitivity

**Azathioprine or mercaptopurine:** increase toxicity of these drugs

**Cyclophosphamide:** increases bone marrow suppression

**Diuretics (e.g., furosemide, thiazides), diazoxide:** increases uric acid levels

**Trimethoprim/sulfamethoxazole:** thrombocytopenia

**Urinary acidifiers (e.g., methionine, ammonium chloride):** urolithiasis

### MONITORING

- Efficacy and adverse effects
- CBC, liver and renal function tests every 2 weeks, especially early in therapy

## Alprazolam

**Trade/brand name:** *Xanax®* (US, CA, UK), *Xanax® XR* (US), *Niravam®* (US), *Alprazolam Intensol®* (US), generic (Rx)
**Classification:** Tranquilizer, CNS depressant, Benzodiazepine

### INDICATIONS

Management of psychogenic or compulsive dermatoses, mostly associated with anxiety. Very effective for acute episodes of anxiety due to its rapid onset of action. It may be used alone or as adjunctive therapy.

**Dogs:** Self-mutilations, acral lick dermatitis, excessive tail or nail biting/chewing, excessive anal or foot licking, flank sucking, tail dock neuroma.

**Cats:** Psychogenic self-induced alopecia, tail sucking, excessive nail or foot biting/chewing, hyperesthesia syndrome.

### CONTRAINDICATIONS

Patients with known hypersensitivity to alprazolam or other benzodiazepines. Use cautiously in debilitated or geriatric animals, patients in coma or shock, with CNS depression, narrow-angle glaucoma, and hepatic or renal impairment. Caution in aggressive patients and working animals. Avoid in pregnant or lactating animals. It may be teratogenic. It should not be discontinued abruptly. Benzodiazepines have been reported to exacerbate myasthenia gravis in humans.

### MECHANISM OF ACTION

Alprazolam is a potent short-acting benzodiazepine exerting its maximum effect within 1 to 2 hours. More specifically, it is a triazolobenzodiazepine, a benzodiazepine with a *triazole ring* attached to its structure. Alprazolam possesses anxiolytic, sedative, hypnotic, anticonvulsant, and muscle relaxant properties. Its clinical effect may last longer and may have less effect on motor function and liver at low doses compared to other benzodiazepines such as diazepam. Exact mechanism of action is unknown. Postulated mechanisms include potentiation of the effects of GABA, an inhibitory neurotransmitter, by binding to specific benzodiazepine receptors, antagonism of serotonin, and diminished release or turnover of acetylcholine in the CNS system.

### DOSAGES

Alprazolam may be used in combination with tricyclic antidepressants, such as clomipramine, for the management of more severe behavioral abnormalities such as cases presenting acute panic attacks.

**Dogs:** 0.05–0.25 mg/kg PO q12–24h

**Cats:** 0.025–0.2 mg/kg PO q12–24h

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg; *Xanax®*, generic
- Disintegrating oral tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg; *Niravam®*, generic
- Extended release oral tablets: 0.5 mg, 1 mg, 2 mg, 3 mg; *Xanax® XR*, generic
- Oral solution: 1 mg/mL in 30 mL; *Alprazolam Intensol®*

## SIDE EFFECTS

Chronic administration of alprazolam may lead to dependence and withdrawal syndrome if discontinued. Benzodiazepines may impede the ability of the animal to learn and may retard training.

**Dogs**
- Common: variable and individual sedation effects, transient ataxia, polyphagia
- Rare: tolerance to the drug, paradoxical CNS excitement, aggression or other unusual behaviors

**Cats**
- Common: sedation, transient ataxia, polyphagia, changes in behavior (irritability, depression, increased affection, aberrant demeanor)
- Rare: paradoxical CNS excitement, anorexia, lethargy, increased ALT/AST, hyperbilirubinemia, tolerance to the drug

## DRUG INTERACTIONS

**Antacids:** may slow the rate, but not the extent of oral alprazolam absorption. This can be managed by separating the medications by 2 hours

**CNS depressant drugs (e.g., barbiturates, narcotics, anesthetics):** may increase alprazolam serum levels and additive effects may occur

**Digoxin:** alprazolam may increase serum levels of digoxin

**Fluoxetine:** increase in alprazolam serum concentration

**Hepatic metabolized drugs (e.g., amiodarone, cimetidine, chloramphenicol, clarithromycin, cyclosporine, diltiazem, erythromycin, isoniazid, ketoconazole, itraconazole):** alprazolam metabolism may be reduced and excessive sedation may occur

**Omeprazole, propanolol, valproic acid:** may decrease metabolism of benzodiazepines and cause excessive sedation

**Phenobarbital, phenytoin:** may decrease alprazolam serum levels

**Rifampin:** may induce hepatic microsomal enzyme activity and decrease alprazolam's efficacy

**Tricyclic antidepressants (e.g., amitriptyline, clomipramine, imipramine):** alprazolam may increase serum levels of these drugs

## MONITORING
- Efficacy and adverse effects
- Hepatic enzymes (particularly with chronic treatment in cats)

## Amino Acids

**Trade/brand name**: *Aminosyn*® (US), *Travasol*® (US, CA), *ProPass*® (US, CA), *Promod*® (US, CA), many brand names available
**Classification**: Nutritional supplement

### INDICATIONS

**Dogs:** Superficial necrolytic dermatitis.

**Cats:** Cats with superficial necrolytic dermatitis might also benefit from amino acid supplementation, as they have been reported to have hypoaminoacidemia; however, no information regarding products and dosages is available.

### CONTRAINDICATIONS

Dehydration, electrolyte imbalances, shock and inadequate oxygen supply.

### MECHANISM OF ACTION

A metabolic hepatopathy in which there is increased hepatic catabolism of amino acids is hypothesized to explain the hypoaminoacidemia seen in superficial necrolytic dermatitis. Thus, amino acid supplementation might replace the deficiency of amino acids associated with this disease.

### DOSAGES

Varying degrees of clinical success have been seen in dogs. Supplementation seems to be more successful when treatment is instituted early in the course of the disease.

**Dogs**

- Intravenous administration: 24 mL/kg (or 500 mg total volume per dog) IV slowly over 8–12 hours in a large central vein (jugular) because the solution is hypertonic and could cause phlebitis. After the initial therapy, the patient should be re-examined in 7–10 days. If significant improvement is noted, then no further infusions are needed. Prolonged remissions have been noted after only one infusion. If minimal to no response is noted, the infusions should be repeated every 7–10 days for four treatments. If there is no improvement in 4–6 weeks, the prognosis is guarded. Exacerbation of skin lesions in dogs that respond to amino acid treatment is common. The timing of these exacerbations is highly variable and amino acids should be re-administered with each exacerbation. Some dogs may require monthly IV amino acid infusions, but many dogs can go several months between infusions. As the disease progresses, the need for infusions will likely increase. Alternatively, the treatment could be performed 3 days in a row or every other day for the first week, and repeated every 1–2 weeks as signs relapse.

**Note:** The use of parenteral amino acids solutions should be undertaken with specific training and intensive care monitoring.

- Oral administration: oral protein supplements can be given either in conjunction with or instead of IV amino acid infusion; however, the IV amino acid infusion appears to be the most effective. There are different supplement options available, and appropriate dosage for dogs has not been established. Whey protein

supplements are commonly used and can be found in health-food stores and some grocery/drug stores. Another choice for specific amino acids is a daily oral supplement of 3–6 egg yolks.

Amino acid powder: *ProPass*® (similar to *Promod*®): 1 scoop/4.5 kg (10 lb) of body weight q24h.

**Cats:** No information available.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Crystalline solution for injection 8.5% and 10%: 10 g/100 mL; *Aminosyn*®, *Travesol*®
- Oral liquid: 32oz btl fruit punch flavor; *Promod*® (protein source: hydrolyzed beef collagen)
- Oral powder: *ProPass*® Packet High Quality Protein (protein source: whey) 7.5 oz can and ProPass Protein Supplement

**Note:** *Promod*® powder was discontinued.

### SIDE EFFECTS

There is limited experience in veterinary medicine.

**Dogs**

- Rare: exacerbation of encephalopathy (may resolve within 12 hours of discontinuing the infusion), imbalance of serum electrolytes and metabolites, catheter-associated thrombophlebitis (mainly if central vein is not used), bacterial colonization of catheter and resultant bacteremia and septicemia can be seen with intravenous administration. Because solutions are hyperosmolar severe tissue damage can occur if the solution is extravasated. Gastrointestinal signs (vomiting, diarrhea) can occur with oral administration

**Cats:** no information available.

### DRUG INTERACTIONS

**Monoamine oxidase (MAO) inhibitors and selective serotonin reuptake inhibitors (SSRIs):** contraindicated in humans taking certain amino acid supplements

### MONITORING

- Efficacy and adverse effects
- Measure blood ammonia before amino acid infusion due to possible exacerbation of hepatic encephalopathy and monitor serum electrolytes

## Amitriptyline Hydrochloride

**Trade/brand name:** *Amitid*® (US), *Elavil*® (CA, UK), generic (Rx)
**Classification:** Behavior modifying drug (tricyclic antidepressant), Antihistamine (first-generation)

### INDICATIONS

Management of behavior disorders, neuropathic pain, and psychogenic and allergic dermatoses.

**Dogs:** Tail biting, flank sucking, anal licking, acral lick dermatitis, neuropathic pain and pruritus, allergic skin diseases. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of oral type 1 antihistamines for treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010).

**Cats:** Psychogenic alopecia and dermatitis, tail sucking, excessive grooming, hyperesthesia syndrome, neuropathic pain and pruritus, allergic skin diseases.

**Note:** For management of allergic skin diseases, the response to amitriptyline in dogs and cats, as with other antihistamines, is individualized and unpredictable. Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Hypersensitivity to tricyclic antidepressants. Should not be used with monoamine oxidase (MAO) inhibitors. Caution in patients with seizures, thyroid disorders, hepatic, renal, or cardiac disorders, xerostomia, keratoconjunctivitis sicca, glaucoma, diabetes, adrenal tumors, pregnant or lactating animals. Amitriptyline will interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Amitriptyline increases neurotransmitter levels of serotonin and norepinephrine by inhibiting their uptake at presynaptic nerve terminals, and it is also a variable competitive antagonist at acetylcholine (muscarinic) and alpha-1 and alpha-2-adrenergic receptors. It also has substantial antihistamine properties by blocking $H_1$ receptors.

### DOSAGES

Dosage schedules vary widely, and the optimal dosage has not been established. Inter-individual variability in response is to be expected; therefore, dosage should be adjusted based on response. Usually a 2- to 4-week trial is recommended, as it may take several weeks before efficacy is noted. After long-term use, discontinuation of the drug should be gradual (over 1–3 weeks).

**Dogs**

- Pruritic dermatoses: 1–2 mg/kg PO q12h
- Behavior-associated disorders: begin with 1–2 mg/kg PO q12h for 2 weeks, then dosage can be increased by 1 mg/kg (up to a maximum dose of 4 mg/kg) every 2 weeks as necessary to improve clinical response

**Cats**

- 0.5–1 mg/kg PO q12–24h or 5–10 mg per cat PO q12–24h
- Transdermal use: amitriptyline has been found to have minimal absorption after a single transdermal dose in cats at 5 mg per cat (much lower bioavailability than oral); therefore, until supporting pharmacokinetic data are available, veterinarians should not rely on the transdermal route for amitriptyline

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 25 mg; *Elavil*®
- Oral tablets: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg; *Amitid*®, generic

### SIDE EFFECTS

**Dogs**
- Common: sedation, constipation, urinary retention
- Rare: hyperexcitability, seizures, cardiac dysrhythmias, bone marrow suppression, gastrointestinal effects (diarrhea, vomiting), endocrine effects

**Cats**
- Rare: sedation, reduced grooming, unkempt hair coat, weight gain, hypersalivation, urinary retention, anorexia, thrombocytopenia, neutropenia, vomiting, ataxia, disorientation, and cardiac conductivity disturbances

### DRUG INTERACTIONS

**Diazepam, fluoxetine, selective serotonin reuptake inhibitors (SSRIs):** possible increase in amitriptyline levels

**Monoamine oxidase (MAO) inhibitors (e.g., selegiline and amitraz), methimazole, cimetidine, ketoconazole, other agents with anticholinergic or CNS depressant effects:** increased risk of toxicity

**Rifampin:** decreases the effect of amitriptyline

**Sympathomimetic agents, cisapride:** increased risk of cardiac effects

**Thyroid medications (e.g., levothyroxine):** amitriptyline may interfere with these drugs; increase risk of cardiac effects

### MONITORING
- Efficacy and adverse effects
- Cardiac evaluation (heart rate and rhythm), CBC and serum chemistry panel: baseline and annual evaluations

## Amoxicillin+Clavulanic Acid

**Trade/brand name:** *Augmentin*® (US, UK), *Clavamox*® (US), *Nisamox*® (UK), *Clavulin*® (CA), *Synulox*® (UK), *Clavaseptin*® (EU), generic (Rx)
**Classification:** Antibacterial (beta-lactam)

### INDICATIONS

**Dogs and cats:** Skin, soft tissue and ear infections such as wounds, abscesses, cellulitis, otitis media, anal sacculitis, superficial and deep pyoderma caused by susceptible Gram-positive and Gram-negative aerobes and anaerobes. Susceptible organisms: *Staphylococcus*, *Streptococcus*, *Corynebacterium*, *Escherichia*, *Klebsiella*, *Proteus*, *Pasteurella*, *Clostridium*. It is ineffective against *Pseudomonas* or *Enterobacter*.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Caution in animals allergic to penicillins or cephalosporins. Safety in pregnant or breeding animals has not been determined.

### MECHANISM OF ACTION

Amoxicillin is bactericidal in action and acts through the inhibition of biosynthesis of cell wall mucopeptide of susceptible organisms. The action of clavulanic acid extends the antimicrobial spectrum of amoxicillin to include organisms resistant to amoxicillin and other beta-lactam antibiotics. It may also possess anti-inflammatory effects, as it was shown to decrease transmigration of leukocytes through endothelial cell monolayers.

### DOSAGES

**Dogs:** 13.75 mg/kg PO q12h

**Note:** The authors usually use a higher extra-label dosage for superficial and deep pyoderma and otitis media: 20–25 mg/kg PO q12h.

**Cats:** 62.5 mg per cat PO q12h or 10–20 mg/kg PO q12h

**Note:** The labeled treatment duration for dogs and cats is 30 days. However, dermatologists usually recommend treatment for 1–2 weeks past resolution of clinical signs.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats

- Oral tablets (amoxicillin/clavulanic acid): 62.5 mg (50 mg/12.5 mg), 125 mg (100 mg/25 mg), 250 mg (200 mg/50 mg), 375 mg (300 mg/75 mg); *Clavamox® Tablets*
- Oral suspension (amoxicillin/clavulanic acid): 62.5 mg (50 mg/12.5 mg) per mL in 15 mL btl; *Clavamox® Drops*

**Human-labeled products**

- Oral tablets (amoxicillin/clavulanic acid): 400 mg/57 mg (chewable); *Augmentin®*
- Oral tablets (amoxicillin/clavulanic acid): 250 mg/125 mg, 500 mg/125 mg; *Clavulin®*
- Oral tablets (amoxicillin/clavulanic acid): 250 mg/125 mg, 500 mg/125 mg, 875 mg/125 mg, 125 mg/31.25 mg (chewable), 200 mg/28.5 mg (chewable), 250 mg/62.5 mg (chewable); generic
- Powder for oral suspension (amoxicillin/clavulanic acid): 400 mg/57 mg cid per 5 mL in 50, 75, and 100 mL; *Augmentin®*
- Powder for oral suspension (amoxicillin/clavulanic acid): 125 mg/31.25 mg per 5 mL in 75, 100, and 150 mL; 200 mg/28.5 mg per 5 mL in 50, 75 and 100 mL; 250 mg/62.5 mg per 5 mL in 75, 100 and 150 mL; generic

### SIDE EFFECTS

**Dogs**

- Common: vomiting, diarrhea, anorexia
- Rare: cutaneous adverse reactions (erythema multiforme, maculopapular reaction, fixed eruption), lethargy, depression, polyuria, polydipsia, lameness, personality change, neurotoxicity (e.g., ataxia) associated with high doses or very prolonged use; elevated liver enzymes, tachypnea, dyspnea, edema and tachycardia

**Cats**
- Common: vomiting, diarrhea, anorexia
- Rare: pruritus and self-induced lesions

### DRUG INTERACTIONS

**Aminoglycosides, cephalosporins:** synergistic or additive activity

**Bacteriostatic antimicrobials (e.g., chloramphenicol, erythromycin, tetracyclines, and sulfonamides):** because of evidence of in-vitro antagonism, concurrent use is not recommended

**Methotrexate:** renal excretion is decreased by amoxicillin, causing increased levels and potential toxic effects

**Probenecid:** competitively blocks tubular secretion of most penicillins, causing increased serum levels and half-lives

### MONITORING
- Efficacy and adverse effects

## Amphotericin B

**Trade/brand name:** Traditional desoxycholate formulation: *Fungizone*® (US, CA, UK). Lipid-based formulations: *Abelcet*® (US, UK), *Ambisome*® (US, CA, UK), *Amphotec*® (US), *Amphotericin*® (US) (Rx)
**Classification:** Antifungal (polyene)

### INDICATIONS

**Dogs and cats:** Leishmaniasis, pythiosis and many systemic mycoses including blastomycosis, histoplasmosis, cryptococcosis, sporotrichosis, zygomycosis, aspergillosis, candidiasis and protothecosis.

### CONTRAINDICATIONS

Hypersensitivity to amphotericin B or its drug class. Caution in animals with impaired renal or hepatic function. Do not use in animals with electrolyte imbalances or dehydration. Use is not advised in pregnant animals although there is no reported toxicity.

### MECHANISM OF ACTION

Amphotericin B is usually fungistatic but it can be fungicidal against some organisms, depending on drug concentration. It binds to sterols (primarily ergosterol) in the fungal cell membrane and alters the permeability, allowing leakage of intracellular components. Amphotericin B also has immunomodulatory properties by activating macrophages and potentiating their phagocytic, tumoricidal and microbicidal actions due to induced production of IL-1 and TNF-alpha.

### DOSAGES

Nephrotoxicity is the dose-limiting factor; may have to interrupt therapy, reduce dosage, or use alternative drugs. Drug needs to be administered intravenously via slow infusion diluted in 5% dextrose in water.

**Dogs**

Traditional formulations

- Systemic mycosis: 0.1–0.5 mg/kg slowly IV q48h for 6 weeks or until a cumulative dose of 8–11 mg/kg is reached
- Leishmaniasis: 0.5–0.8 mg/kg slowly IV q48h until a cumulative dose of 8–16 mg/kg is reached

Liposomal formulations

- Pythiosis: 2–3 mg/kg slowly IV q48h for 4 weeks or until a cumulative dose of 24–27 mg/kg is reached
- Blastomycosis: 3.3 mg/kg slowly IV q48 h for 4 weeks or until a cumulative dose of 12–30 mg/kg is reached
- Systemic mycosis (except blastomycosis): 1–2.5 mg/kg slowly IV q48h for 4 weeks or until a cumulative dose of 12 mg/kg is reached
- Resistant systemic mycosis: 2–2.5 mg/kg slowly IV q48h for 4 weeks or until a cumulative dose of 24–30 mg/kg is reached
- Leishmaniasis: 3–3.3 mg/kg slowly IV q72–96 h until a cumulative dose of 15 mg/kg is reached (duration varies). May be possible to give the same cumulative dose at a lower level q48h

**Note:** For treatment of systemic mycosis, amphotericin B can be combined with ketoconazole at 10–20 mg/kg PO q24h or divided q12h.

**Cats**

Traditional formulations

- Systemic mycosis: 0.1–0.25 mg/kg slowly IV q48h for 6 weeks or until a cumulative dose of 4–8 mg/kg is reached

Liposomal formulations

- Systemic mycosis: 1 mg/kg slowly IV q48h for 4 weeks or until a cumulative dose of 12 mg/kg is reached

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Intravenous desoxycholate powder for injection: 50 mg/vial; *Fungizone*®
- Lipid-based suspension for injection: 100 mg/10–20 mL (as lipid complex); *Abelcet*®
- Lipid-based powder for injection: 50 mg/20 mL vial (as cholesteryl); *Amphotec*®, *Ambisome*®
- Lipid-based powder for injection: 100 mg/50 mL (as cholesteryl); *Amphotec*®

## SIDE EFFECTS

**Dogs and cats:** Amphotericin B lipid-based formulations are much less nephrotoxic than traditional forms. Cats are more sensitive than dogs to the nephrotoxic effects of this drug. Lipid formulations have a greater tendency to develop infusion-related reactions, which can be reduced by slowing the infusion rate.

- Common: dose-related nephrotoxicity
- Uncommon: anorexia, vomiting, tremors, anaphylaxis, hypokalemia, distal renal tubular acidosis, hypomagnesaemia, phlebitis, myalgia, cardiac arrhythmias, non-regenerative anemia and fever, calcinosis cutis, increase in creatine kinase levels, weight loss, and normochromic normocytic anemia with long-term treatment

### DRUG INTERACTIONS

**Aminoglycosides (e.g., gentamicin, amikacin), polymyxin B, colistin, cisplatin, cyclosporine, methoxyflurane or vancomycin:** potential additive nephrotoxicity

**Cardiac glycosides (e.g., digoxin), skeletal muscle relaxants, or other potassium-depleting drugs (e.g., thiazide or loop diuretics), glucocorticoids, flucytosine:** potentiate hypokalemia

**Ketoconazole:** potentiates effect against blastomycosis and histoplasmosis

**Rifampin:** potentiates effect against aspergillosis, candidiasis and histoplasmosis

### MONITORING

- Efficacy and adverse effects
- Renal function pre-treatment and during treatment: BUN and serum creatinine every other day during dosage increase, and at least weekly thereafter during therapy
- Serum electrolytes (sodium, potassium and magnesium), liver function tests, CBC and urinalysis: on a weekly basis
- Animal's body weight

## Auranofin

**Trade/brand name:** *Ridaura*® (US, CA) (Rx)
**Classification:** Immunomodulatory (immunosuppressive, Gold salt)

### INDICATIONS

There is limited experience in dogs and cats. Gold salts should be saved for cases that are unresponsive to or do not tolerate more conventional therapy, such as glucocorticoids and azathioprine. Auranofin appears to be less toxic but less efficacious than injectable gold. Response to treatment is variable.

**Dogs:** Immune-mediated skin diseases such as pemphigus complex.

**Cats:** Immune-mediated skin diseases such as pemphigus complex, eosinophilic granuloma complex, and plasma cell pododermatitis and stomatitis.

### CONTRAINDICATIONS

Do not use in animals with suppressed bone marrow or animals receiving other bone marrow suppressive agents such as azathioprine and cyclophosphamide. It is contraindicated in severely debilitated animals, animals with uncontrolled diabetes, and pregnant animals, and in systemic lupus erythematosus (may exacerbate the disease).

### MECHANISM OF ACTION

The exact mechanism of action of gold salts is unknown, but auranofin was shown to have anti-inflammatory, immunomodulating, and antimicrobial in-vitro effects. Gold salts inhibit macrophage phagocytosis, reduce the release of inflammatory mediators, such as lysosomal enzymes, histamine and prostaglandin, inactivate complement components, interfere with immunoglobulin-synthesizing

cells, inhibit antigen- and mitogen-induced T-cell proliferation, and suppress IL-2 and IL-2 receptor synthesis. Oral gold also has in-vitro inhibitory effect on DNA, RNA, and protein synthesis. Auranofin contains 29% gold.

### DOSAGES

There is limited experience in dogs and cats.

**Dogs:** 0.05–0.2 mg/kg (up to 9 mg/day total dose) PO q12h

**Cats:** 0.2–0.3 mg/kg (up to 9 mg/day total dose) PO q12h

**Note:** Once remission has been achieved, 1–2 mg/kg is given every other week for 1 month, then once monthly. If complete remission after 6 months, can try to stop treatment. Lag phase of 6–12 weeks. Often used in conjunction with glucocorticoids initially. Allow for a 4-week washout period if using after azathioprine.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 3 mg; *Ridaura*®

### SIDE EFFECTS

**Dogs and cats**

- Common: dose-dependent (high doses) blood dyscrasias (immune-mediated thrombocytopenia, hemolytic anemia, or leukopenia) and dose-dependent gastrointestinal disturbances (particularly diarrhea). It is a known teratogen and maternotoxic. Rapid reversal of these side effects can be expected after cessation of therapy and glucocorticoid administration
- Rare: nephrotoxicity (proteinuria), hepatotoxicity (increased liver enzymes), dermatosis, and corneal and oral ulcers

### DRUG INTERACTIONS

**Other cytotoxic agents (e.g., azathioprine, chlorambucil and cyclophosphamide and high dose glucocorticoids):** safety has not been established; use with caution

**Penicillamine or antimalarial drugs:** potential additive hematologic or renal toxicity

### MONITORING

- Efficacy and adverse effects
- Chemistry profile, urinalysis and CBC (eosinophilia may precede the development of adverse reaction) including platelet count: baseline, once monthly for 2–3 months then every other month

## Aurothiomalate, Sodium

**Trade/brand name:** *Aurolate*® (US), *Myochrisine*® (US, CA), *Myocrisin*® (UK), generic: aurolate; sodium aurothiomalate; gold sodium thiomalate (Rx)
**Classification**: Immunomodulatory (immunosuppressive Gold salt)

Most of the information presented here is extrapolated from aurothioglucose, which is no longer commercially available. Similarities between the two drugs may allow replacement of aurothioglucose with sodium aurothiomalate.

### INDICATIONS

There is limited experience in dogs and cats. It should be saved for cases that are unresponsive to or do not tolerate more conventional therapy, such as glucocorticoids and azathioprine. Response to treatment is variable.

**Dogs:** Immune-mediated skin diseases such as pemphigus complex.

**Cats:** Immune-mediated skin diseases such as pemphigus complex and plasma cell pododermatitis/stomatitis and eosinophilic granuloma complex.

### CONTRAINDICATIONS

Do not use in animals with renal or hepatic disease or bone marrow suppression, or in animals receiving other bone marrow suppressive agents such as azathioprine and cyclophosphamide. It is contraindicated in severely debilitated animals, animals with uncontrolled diabetes, and pregnant animals, and in systemic lupus erythematosus (may exacerbate the disease). Do not use intravenously.

### MECHANISM OF ACTION

The exact mechanism of action of sodium aurothiomalate is unknown, but it was shown to have anti-inflammatory, immunomodulating, and antimicrobial (in-vitro) effects. In general, gold salts inhibit macrophage phagocytosis, reduce the release of inflammatory mediators, such as lysosomal enzymes, histamine, and prostaglandin, inactivate complement components, interfere with immunoglobulin-synthesizing cells, inhibit antigen- and mitogen-induced T-cell proliferation, and suppress IL-2 and IL-2 receptor synthesis.

### DOSAGES

There is limited experience in dogs and cats.

**Dogs and cats:** 1 mg/kg IM once weekly.

**Note:** Some authors recommend test dosing at 1–5 mg IM (1 mg for small patients and 5 mg for large patients) at first week, then 2–10 mg IM at second week, then 1 mg/kg IM once weekly until remission, then once monthly. If complete remission after 6 months, can try to stop treatment. Lag phase of 6–12 weeks. Often used in conjunction with glucocorticoids initially. Allow for a 4-week washout period if using after azathioprine.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Injection: 10 mg/mL, 25 mg/mL, and 50 mg/mL in 2 mL and 10 mL vials; *Aurolate®*, *Myochrisine®*, generic

### SIDE EFFECTS

**Dogs and cats**

- Common: pain at the injection site. Blood dyscrasias (immune-mediated thrombocytopenia, hemolytic anemia or leukopenia) and gastrointestinal disturbances (particularly diarrhea). It is a known teratogen
- Rare: nephrotoxicity (proteinuria), hepatotoxicity, toxic epidermal necrolysis, stomatitis

### DRUG INTERACTIONS

**Other cytotoxic agents (e.g., azathioprine, chlorambucil and cyclophosphamide and high dose glucocorticoids):** safety has not been established; use with caution

**Penicillamine or antimalarial drugs:** potential additive hematologic or renal toxicity

### MONITORING

- Efficacy and adverse effects
- Urinalysis: baseline then weekly
- CBC: baseline then every 2 weeks (e.g., eosinophilia may precede the development of adverse reactions)
- Hepatic and renal function tests: baseline, every 2 weeks initially, then every 1–2 months during maintenance

## Azathioprine

**Trade/brand name:** *Imuran*® (US, CA, UK), *Azasan*® (US) (Rx)
**Classification:** Immunomodulatory (immunosuppressive)

### INDICATIONS

**Dogs:** Various immune-mediated skin diseases including pemphigus complex, blistering skin diseases (e.g., epidermolysis bullosa acquisita, bullous pemphigoid, mucous membrane pemphigoid), discoid lupus erythematosus, systemic lupus erythematosus, vesicular cutaneous lupus erythematosus, exfoliative cutaneous lupus erythematosus, erythema multiforme, cutaneous vasculitis, sterile pyogranulomatous disorders, familial dermatomyositis, uveodermatologic syndrome, perianal fistula, symmetrical lupoid onychodystrophy, cryoglobulinemia, cryofibrinogenemia, graft-versus-host disease, and reactive histiocytosis.

**Note:** Azathioprine can be used as a glucocorticoid sparing agent, in combination with glucocorticoids or other immunosuppressive agents in more refractory cases, or as a sole therapy.

**Cats:** Even though effective in cats, azathioprine is generally contraindicated because of its potential severe side effects.

### CONTRAINDICATIONS

Hypersensitivity to azathioprine or its drug class. Contraindicated in cats because of difficulty in accurately dosing and potential for profound myelosuppression and fatal toxicity. Caution in patients with hepatic dysfunction. Avoid use in pregnant animals.

### MECHANISM OF ACTION

Azathioprine is an immunosuppressive agent that antagonizes purine metabolism, thereby inhibiting RNA and DNA synthesis and mitosis. Azathioprine inhibits T-cell-mediated immune function, decreases T-cell-dependent antibody synthesis, and decreases the number of Langerhans cells and antigen-presenting

cells. It is metabolized by thiopurine methyltransferase, xanthine oxidase, and hypoxanthine-guanine phosphoribosyltransferase.

### DOSAGES

**Dogs:** 1.5–2.5 mg/kg PO q24h until remission, then dosage can be reduced to q48h. Long-term management may be possible with doses as low as 0.5–2 mg/kg q72h.

**Note:** Clinical response may require 4–8 weeks. It may be combined with other immunosuppressive drugs (e.g., oral glucocorticoids: prednisone/prednisolone) for the first weeks or months.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 25 mg, 50 mg; *Imuran*®
- Oral tablets: 75 mg, 100 mg; *Azasan*®

### SIDE EFFECTS

**Dogs:** Most of the side effects are reversible with early discontinuation of the drug. Susceptibility to adverse effects may be due to a metabolism deficiency of thiopurine methyltransferase, reported in 10% of the dogs. There might be variations in the activity of this enzyme between dog breeds, with giant schnauzers having much lower enzyme activity (potentially more susceptible to azathioprine side effects) and Alaskan malamutes having much higher enzyme activity (perhaps needing higher dosages of azathioprine). There are also anecdotal reports that generics have a higher incidence of hepatic toxic reactions, but the authors have not observed this problem in practice. In general, dosage adjustments can be made based on the results of laboratory monitoring and clinical improvement.
- Common: diarrhea (may be hemorrhagic), myelosuppression (leukopenia, lymphopenia, thrombocytopenia and non-regenerative anemia). Myelosuppression has been reported to occur after 4–16 weeks of administration
- Rare: vomiting, anorexia, hepatotoxicity (usually responds to drug withdrawal), occasional clinical hepatitis, acute pancreatitis (mostly reported in association with glucocorticoids), poor hair growth, alopecia, cutaneous eruptions, increased susceptibility to opportunistic infections when used long-term (pyoderma, demodicosis, dermatophytosis), parasitic and neoplastic illnesses with long-term use

### DRUG INTERACTIONS

**Allopurinol:** potential decrease in hepatic metabolism of azathioprine

**Aminosalicylates (e.g., sulfasalazine, mesalamine, olsalazine):** increased risk for azathioprine toxicity

**Angiotensin-converting enzyme (ACE) inhibitors (e.g., benazepril, enalapril):** increase risk for hematological toxicity/bone marrow suppression

**Drugs affecting myelopoiesis (e.g., cyclophosphamide, trimethoprim sulfa):** increase risk for hematological toxicity/bone marrow suppression

**Glucocorticoids:** increased risk of pancreatitis

**Leflunomide:** increased risk of infection

**Non-depolarizing muscle relaxants (e.g., pancuronium and tubocurarine):** inhibition of neuromuscular blocking activity

**Warfarin:** potential for reduced anticoagulant effect

### MONITORING

- Efficacy and adverse effects
- CBC including platelet count: baseline and at least every 2–3 weeks for the first 3–4 months of therapy. Once in remission every 1–3 months. Thrombocytopenia may be the first indication of bone marrow suppression. If leukocyte counts decrease to <5000 cells/mm$^3$ treatment should be discontinued until leukopenia resolves
- Chemistry profile: baseline and initially at least every 2–3 months. Once in remission, every 6 months
- Pancreatic enzyme levels: initially at least every 4 weeks (mainly combined with glucocorticoid therapy)

**Note:** Currently there is no evidence supporting the routine measurement of red blood cell thiopurine methyltransfarase activity in dogs treated with azathioprine, as toxic events do not appear to be associated with low enzyme activity levels.

## Azithromycin

**Trade/brand name:** *Azithrocin*® (US), *Zithromax*® (US, CA, UK), *Zmax*® (US), generic (Rx)
**Classification:** Antibacterial (macrolide/azalide)

### INDICATIONS

**Dogs:** Bacterial skin and soft tissue infections (superficial and deep pyoderma), oral and cutaneous papillomatosis (variable response), cyclosporine-induced gingival hyperplasia (variable response), and infections caused by *Mycobacterium leprae* or *Mycobacterium avium* complex.

**Cats:** Bacterial skin and soft tissue infections, ascending or primary otitis media usually associated with susceptible organisms that cause upper respiratory tract infections mainly *Staphylococci*, *Streptococci*, *Chlamydia*, *Mycoplasma* (except for *Mycoplasma haemofelis*) and *Bordetella*, and infections caused by *Mycobacterium leprae*, *Mycobacterium fortuitum* or *Mycobacterium avium* complex. It has also been indicated for *Nocardia* and L-form bacterial infections.

**Note:** Despite indication for bacterial skin infections, this drug is not commonly used by the authors to treat pyodermas, but if used for this purpose, ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Hypersensitivity to azithromycin or its drug class. Caution in patients with history of vomiting or hepatic function and/or biliary dysfunction, and in animals with arrhythmias.

### MECHANISM OF ACTION

Azithromycin inhibits bacterial RNA-dependent protein synthesis by penetrating the cell wall and binding to the 50S ribosomal subunit. Although usually classified as bacteriostatic, it may be bactericidal at higher concentrations against selected organisms. It is unclear if azithromycin and other macrolide antimicrobials modulate the host immune response or if they eliminate latent pathogens that could possibly trigger chronic inflammation; however, they have been shown to modulate in-vitro neutrophil oxidant production, and pro-inflammatory cytokine synthesis and release by leukocytes. The mechanism by which azithromycin improves cyclosporine-induced gingival overgrowth, particularly in humans, is currently unknown. It is speculated that azithromycin may kill oral bacteria, decreasing gingival stimulation and reducing cyclosporine-induced gingival overgrowth by suppressing protein synthesis and concentrating in phagocytes and fibroblasts. Despite potential indication for canine papillomatosis, it is currently unknown if azithromycin has an antiviral effect.

### DOSAGES

Administer without food for better absorption.

**Dogs**

- Bacterial skin infections: 5–10 mg/kg PO q12–24h for 1–2 weeks past resolution of clinical signs
- Oral and cutaneous papillomatosis: 10 mg/kg PO q24h for 10 days
- Cyclosporine induced gingival hyperplasia: 10 mg/kg PO q24h for 14 weeks – treatment trial (at least partial improvement should be observed after 4 weeks)

**Cats**

- Bacterial skin infections: 7–15 mg/kg PO q12–24h for 1–2 weeks past resolution of clinical signs
- Ascending or primary otitis media: 10 mg/kg PO q48h for 2–3 treatments

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 250 mg; *Zithromax*®, generic
- Oral tablets: 250 mg, 500 mg, 600 mg; *Azithrocin*®, *Zithromax*®, generic
- Oral suspension: 100 mg/5 mL, 200 mg/5 mL; *Zithromax*®, generic
- Extended-release oral suspension: 27 mg/mL; *Zmax*®

### SIDE EFFECTS

**Dogs and cats:** There is limited experience in dogs and cats.

- Common: vomiting, diarrhea, anorexia, abdominal pain (less gastrointestinal side effects than erythromycin)
- Rare: hepatomegaly, cholestatic hepatitis, increased liver enzymes, phospholipidosis (unknown clinical significance)

### DRUG INTERACTIONS

Azithromycin, unlike erythromycin, does not inhibit hepatic microsomal enzyme CYP3A4 (formerly cytochrome P450 IIIA4), thereby reducing the potential for drug interactions.

**Antacids (oral magnesium and aluminum based):** may reduce absorption rate of azithromycin. Separate dosages 2 hours

**Chloramphenicol and other macrolides and lincosamides:** decreased antibiotic effect of these drugs due to competition for the same binding sites

**Cisapride:** contraindicated with other macrolides; no data on azithromycin

**Cyclosporine, methylprednisolone, theophylline:** serum levels of these drugs may be increased

**Digoxin:** other macrolides can increase digoxin serum levels; no data on azithromycin

**Pimozide:** contraindication with azithromycin because of possible acute death (pimozide is not commonly used in veterinary medicine)

**Warfarin, dicumarol, anisindione, and acenocoumarol:** may increase anticoagulant effect of these drugs

### MONITORING

- Efficacy and adverse effects
- Hepatic profile if indicated

## Calcitriol

**Trade/brand name:** *Calcitriol*® (US), *Rocaltrol*® (US, CA, UK), *Silkis*® (UK), Trikal® (UK) (Rx)
**Classification:** Vitamin (vitamin D analog)

### INDICATIONS

**Dogs:** Primary idiopathic seborrhea (especially in spaniel breeds).

**Note:** Calcitriol is not commonly used by the authors as a first-line therapy for idiopathic or primary seborrhea in dogs, but it can be used as an alternative therapy for more severe and refractory cases.

### CONTRAINDICATIONS

Patients with hypercalcemia, vitamin D toxicity, malabsorption syndrome, and hyperphosphatemia. Safety in pregnant and lactating animals has not been established.

### MECHANISM OF ACTION

Calcitriol, or 1,25-dihydroxyvitamin $D_3$, a vitamin D metabolite, is a hormone that regulates serum calcium levels by stimulating calcium mobilization from bones, by increasing the intestinal absorption of calcium, and by reducing its renal excretion. Vitamin D analogs inhibit keratinocyte proliferation, induce keratinocyte terminal differentiation, and decrease immunologic reactivity by reducing the production or transcription of various cytokines and reducing the antigen-presenting function of Langerhans cells. It has been shown to significantly decrease cell proliferation, as measured by cell labeling indices, in the epidermis and hair follicles of dogs with idiopathic seborrhea.

### DOSAGES

There is limited experience in dogs.

**Dogs:** 10 ng/kg (0.01 mcg/kg) PO q24h

**Note:** It should be given as far away from the main meal as possible to minimize the risk of increased calcium absorption and hypercalcemia. Dose may need to be adjusted as necessary to maintain normal calcium concentration. Reformulation by a compounding pharmacy may be needed to assure accurate dosing.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 0.25 mcg, 0.5 mcg; *Calcitriol®*, *Rocaltrol®*
- Oral solution: 1 mcg/mL in 15 mL btl; *Calcitriol®*, *Rocaltrol®*

### SIDE EFFECTS

**Dogs**

- Rare: hypercalcemia (polydipsia, polyuria, anorexia, and vomiting), hyperphosphatemia and hypocalcemia (muscle weakness, muscle tremors or twitching, behavior changes, or seizures). Hypercalcemia occurs mostly as a result of calcitriol drug interactions. Accidental overdose may cause soft tissue metastatic calcification and can be fatal

### DRUG INTERACTIONS

**Calcium-containing phosphorus binding agents (e.g., calcium carbonate) or thiazide diuretics:** increased risk of hypercalcemia

**Digoxin, verapamil:** hypercalcemia may potentiate their toxicity

**Glucocorticoids:** can abolish the effects of vitamin D analogs

**Phenytoin, barbiturates, primidone:** may decrease the activity of vitamin D analogs by increasing their metabolism

**Sucralfate:** decreases calcitriol absorption

### MONITORING

- Efficacy and adverse effects
- Serum calcium, phosphate and creatinine – baseline, 1 week and 1 month during treatment, then monthly thereafter
- Urine calcium baseline and as needed
- Serum electrolyte and parathyroid hormone levels

## Caspofungin Acetate

**Trade/brand name:** *Cancidas®* (US, CA, UK) (Rx)
**Classification:** Antifungal (echinocandin)

### INDICATIONS

**Dogs and cats:** Invasive or disseminated infections caused by *Aspergillus*, *Candida*, and *Sporothrix*. Other indications include pythiosis and lagenidiosis.

**Note:** Very expensive therapy.

### CONTRAINDICATIONS

Caspofungin should be contraindicated in patients with hypersensitivity to it or its drug class. Based on information extrapolated from humans, it needs to be used with caution and dosage may need to be reduced in patients with hepatic dysfunction. Caspofungin has been shown to cross the placenta in animal studies and to be embryotoxic in rats and rabbits, but no studies have been performed in dogs and cats.

### MECHANISM OF ACTION

Caspofungin interferes with fungal cell wall biosynthesis by non-competitive inhibition of 1,3-beta-D-glucan synthase. It inhibits hyphal tip and branch point growth, converting mycelium to small clumps. Generally fungicidal in vitro but fungistatic against most fungal and yeast organisms in vivo.

### DOSAGES

There is very limited experience in dogs and cats. This medication is recommended for inpatient use only. It should be considered an alternative therapy for resistant and refractory cases, or for patients that do not tolerate conventional antifungals.

**Dogs and cats:** 0.5–2 mg/kg q24h IV infused over 1 hour (anecdotal)

**Note:** Frequency of administration can be reduced after clinical remission. Average duration of therapy: 1 month.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Powder for injection: 50 mg and 70 mg in single-use vials; *Cancidas®*

### SIDE EFFECTS

**Dogs and cats:** Because of limited experience in dogs and cats, no specific information is available.

**Note:** In humans it is usually well tolerated, with reported histamine-mediated reactions (urticaria, facial swelling, pruritus), anaphylaxis, intravenous-site reactions (pain, redness, phlebitis), vomiting, diarrhea, anemia, hepatotoxicity, and increased alkaline phosphatase.

### DRUG INTERACTIONS

**Carbamazepine, dexamethasone, phenytoin, efavirenz, nevirapine, rifampin:** reduce caspofungin serum levels

**Cyclosporine:** increases caspofungin serum levels and increases risk for elevation in hepatic enzymes

### MONITORING

- Efficacy and adverse effects
- Periodic liver function tests, CBC, and electrolytes

# Cefadroxil

**Trade/brand name:** *Cefa-Tabs*® (US, CA), *Cefa-Cure*® (US), *Cefa-Drops*® (US, CA), *Duricef*® (US, CA), *Ultracef*® (US), generic (Rx)
**Classification:** Antibacterial (beta-lactam, first-generation cephalosporin)

## INDICATIONS

**Dogs and cats:** Superficial and deep pyodermas, cellulitis, wound infections, and abscesses caused mostly by susceptible Gram-positive bacteria such as *Staphylococcus*, beta-hemolytic *Streptococcus*, and some Gram-negative bacteria such as *Proteus mirabilis*, *Escherichia coli*, *Klebsiella*, *Actinobacillus*, *Pasteurella*, and *Corynebacterium*. Not effective against *Pseudomonas aeruginosa* or methicillin-resistant staphylococcal infections.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

## CONTRAINDICATIONS

Do not use in animals hypersensitive to cephalosporins and penicillins. Use with caution in patients receiving other beta-lactam antibiotics (e.g., penicillins, carbapenem) or nephrotoxic drugs, and in patients with seizures or impaired renal function (may need to reduce dose).

## MECHANISM OF ACTION

Cefadroxil is a bactericidal agent that inhibits bacterial cell wall synthesis, leading to cell lysis and death.

## DOSAGES

**Dogs:** 22–35 mg/kg PO q12h

**Cats:** 22–35 mg/kg PO q24h

**Duration of treatment:** the manufacturer recommends not exceeding 30 days of treatment in dogs and 21 days in cats; however, dermatologists typically recommend treating for 1–2 weeks past resolution of clinical signs.

**Note:** Despite the once-daily administration recommended by the manufacturer to treat cats, the authors recommend administering cefadroxil twice a day.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats.
- Oral tablets: 50 mg, 100 mg, 200 mg, 1 g; *Cefa-Tabs*®, *Cefa-Cure*®
- Powder for oral suspension: 50 mg/mL in 15 mL and 50 mL vials; *Cefa-Drops*®

**Human-labeled products**
- Oral tablets: 1 g; *Duricef*®, generic
- Oral capsules: 50 mg, 100 mg, 200 mg, 500 mg; *Duricef*®, generic
- Oral capsules: 500 mg; *Ultracef*®
- Powder for oral suspension: 125 mg/5 mL, 250 mg/5 mL, 500 mg/5 mL in 50, 75, and 100 mL vials; *Duricef*®, *Utracef*®, generic

### SIDE EFFECTS

**Dogs and cats**
- Common: anorexia, vomiting, diarrhea, and lethargy. Administration with food may help prevent these side effects
- Rare: hypersensitivity reactions unrelated to dose (cutaneous lesions including granulomatous mural folliculitis, fever, eosinophilia, lymphadenopathy, and anaphylaxis)

**Note:** High doses or prolonged use of cephalosporins have been associated with nephrotoxicity, neutropenia, agranulocytosis, thrombocytopenia, hepatitis, positive Coomb's test, interstitial nephritis, and renal tubular necrosis.

### DRUG INTERACTIONS

**Aminoglycoside or other nephrotoxic drugs:** potential additive nephrotoxicity

**Probenecid:** increases serum levels of cefadroxil

**If mixed with other drugs in a compounded formulation:** inactivation of cefadroxil may occur

### MONITORING
- Efficacy and adverse effects
- Renal monitoring in patients with deficient renal function

## Cefovecin Sodium

**Trade/brand name:** *Convenia*® (US, CA, UK) (Rx)
**Classification:** Antibacterial (beta-lactam, third-generation cephalosporin)

### INDICATIONS

**Dogs:** Skin and soft tissue infections including superficial and deep pyodermas, wounds, and abscesses caused by susceptible strains of *Staphylococcus pseudintermedius* (*intermedius*), hemolytic *Streptococcus canis* (group G), and *Proteus*.

**Cats:** Skin and soft tissue infections including wounds and abscesses caused by susceptible strains of *Staphylococcus*, *Streptococcus*, *Pasteurella multocida*, and *Proteus*, and anaerobic bacteria such as *Bacteroides*, *Clostridium*, and *Fusobacterium*. Cefovecin is not active against *Pseudomonas*, *Enterococcus*, and methicillin-resistant *Staphylococcus* strains. It is a good alternative to oral antibiotics particularly in pets that are difficult for owners to medicate, in pets that experience gastrointestinal side effects from oral medications, and to avoid the risks of non-compliance with oral medications.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to cephalosporins and penicillins. Use with caution in patients receiving other beta-lactam antibiotics (e.g., penicillins,

carbapenem) or nephrotoxic drugs, and in patients with seizures. Safety has not been assessed in renal disease; therefore, it should be used with caution in patients with impaired renal function (may need to reduce dose). Safety in animals less than 4 months of age and in breeding and lactating animals has not been determined. Safety has not been established for intravenous or intramuscular administration.

### MECHANISM OF ACTION

Cefovecin is a bactericidal agent that binds to proteins involved in bacterial cell wall synthesis, thereby decreasing cell wall strength and rigidity and affecting cell wall division. It is resistant to some bacterial beta-lactamases.

### DOSAGES

Cefovecin must be given by or on the order of a veterinarian.

**Dogs and cats:** 8 mg/kg SC single or repeated administration (labeled for q14 days up to a total of two administrations)

**Note:** The authors recommend re-evaluation of the patient's clinical response every 2 weeks to decide if subsequent injections are needed. Once clinical signs resolve, no further injections are needed. Most dogs and cats may require up to three injections for complete clinical resolution of the infection.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats.

- Powder for injection: 80 mg/mL in 10 mL vial; *Convenia*®

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs**

- Common: vomiting, soft feces/diarrhea, decreased appetite/anorexia (gastrointestinal signs may be transient), lethargy, and mild local and transient reactions at injection sites (swelling or itching)
- Rare: blood in feces, flatulence, increased borborygmi and mild to moderate increase in serum gamma-glutamyl transferase or serum alanine aminotransferase (no clinical abnormalities). Injection-site reactions (seroma, alopecia, crusts, necrosis, and erythema), facial edema, tremors, acute pulmonary edema, salivation, pruritus, hemolytic anemia, ataxia, seizures, and death have been reported in foreign markets

**Cats**

- Common: vomiting, soft feces/diarrhea, decreased appetite/anorexia (gastrointestinal signs may be transient), and lethargy
- Rare: "hyper"/acting strange, inappropriate urination, and mild elevation in alanine aminotransferase (no clinical abnormalities). Injection-site reactions (alopecia, crusts, necrosis, and erythema), facial edema, tremors, acute pulmonary edema, salivation, pruritus, hemolytic anemia, ataxia, seizures, anaphylaxis, and death have been reported in foreign markets.

### DRUG INTERACTION

Cefovecin is highly bound to plasma proteins; therefore, caution should be taken when using it in conjunction with other highly protein-bound drugs.

**Carprofen, furosemide, doxycycline, ketoconazole:** potential for increased serum levels of these drugs

**Non-steroidal anti-inflammatory drugs (NSAIDs):** potential myelotoxicity (toxic neutropenia)

### MONITORING

- Efficacy and adverse effects
- Renal monitoring in patients with deficient renal function

## Cefpodoxime Proxetil

**Trade/brand name:** *Simplicef*® (US), *Vantin*® (US), generic (Rx)
**Classification:** Antibacterial (beta-lactam, third-generation cephalosporin)

### INDICATIONS

**Dogs:** Skin and soft tissue infections including wounds, abscesses, superficial and deep pyodermas caused by susceptible Gram-negative bacteria in the family Enterobacteriaceae: *Escherichia coli*, *Proteus mirabilis*, *Pasteurella multocida*, and *Klebsiella*; and Gram-positive bacteria: *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, B-hemolytic). Not active against most obligate anaerobes, *Pseudomonas*, *Enterococcus*, and methicillin-resistant *Staphylococcus* strains. May be used for treatment of infections of the ear canal, particularly otitis media, caused by susceptible organisms; however, tissue concentration is not known for the external or middle ear and this indication is controversial with unpredictable efficacy.

**Cats:** Not currently approved for cats, but it may be useful for the same indications as for dogs.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to cephalosporins and penicillins. Caution in patients receiving other beta-lactam antibiotics (e.g., penicillins, carbapenem) or nephrotoxic drugs, patients with seizures, and patients with impaired renal function (may need to reduce dose). Safety in dogs used for breeding, and in pregnant or lactating bitches, has not been determined.

### MECHANISM OF ACTION

Cefpodoxime is a bactericidal agent that inhibits bacterial cell wall synthesis, leading to cell lysis and death.

### DOSAGES

Cefpodoxime may be given with or without food.

**Dogs:** 5–10 mg/kg PO q24h (10 mg/kg dosage appears to be more effective than 5 mg/kg)

**Cats:** 5 mg/kg PO q12h or 10 mg/kg q24h (dosage extrapolated from dogs)

**Duration of treatment:** labeled for 5–7 days, or for 2–3 days beyond the cessation of clinical signs, up to a maximum of 28 days. However, dermatologists usually recommend until 1–2 weeks past resolution of clinical signs.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs.
- Oral tablets: 100 mg, 200 mg; *Simplicef®*

**Human-labeled products**
- Oral tablets: 100 mg, 200 mg; *Vantin®*, generic
- Granules for oral suspension: 50 mg/5 mL and 100 mg/5 mL in 50, 75 and 100 mL btl; *Vantin®*; generic

### SIDE EFFECTS

**Dogs and cats**
- Common: vomiting, diarrhea, anorexia
- Rare: lethargy, hypersensitivity reaction, nephrotoxicity, bleeding disorders

**Note:** High doses or prolonged use of cephalosporins have been associated with nephrotoxicity, neutropenia, agranulocytosis, thrombocytopenia, hepatitis, positive Coomb's test, interstitial nephritis, and renal tubular necrosis.

### DRUG INTERACTIONS

**H-2 antagonists (e.g., ranitidine, cimetidine), antacids or proton pump inhibitors (e.g., omeprazole):** potential for decreased cefpodoxime absorption

**Parenteral aminoglycoside or other nephrotoxic drugs:** potential additive nephrotoxicity

**Probenecid:** increase serum levels of cefpodoxime

**If mixed with other drugs in a compounded formulation:** inactivation of cefpodoxime may occur

### MONITORING
- Efficacy and adverse effects
- Renal monitoring in patients with deficient renal function

## Cephalexin

**Trade/brand name:** *Keflex®* (US, CA), *Ceporex®* (CA, UK), *Relexine®* (UK), many brand names available (Rx)
**Classification:** Antibacterial (beta-lactam, first-generation cephalosporin)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including superficial and deep pyodermas, wounds, and abscesses caused by susceptible Gram-positive bacteria such as *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, *Streptococcus canis* and some Gram-negative bacteria such as *Escherichia coli*,

*Pasteurella multocida*, *Proteus mirabilis*, and *Klebsiella*. Not efficacious against *Pseudomonas aeruginosa*, some *Proteus*, *Bacteroides*, *Enterococcus*, anaerobes, and methicillin-resistant *Staphylococcus* strains. May be used for treatment of infections of the ear canal, particularly otitis media, caused by susceptible organisms; however, tissue concentration is not known for the external or middle ear and this indication is controversial with unpredictable efficacy.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to cephalosporins or penicillins. Caution in patients with diminished renal function and seizure disorders. Safety in dogs used for breeding, and in pregnant or lactating bitches, has not been determined.

### MECHANISM OF ACTION

Cephalexin is a bactericidal agent that inhibits bacterial cell wall synthesis, leading to cell lysis and death.

### DOSAGES

May be administered with food (especially if gastrointestinal side effects occur).

**Dogs and cats:** 22–30 mg/kg PO q12h for 1–2 weeks past resolution of clinical signs

**Note:** There are also reports of administration q8h and q24h; however, the authors continue to recommend q12h administration

### FORMULATIONS

**Veterinary-labeled products:** None in the US

**Human-labeled products**

- Oral tablets and capsules: 250 mg, 500 mg, 1 g; *Ceporex®*, *Keflex®*, *Relexine®*, generic
- Powder for oral suspension: 125 mg/5 mL, 250 mg/5 mL, 500 mg/5 mL; *Cefaseptin®*, *Ceporex®*, *Keflex®*, generic

### SIDE EFFECTS

**Dogs**

- Common: vomiting, diarrhea, anorexia
- Rare: salivation, tachypnea, excitability or depression/lethargy, hypersensitivity reaction, urticaria, nephrotoxicity, erythema multiforme, drug-induced pemphigus foliaceus, transient increase in hepatic enzymes

**Cats**

- Common: vomiting, diarrhea, anorexia
- Rare: hypersensitivity reaction, nephrotoxicity, pyrexia, toxic epidermal necrolysis, salivation, cholestatic jaundice

**Note:** In cats and dogs, high doses or prolonged use of cephalosporins have been associated with nephrotoxicity, neutropenia, agranulocytosis, thrombocytopenia, hepatitis, positive Coomb's test, interstitial nephritis, and renal tubular necrosis.

### DRUG INTERACTIONS

**Bacteriostatic antibiotics (e.g., chloramphenicol):** avoid use with cephalexin

**Parenteral aminoglycoside or other nephrotoxic drugs:** potential additive nephrotoxicity

**Probenecid:** increases serum levels of cephalexin

### MONITORING

- Efficacy and adverse effects
- Renal monitoring in patients with deficient renal function

## Cetirizine Hydrochloride

**Trade/brand name:** *Zyrtec*® (US), *Zirtec*® (UK), generic
**Classification:** Antihistamine (second-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic skin conditions including urticaria and insect-bite hypersensitivity. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of oral type 1 antihistamines for treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010).

**Note:** The response to cetirizine in dogs and cats, as with other antihistamines, is individualized and unpredictable. Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to cetirizine or hydroxyzine. Dosage adjustment is recommended in humans with severe renal or hepatic impairment, and in elderly people. The formulation containing pseudoephedrine should not be used in dogs and cats. Caution in patients with hepatic disease, pregnant and lactating animals. Cetirizine may interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Cetirizine is a piperazine derivative and carboxylated metabolite of hydroxyzine with selective histamine $H_1$-receptor antagonism and anti-allergic properties inhibiting histamine-induced wheal and flare responses. In addition, it inhibits eosinophil, T-lymphocyte, and monocyte chemotaxis during the late phase of the allergic response and decreases intercellular adhesion molecule (ICAM)-1 expression on epithelial cells. It possesses minimal anticholinergic or antiserotonergic effects.

### DOSAGES

There is limited experience in dogs and cats.

**Dogs:** 1 mg/kg or 10–20 mg per dog PO q12–24h

**Cats:** 1 mg/kg or 5 mg per cat PO q12–24h

**Note:** Cetirizine is labeled as once daily dosage for humans and may have the advantage of once daily administration in dogs and cats as well. Higher doses appear to be more effective.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 5 mg, 10 mg; *Zyrtec*®, generic
- Oral chewable tablets (grape flavor): 5 mg, 10 mg; *Zyrtec*®, generic
- Oral solution (banana-grape flavor): 1 mg/mL in 120 and 480 mL; *Zyrtec*® *Syrup*, generic

### SIDE EFFECTS

**Dogs and cats:** Cetirizine has a low rate of penetration of the blood–brain barrier and it has minimal CNS impairment, showing low incidence of sedation compared to conventional antihistamines commonly used in dogs and cats. Nevertheless, there is limited clinical experience with this drug in dogs and cats.
- Rare: sedation, transient vomiting, hypersalivation.

### DRUG INTERACTIONS

Compared to some other antihistamines, cetirizine has low potential for interaction with drugs metabolized by the hepatic cytochrome P450 system.

**CNS depressants: benzodiazepines (e.g., diazepam), other antihistamines that cause sedation (e.g., diphenhydramine), anti-seizure drugs (e.g., carbamazepine), sedatives, muscle relaxants, narcotic pain relievers (e.g., codeine), tricyclic antidepressants (e.g., amitriptyline):** potential additive sedation effects

### MONITORING

- Efficacy and adverse effects

## Chlorambucil

**Trade/brand name:** *Leukeran*® (US, CA, UK), generic (Rx)
**Classification:** Immunomodulatory (immunosuppressive), Antineoplastic

### INDICATIONS

**Dogs:** Immune-mediated skin diseases including pemphigus complex, cutaneous and systemic lupus erythematosus, blistering skin disorders (e.g., bullous pemphigoid), vasculitis, cold agglutinin disease, and lymphocyte, mast cell, and plasma cell malignancies. It may be used as immunosuppressive therapy in dogs that cannot tolerate azathioprine or corticosteroids. It can also be used as a glucocorticoid-sparing agent.

**Cats:** Immune-mediated skin diseases including pemphigus complex, eosinophilic granuloma complex, cutaneous lymphocytosis, idiopathic refractory pruritus, and lymphocyte and plasma cell malignancies. It is the immunosuppressive drug

of choice for cats and may be used to replace cyclophosphamide or corticosteroids when severe side effects occur. It is often used in combination with glucocorticoid therapy.

### CONTRAINDICATIONS

Do not use in animals allergic to chlorambucil or in immunosuppressed animals. Caution in patients with pre-existing (or susceptible to) bone marrow suppression or infections. Avoid use in pregnant animals because of teratogenic potential. Pregnant women should not handle this medication, nor the urine or feces of animals taking chlorambucil. Tablets should not be split or crushed, and gloves should be worn during administration.

### MECHANISM OF ACTION

Chlorambucil is a cell-cycle non-specific cytotoxic alkylating immunosuppressant and antineoplastic agent derived from nitrogen mustard that cross-links DNA.

### DOSAGES

**Dogs and cats:** Chlorambucil dose varies highly depending on the treatment protocol. In general, 0.1–0.2 mg/kg PO q24–48h is used. When used as a substitute for cyclophosphamide in combination chemotherapy protocols for treatment of lymphoma, such as cyclophosphamide/vincristine/prednisone (COP) or cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP), the dosage is 0.8–1.4 mg/kg PO once. Once remission has been achieved, the dosage may be tapered accordingly.

**Note:** Clinical response may require 4–8 weeks. It is often combined with other immunosuppressive drugs (e.g., oral glucocorticoids: prednisone/prednisolone) for the first weeks or months.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 2 mg; *Leukeran*®, generic

**Note:** Size of tablets makes it most useful in small dogs and cats.

### SIDE EFFECTS

Compared to other alkylating agents, chlorambucil is slow-acting and less toxic. Side effects may occur gradually, with nadirs occurring usually within 7–14 days of the start of therapy. Recovery generally takes 7–14 days; however, severe bone marrow suppression can result in pancytopenia that may take months to years for recovery.

**Dogs**

- Common: myelosuppression (anemia, leukopenia, thrombocytopenia), gastrointestinal toxicity (vomiting, diarrhea, anorexia)
- Rare: pancytopenia, alopecia and delayed hair regrowth of shaved areas (mainly poodles and kerry blue terriers), urticarial reactions

**Cats**

- Common: myelosuppression (anemia, leukopenia, thrombocytopenia), gastrointestinal toxicity (vomiting, diarrhea, anorexia)

- Rare: seizures, facial twitching, jerking of the muscles of the head and limbs and myoclonus were reported in one cat

**Note:** Bronchopulmonary dysplasia with pulmonary fibrosis, uric acid nephropathy, and hepatotoxicity has been rarely reported in humans receiving chronic therapy.

### DRUG INTERACTIONS

**Other antineoplastic, bone marrow suppressant, and immunosuppressant drugs (e.g., chloramphenicol, azathioprine, cyclophosphamide, corticosteroids, flucytosine, amphotericin B, colchicine):** potential additive myelosuppression

### MONITORING

- Efficacy and adverse effects
- CBC and platelet count: baseline and every other week or monthly for the first 3 months, then every 3–4 months
- Uric acid and liver profile: if warranted

## Chloramphenicol/Chloramphenicol Palmitate

**Trade/brand name:** *Chlor Tablets*® (US, CA), *Chloromycetin*® (CA, UK), *Duricol*® (US), *Kemicetine*® (UK), *Viceton*® (US), many generics (Rx)
**Classification:** Antibacterial

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including abscesses, superficial and deep pyodermas, and oral infections (stomatitis, gingivitis) caused by susceptible organisms including Gram-positive bacteria such as *Staphylococcus* (e.g., *S. pseudintermedius* and methicillin-resistant organisms) and *Streptococcus*; Gram-negative bacteria such as *Neisseria*, *Brucella*, *Salmonella*, *Shigella*, *Haemophilus*, *Proteus*, and *Bordetella*; anaerobic bacteria such as *Clostridium*, *Bacteroides*, *Fusobacterium*, and *Veillonella*; and *Nocardia*, *Chlamydia*, *Mycoplasma*, *Borrelia*, and *Rickettsia*. Not effective against *Mycobacterium*, *Pseudomonas*, *Enterobacter*, *Serratia*, and *Klebsiella*. These organisms may be resistant or develop resistance during treatment. High lipid solubility makes it suitable for intraocular infections, and it will also reach the CNS.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals allergic to chloramphenicol. Caution in patients with pre-existing hematologic abnormalities, especially non-regenerative anemia or leucopenia, and patients with impaired hepatic or renal function (dosage may need to be reduced). Avoid high doses and long-term use in cats. Do not use in animals with cardiac abnormalities, and pregnant, neonatal, or breeding animals (may affect gonadal function). Human exposure may pose a risk (warn owners that exposure to even small doses via oral, nasal, or ophthalmic routes can cause

irreversible and fatal aplastic anemia in people). The use of chloramphenicol may interfere with vaccinations.

### MECHANISM OF ACTION

Chloramphenicol is a broad-spectrum bacteriostatic agent that binds to the 50S ribosomal subunit of susceptible bacteria, thus inhibiting bacterial RNA protein synthesis.

### DOSAGES

Chloramphenicol and chloramphenicol palmitate

**Dogs:** 40–60 mg/kg PO q8h

**Cats:** 15–20 mg/kg or 50 mg per cat PO q12h

**Note:** Medication should be handled with care. Powder should not be inhaled and hands should be washed after handling tablets.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs only.

- Oral tablets: 50 mg, 100 mg, 250 mg, 500 mg, 1 g; *Duricol®*, *Viceton®*, *Chlor Tablets®*, generic
- Oral capsules: 50 mg, 100 mg, 250 mg, 500 mg; *Duricol®*, *Viceton®*, generic

**Human-labeled products**

- Oral capsules: 250 mg, 500 mg; *Chloromycetin®*
- Oral liquid (palmitate): 50 mg/mL; *Chloromycetin Palmitate®*
- Powder for oral solution: 25 mg/vial in 15 mL btl; *Chloromycetin®*

### SIDE EFFECTS

**Dogs and cats**

- Common: vomiting, diarrhea, anorexia, depression
- Rare: exercise intolerance or reluctance to move, weakness, tachycardia, weight loss. Bone marrow suppression with high doses or prolonged treatment (reversible with discontinuation of therapy). Cats appear more sensitive to bone marrow suppression than dogs, because of a reduced capacity to metabolize chloramphenicol

**Dogs:** dogs receiving > 2–3 weeks of treatment at > 175 mg/kg/day may develop depression and anorexia, and at > 225 mg/kg/day they may develop myelosuppression and reticulocytopenia. Reversible suppression of erythropoietic response at therapeutic dosages may occur in dogs with pre-existing or concurrent blood loss when therapy commences.

**Cats:** cats receiving 25–40 mg/kg/day for 3 weeks or 120 mg/kg/day for 1 week may develop depression, dehydration, anorexia, weight loss, diarrhea, vomiting, and myelotoxicity. Reversible erythroid maturation arrest, vacuolation of marrow elements, and pancytopenia may occur.

### DRUG INTERACTIONS

Chloramphenicol inhibits cytochrome P450 activity and resultant hepatic biotransformation of drugs.

**Anti-anemia drugs (e.g., iron, folic acid, vitamin B12):** decreased effectiveness due to potential delayed hematopoietic response caused by chloramphenicol

**Beta-lactam antibiotics (e.g., penicillins, cephalosporins), aminoglycosides, fluoroquinolones, macrolides, lincosamides:** antagonism of bactericidal activity

**Calcium lactate, kaolin-pectin, aluminum hydroxide:** may increase bioavailability

**Lidocaine:** delays hepatic metabolism of lidocaine

**Methotrexate:** decreases efficacy of methotrexate

**Myelosuppressive drugs (e.g., cyclophosphamide), cimetidine:** increase potential for bone marrow suppression

**Phenobarbital, rifampin:** decrease chloramphenicol levels

**Phenytoin, primidone, phenobarbital, pentobarbital, cyclophosphamide, digoxin, warfarin, inhalation anesthetics, salicylates, cyclosporine:** prolonged action of these drugs and potential for toxicity

**Primidone:** anorexia and CNS effects may occur in dogs

**Propofol:** potential prolonged anesthesia in dogs

### MONITORING

- Efficacy and adverse effects
- Routine CBC with chronic therapy

## Chlorpheniramine Maleate

**Trade/brand name:** *Aller-Chlor*® (US), *Chlor-Phen*® (US), *Chlor-Trimeton*® (US), Chlor-*Tripolon*® (CA), *Phenetron*® (US), generic
**Classification:** Alkylamine antihistamine (first-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic skin conditions including urticaria and insect-bite hypersensitivity. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of oral type 1 antihistamines for the treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010).

**Note:** The response to chlorpheniramine in dogs and cats, as with other antihistamines, is individualized and unpredictable. A better result may be achieved with the combination of chlorpheniramine and hydroxyzine than with chlorpheniramine used as sole therapy, since this treatment modality has been reported to be efficacious in ameliorating the clinical signs of canine atopic dermatitis (Olivry *et al*. 2010). Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released. It is one of the most common antihistamines used in cats for control of pruritic conditions. May also be used as adjunctive therapy for mast cell tumors.

### CONTRAINDICATIONS

Do not use in animals allergic to chlorpheniramine.

Caution in patients with hyperthyroidism, cardiovascular disease, hypertension, glaucoma, prostatic hypertrophy, pyeloduodenal or bladder neck obstruction. Caution in patients with hepatic disease, and in pregnant and lactating animals. Chlorpheniramine will interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Chlorpheniramine is a histamine $H_1$-receptor antagonist with anti-allergic properties inhibiting histamine-induced wheal and flare responses. Has anticholinergic and CNS activity, with variable degrees of sedation in dogs and cats.

### DOSAGES

**Dogs:** 4–8 mg per dog (maximum of 0.5 mg/kg) PO q8–12h

**Cats:** 2–4 mg per cat PO q8–12h

**Note:** Chlorpheniramine maleate has a bitter taste.

### FORMULATIONS

**Veterinary-labeled products:** None as a single entity

**Human-labeled products**

- Chewable oral tablets: 2 mg, 4 mg; *Aller-Chlor®*, *Chlor-Phen®*, *Chlor-Trimeton®*, generic
- Timed-release oral tablets and capsules: 8 mg, 12 mg; *Chlor-Trimeton®*, *Chlor-Phen®*, generic (should not be crushed or chewed)
- Oral syrup: 1 mg/5 mL, 2 mg/5 mL in 118 mL; *Aller-Chlor®*

**Note:** Many formulations are available combining chlorpheniramine with decongestants, analgesics, and/or antitussives, and those are not recommended because of potential unpredictable side effects.

### SIDE EFFECTS

**Dogs and cats**

- Common: CNS depression (lethargy, somnolence)
- Rare: paradoxical excitement (reported in cats), diarrhea, vomiting, anorexia, dry mouth

**Note:** Sedative effects may diminish with time.

### DRUG INTERACTIONS

**Anticoagulants (e.g., heparin, warfarin):** counteraction of anticoagulation effects

**Other CNS depressant drugs:** increase sedation

**Monoamine oxidase (MAO) inhibitors (e.g., amitriptyline, amitraz):** may potentiate anticholinergic effects

**Phenytoin:** increases pharmacological effects of phenytoin

### MONITORING

- Efficacy and adverse effects

## Ciprofloxacin Hydrochloride

**Trade/brand name:** *Ciloxan*® (US, CA, UK), *Cipro*® (US, CA), *Cipro XR*® (US), *Ciproxin*® (UK), generic (Rx)
**Classification:** Antibacterial (second-generation fluoroquinolone)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including superficial and deep pyodermas caused by susceptible Gram-positive bacteria such as *Staphylococcus* (including *S. pseudintermedius*, penicillinase-producing, and methicillin-resistant strains) and Gram-negative bacteria such as *Pseudomonas aeruginosa*, *Klebsiella*, *Escherichia coli*, *Enterobacter*, *Campylobacter*, *Shigella*, *Salmonella*, *Aeromonas*, *Haemophilus*, *Proteus*, *Yersinia*, *Serratia*, and *Vibrio*. Other susceptible organisms include *Brucella*, *Chlamydia trachomatis*, *Mycoplasma*, and *Mycobacterium*. Most anaerobes and some *Streptococcus* are resistant. May be used for treatment of infections of the ear canal, particularly otitis media, caused by susceptible organisms; however, tissue concentration is not known for the external or middle ear and this indication is controversial because of unpredictable efficacy.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to ciprofloxacin. Because of potential damage to articular cartilage in skeletally immature dogs, ciprofloxacin should not be used in small and medium-breed dogs between 2 and 8 months of age, large-breed dogs until 12 months of age, and giant-breed dogs until 18 months of age. Avoid high concentrations in patients with renal failure, because of potential CNS toxicity. Also avoid use in pregnant, lactating, or breeding animals. Caution in patients prone to seizures because of possible CNS stimulation and dehydrated animals because of possible crystalluria. Despite low risk of retinal toxicity in cats receiving ciprofloxacin, high doses in cats should be used with caution. Minimize or avoid sun exposure, as photosensitivity is reported in humans.

### MECHANISM OF ACTION

Ciprofloxacin is a broad-spectrum bactericidal agent that inhibits bacterial DNA gyrase, thereby preventing bacterial DNA synthesis. Interestingly, ciprofloxacin was shown in vitro to modulate cell cycle progression and apoptosis in neoplastic cells; however, the clinical application as a chemotherapeutic agent in dogs and cats is unknown.

### DOSAGES

Administer preferably on an empty stomach.

**Dogs:** 10–30 mg/kg PO q24h or 5–15 mg/kg PO q12h

**Cats:** 20 mg/kg PO q24h

**Duration of treatment:** 1–2 weeks past resolution of clinical signs. Higher dosages might be needed for treatment of infections of the ear canals.

**Note:** Compared to other fluoroquinolones, oral availability may be variable and unpredictable in dogs and cats (Abadia *et al.* 1995; Allbarellos *et al.* 2004).

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 100 mg, 250 mg, 500 mg, 750 mg; *Cipro*®, *Ciproxin*®, *Ciloxan*®, generic
- Extended-release oral tablets: 500 mg, 1000 mg; *Cipro XR*®, generic
- Powder for oral suspension: 50 mg/mL and 100 mg/mL; *Cipro*®, *Ciproxin*®, *Ciloxan*®, generic

### SIDE EFFECTS

**Dogs and cats**
- Uncommon: nausea, vomiting, diarrhea, anorexia, permanent cartilage abnormalities and lameness in growing animals (see contraindications)

**Note:** Hypersensitivity reactions, crystalluria, CNS effects (dizziness, stimulation), photosensitivity, tendinitis, and tendon rupture have been reported in humans.

### DRUG INTERACTIONS

**Antibiotics (e.g., aminoglycosides, cephalosporins, penicillins):** potential unpredictable synergism

**Cyclosporine:** potential reduction in the metabolism and exacerbated nephrotoxicity of cyclosporine in humans

**Glyburide:** potential severe hypoglycemia

**Nitrofurantoin:** concomitant use is not recommended because of potential antagonism of antimicrobial effect

**Phenytoin:** potential alteration in phenytoin blood levels

**Probenecid:** potential increase in ciprofloxacin blood levels

**Products containing aluminum (sucralfate), iron, zinc, and/or calcium:** decrease absorption of ciprofloxacin; separate medications by at least 2 hours

**Theophylline, methotrexate:** potential increase in the blood levels of these drugs

**Warfarin:** potential for increased warfarin effects

### MONITORING
- Efficacy and adverse effects
- Monitor cats for mydriasis which can be an indication of retinal toxicity

## Clarithromycin

**Trade/brand name:** *Biaxin*® (US, CA), *Biaxin*® *XL*(US, CA), *Klaricid*® (UK), generic (Rx)
**Classification:** Antibacterial (macrolide)

## INDICATIONS

**Dogs and cats:** Bacterial skin infections caused by susceptible organisms such as Gram-positive anaerobes including *Bacteroides*, *Clostridium*, *Peptococcus*, *Propionibacterium*, *Streptococcus*, and *Staphylococcus*, Gram-negative aerobes such as *Haemophilus*, *Pasteurella multocida*, *Legionella*, *Bordetella* and *Campylobacter*; diseases caused by opportunistic mycobacteria including feline mycobacterial panniculitis, feline leprosy, and canine leproid granuloma syndrome. Other target organisms include *Nocardia*, *Toxoplasma gondii*, *Helicobacter pylori*, *Borrelia burgdorferi*, and *Cryptosporidium parvum*.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

## CONTRAINDICATIONS

Hypersensitivity to clarithromycin or any of the macrolides. Caution in patients with renal or hepatic failure (reduce dose). Avoid in pregnant animals.

## MECHANISM OF ACTION

Clarithromycin is bacteriostatic and inhibits bacterial RNA-dependent protein synthesis by penetrating the cell wall and binding to the 50S ribosomal subunit. May be bactericidal at high concentrations in very susceptible organisms.

## DOSAGES

May be administered without food for faster absorption.
There is limited clinical experience in dogs and cats.

### Dogs

- Susceptible infections: 5–10 mg/kg PO q12h
- Severe/refractory cases of canine leproid granuloma syndrome: combine clarithromycin at 15–25 mg/kg PO total daily dose PO divided q8–12h and rifampin at 10–15 mg/kg PO q24h. Treatment should be continued until lesions have completely resolved (typically 4–8 weeks)

### Cats

- Susceptible infections: 7.5 mg/kg PO q12h
- Mycobacterial infections: combination therapy using two or more antibiotics has been recommended and appears to be more efficacious than single antibiotic therapy. Long treatment courses are often needed (2–14 months), mainly for severe/refractory cases, until lesions completely resolve, and treatment should be continued for at least 2 months beyond resolution of the lesions
  - Clarithromycin alone at 62.5 mg per cat PO q12h or combined with doxycycline at 5 mg/kg PO q12h, or enrofloxacin or marbofloxacin at 5 mg/kg PO q24 h
  - Clarithromycin alone at 62.5 mg per cat PO q12h or combined with clofazimine at 8–12 mg/kg PO q24, and/or rifampin at 10–15 mg/kg PO q24h

**Note:** Clarithromycin is generally associated with high rates of bacterial resistance; therefore, care should be taken with prolonged therapy.

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Film-coated oral tablets: 250 mg, 500 mg; *Biaxin®*, *Klaricid®*, generic
- Extended-release oral tablets: 500 mg, 1000 mg; *Biaxin® XL*, generic
- Powder for oral suspension: 25 mg/mL, 50 mg/mL in 50 mL and 100 mL vials; *Biaxin®*, *Klaricid®*, generic

### SIDE EFFECTS

**Dogs and cats**
- Common: diarrhea, vomiting, nausea and anorexia
- Rare: generalized or pinnal erythema in cats and orange staining of the skin

**Note:** Eosinophilia, increased liver enzymes, cholestatic hepatitis, thrombocytopenia, allergic skin reaction, and prolonged QT interval (torsades de pointes) have been reported in humans but not in animals.

### DRUG INTERACTIONS

**Clarithromycin inhibits the metabolism of drugs that use the CYP3A subfamily of the cytochrome P450 enzyme system with need for monitoring and/or dosage reduction of these drugs if used together with clarithromycin:** quinidine, buspirone, disopyramide, ergotamine derivatives such as bromocriptine or cabergoline, triazolam, midazolam, alprazolam, lovastatin, simvastatin, cyclosporine, systemic tacrolimus, carbamazepine, theophylline, buspirone, alfentanil, rifabutin, methylprednisolone, benzodiazepine, cisapride, and azole antifungals.

**Anticoagulant drugs (e.g., warfarin):** may potentiate the effects of oral anticoagulants

**Digoxin:** potential increase in digoxin blood levels

**Fluconazole:** potential increase in clarithromycin blood levels

**Omeprazole:** potential increase of blood levels of one another

**Zidovudine:** potential decrease in blood levels of zidovudine

### MONITORING
- Efficacy and adverse effects

## Clemastine Fumarate

**Trade/brand name:** *Tavist®* (US, CA), *Tavegil®* (UK), generic
**Classification:** Ethanolamine antihistamine (first-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic skin conditions including urticaria and insect-bite hypersensitivity. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of oral type 1 antihistamines for treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010).

**Note:** The response to clemastine in dogs and cats, as with other antihistamines, is individualized and unpredictable. Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Do not use in animals allergic to clemastine. Caution in patients with prostatic hypertrophy, bladder neck obstruction, severe cardiac failure, angle-closure glaucoma, pyeloduodenal obstruction, or hepatic disease. Caution in pregnant and lactating animals. Clemastine may interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Clemastine is a histamine $H_1$-receptor antagonist with anti-allergic properties inhibiting histamine-induced wheal and flare responses. Has greater anticholinergic activity but less sedation than other first-generation antihistamines.

### DOSAGES

**Dogs:** 0.05–1.5 mg/kg PO q12h

**Note:** Oral bioavailability was shown to be low in dogs receiving 0.5 mg/kg doses (Hansson H *et al*. 2004). Higher doses might be more beneficial.

**Cats:** 0.34–0.68 mg per cat PO q12h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 1.34 mg (equivalent to 1 mg clemastine), 2.68 mg (equivalent to 2 mg clemastine); *Tavist®*, generic
- Oral tablet: 1 mg; *Tavegil®*
- Oral suspension/syrup: 0.67 mg/5 mL (equivalent to 0.5 mg/5 mL clemastine) in 120 mL btl; *Tavist®*, generic

### SIDE EFFECTS

**Dogs**

- Common: sedation, anticholinergic effects (dry mouth, decreased GI secretions, etc.), paradoxical hyperactivity

**Cats**

- Common: diarrhea
- Rare: fixed drug eruption

### DRUG INTERACTIONS

**Monoamine oxidase (MAO) inhibitors (e.g., amitraz, selegiline, furazolidone):** may increase the anticholinergic effects of celmastine
**Other CNS depressant drugs (e.g., barbiturates, tranquilizers):** additive CNS depression

### MONITORING

- Efficacy and adverse effects

## Clindamycin Hydrochloride/Palmitate

**Trade/brand name:** *Aquadrops*® (US), *Antirobe*® (US, CA, UK), *Clindrops*® (US), *Cleocin*® (US), *ClinCaps*® (US), *Clinacin*® (UK), *Clintabs*® (US), generic (Rx)
**Classification:** Antibacterial (lincosamide)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including superficial and deep pyodermas, wounds, abscesses, oral infections (e.g., stomatitis) caused by susceptible organisms including aerobic Gram-positive cocci such as *Staphylococcus aureus*, *S. pseudintermedius* (including methicillin-resistant organisms), and *Streptococcus*, and anaerobes such as *Actinomyces*, *Clostridium*, *Bacteroides*, and *Fusobacterium*. Also effective against *Nocardia*, *Pseudomonas*, *Corynebacterium*, and protozoa. May be used for treatment of infections of the ear canal, particularly otitis media, caused by susceptible organisms; however, tissue concentration is not known for the external or middle ear, and this indication is controversial with unpredictable efficacy.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals allergic to clindamycin or lincomycin, or in those with bacterial resistance to these antibiotics. Caution in patients with severe renal and/or hepatic disease (reduce dose). Avoid use in neonatal animals. Safety in pregnant and breeding animals has not been established.

### MECHANISM OF ACTION

Clindamycin is a broad-spectrum antibiotic and antiprotozoal agent that binds to the 50S ribosomal subunit of susceptible bacteria and protozoa, thus inhibiting their protein synthesis. Complete cross-resistance occurs between clindamycin and lincomycin, and at least partial cross-resistance occurs between these two antibiotics and the macrolide erythromycin. Lincosamides are typically bacteriostatic at the recommended dose but can be bactericidal, depending on the susceptibility of the organism and drug concentration at the infection site.

### DOSAGES

**Dogs**

- Label dose: 5.5–33 mg/kg PO q12h
- Wounds, abscesses, otitis, oral infections: 5–11 mg/kg PO q12h
- Pyoderma: 11 mg/kg PO q12 h. One study has also shown efficacy at 11 mg/kg PO q24h for deep pyoderma (Scott *et al*. 1998).
- Refractory infections: up to 33 mg/kg PO q12h

**Duration of treatment:** 1–2 weeks past resolution of infection.

**Cats**
- Label dose: 11–33 mg/kg PO q24h
- Skin and soft tissue infections (wounds, abscesses), oral infections: 5–11 mg/kg PO q12h or 11–33 mg/kg PO q24h
- Refractory infections: up to 33 mg/kg PO q12h

Duration of treatment: Recommended by the manufacturer to use for 7–28 days; however, the authors recommend treatment until 1–2 weeks past resolution of clinical signs.

**Note:** Oral liquid formulation may be unpalatable to cats (high alcohol content). Refrigerating the medication may reduce unpleasant flavoring. If given as oral tablets or capsules, especially to cats, medication should be followed by at least 4–6 mL of liquid or food bolus (pill pockets might be helpful) to avoid esophageal injuries. Faster absorption occurs if administered on an empty stomach. Bacterial resistance may occur during treatment.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats.
- Oral capsules (as hydrochloride): 25 mg, 75 mg, 150 mg, 300 mg; *Antirobe*®, *ClinCaps*®, *Clinacin*®
- Oral tablets (as hydrochloride): 25 mg; *Clintabs*®
- Oral solution (as hydrochloride): 25 mg/mL in 30 mL btl; *Antirobe*®, *Aquadrops*®

**Human-labeled products**
- Oral capsules (as hydrochloride): 75 mg, 150 mg, 300 mg; *Cleocin*®, generic
- Granules for oral suspension (as palmitate): 15 mg/mL in 100 mL btl; *Cleocin Pediatric*®

## SIDE EFFECTS

**Dogs and cats**
- Common: vomiting, diarrhea, anorexia
- Rare: bloody diarrhea in dogs (colitis), esophagitis or esophageal stricture in cats with capsules or tablets without food or water, hypersalivation in cats, allergic skin eruption, neuromuscular blockade, leukopenia, increased serum hepatic enzyme activity

## DRUG INTERACTIONS

**Cyclosporine:** reduction in cyclosporine blood levels

**Macrolides, other lincosamides, chloramphenicol:** antagonism. Avoid concomitant use of any of these medications with clindamycin

**Neuromuscular blocking agents (e.g., atracurium, tubocurarine, pancuronium):** prolonged neuromuscular blockade associated with intrinsic neuromuscular blocking activity of clindamycin

## MONITORING
- Efficacy and adverse effects (mainly severe diarrhea)
- Periodic (once monthly) liver and kidney function tests and CBC if therapy persists for >30 days

# Clofazimine

**Trade/brand name:** *Lamprene*® (US, UK), generic (Rx)
**Classification:** Antibacterial (antimycobacterial)

## INDICATIONS

**Dogs and cats:** Skin and soft tissue infections such as leprosy, opportunistic mycobacteriosis, or localized atypical mycobacterial infections caused by mycobacteria, including *Mycobacterium leprae*, *M. tuberculosis*, *M. avium* complex (MAC), *M. bovis*, and *M. chelonei*.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

## CONTRAINDICATIONS

Caution in patients with hepatic or renal impairment or pre-existing gastrointestinal conditions such as diarrhea or abdominal pain. Its safety in pregnant animals has not been evaluated.

## MECHANISM OF ACTION

Clofazimine is a bactericidal agent that binds to mycobacterial DNA and inhibits growth. It also has anti-inflammatory and immunosuppressive effects, but the mechanism of action is not well understood. It may also have anti-leishmanial activity.

## DOSAGES

There is limited experience in dogs and cats. It may be difficult to dose accurately. Clofazimine is often used in combination with other recommended drugs.

### Dogs

- *M. avium* complex (MAC): 4–12 mg/kg PO q24h for 6–9 months (until 2–3 months after clinical resolution). May be combined with one or two of the following antibiotics: doxycycline (10 mg/kg PO q12h), clarithromycin (7.5–12.5 mg/kg PO q12h), enrofloxacin (5–15 mg/kg PO q24h), rifampin (10–20 mg/kg PO q24h)
- *M. avium–intracellulare* complex infections, leprosy, or atypical mycobacteriosis: 4–8 mg/kg PO q24h for 4–12 weeks. May be combined with one or two of the following antibiotics: doxycycline (10 mg/kg PO q12h), clarithromycin (10–15 mg/kg PO q12h), enrofloxacin (5–15 mg/kg PO q24h), rifampin (10–20 mg/kg PO q24h)

### Cats

- Leprosy (*Mycobacterium lepraemurium* or other mycobacteria): 25–50 mg per cat PO q24–48h for 6–9 months (until 2–3 months after clinical resolution). May be combined with clarithromycin (62.5 mg per cat PO q12h) or rifampin (10–15 mg/kg PO q24h)
- Localized atypical mycobacterial infections: 8 mg/kg PO q24h for 6–9 months (until 2–3 months after clinical resolution). May be combined with marbofloxacin (5 mg/kg PO q24h), doxycycline (5–10 mg/kg PO q12h), clarithromycin (62.5 mg per cat PO q12h), or minocycline (5–12.5 mg/kg PO q12h)

- Disseminated *M. avium–intracellulare* complex infection: 4–8 mg/kg PO q24h for 5–14 months. May be combined with marbofloxacin (5 mg/kg PO q24h), doxycycline (5 mg/kg PO q12h), clarithromycin (62.5 mg per cat PO q12h), or minocycline (5–12.5 mg/kg PO q12h)

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral capsules: 50 mg, 100 mg; generic (its use is FDA-controlled; may be available through compounding pharmacies)

**Note:** Clofazimine may be difficult for veterinarians to obtain.

### SIDE EFFECTS

**Dogs and cats:** The side effects are not well documented, since there is limited experience using this drug in dogs and cats. Gastrointestinal signs (vomiting, diarrhea), dose-related skin, eye, and body fluid orange-brown discoloration, hepatic and renal abnormalities, electrolytes dysfunction, and CNS toxicity, as reported in humans, may also occur in animals. Erythema of the pinna has been reported in cats.

### DRUG INTERACTIONS

**Dapsone:** potential reduction of anti-inflammatory effects of clofazimine (unclear clinical significance)

**Isoniazid:** potential reduction of clofazimine levels in the skin and increase in serum and urine levels (unclear clinical significance)

**Rifampin:** alters pharmacodynamics of rifampin

### MONITORING

- Efficacy and adverse effects
- Chemistry profile (liver enzymes, electrolytes, renal function) and urinalysis: baseline then monthly during initial treatment

## Clomipramine Hydrochloride

**Trade/brand name:** *Clomicalm*® (US, CA, UK), *Anafranil*® (US, CA, UK), generic (Rx)
**Classification:** Behavior modifying drug (tricyclic antidepressant), Antihistamine

### INDICATIONS

Management of psychogenic or compulsive dermatoses.

**Dogs:** Self-mutilations, acral lick dermatitis, excessive tail or nail biting/chewing, excessive anal or foot licking, flank sucking, tail dock neuroma.

**Cats:** Excessive grooming or psychogenic self-induced alopecia, tail sucking, excessive nail or foot biting/chewing, hyperesthesia syndrome.

## CONTRAINDICATIONS

Do not use in animals allergic to tricyclic antidepressants. It should not be used in breeding male dogs. Caution in patients with decreased gastrointestinal motility, urinary or stool retention, cardiac rhythm disturbances, glaucoma, keratoconjunctivitis sicca, pre-existing seizure disorders, and liver impairment. Caution in patients with hyperthyroidism or those that are receiving thyroid supplementation, because of increased risk of cardiac rhythm abnormalities. Avoid use in patients with diabetes mellitus, as clomipramine may alter glucose blood levels. Clomipramine may interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

## MECHANISM OF ACTION

Clomipramine selectively inhibits serotonin (5-HT) reuptake, and its metabolite, dimethylclomipramine, blocks norepinephrine reuptake at the presynaptic neuron terminals; thereby it increases serotonin and norepinephrine concentrations at the synapse sites. Clomipramine also has moderate antihistaminic and anticholinergic activities and is an alpha-1 adrenergic antagonist.

## DOSAGES

### Dogs

- Label dose: 2–4 mg/kg PO q24h or divided q12h
- Psychogenic dermatoses: 1–3 mg/kg PO q12h for at least 4 weeks

### Cats

- General dose: 0.25–1 mg/kg PO q12–24h
- Hyperesthesia syndrome: 0.5–1 mg/kg PO q24h
- Psychogenic alopecia: clomipramine administered at 0.5 mg/kg PO q24h for 56 days failed to demonstrate significant improvement in psychogenic alopecia; therefore, higher doses (1 mg/kg PO q12–24h) and longer duration of treatment may be needed for treatment of psychogenic alopecia (Mertens *et al*. 2006)

**Note:** Clomipramine is often used in combination with other behavior-modification drugs. It may be combined with behavior management for better efficacy. Clomipramine may be given with food to minimize vomiting. It may take 4–6 weeks to see improvement. Clomipramine dose should be started low and increased gradually every 2 weeks to determine the lowest effective dose and minimize side effects. Treatment can be maintained for 4–6 months, if clinical signs are well controlled, before gradually reducing the dose (reduce by 25% every 1–2 weeks). Abrupt cessation should be avoided to prevent rebound effects. Continue the weaning process until the animal is either completely off the drug or until the abnormal behavior reoccurs. At this point, return to the previously effective dose and continue for a longer period before trying to wean again.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs

- Oral tablets: 5 mg, 20 mg, 40 mg, 80 mg; *Clomicalm*®

**Human-labeled products**
- Oral capsules: 25 mg, 50 mg, 75 mg; *Anafranil®*, generic

## SIDE EFFECTS

**Dogs**
- Common: anorexia, vomiting, diarrhea, lethargy, elevation of liver enzymes, and anticholinergic effects (e.g., dry mouth, polydipsia, tachycardia, urine retention, reduced intestinal motility). Clomipramine may decrease total T4 and free T4 levels in dogs; therefore, thyroid tests should be interpreted with caution in patients receiving clomipramine to avoid misdiagnosis of hypothyroidism (Gulikers *et al*. 2003)
- Rare: aggression, lowered seizure threshold and cardiac effects are possible, although clomipramine was shown not to cause any concerning cardiac abnormalities in healthy dogs

**Cats**
- Common: lethargy, constipation, mydriasis, and anticholinergic effects (e.g., dry mouth, polydipsia, tachycardia, urine retention, reduced intestinal motility)
- Rare: anorexia, vomiting, diarrhea, weight gain, disorientation, hypothermia

**Note:** Cats have been reported to be more susceptible to the adverse effects of clomipramine than dogs. Overdoses can produce life-threatening arrhythmias, seizures, and cardiorespiratory collapse.

## DRUG INTERACTIONS

**Anticholinergic agents (e.g., atropine) and CNS depressants (e.g., other tricyclic antidepressants, benzodiazepines, barbiturates, general anesthetics):** additive effects

**Antithyroid agents:** potential risk of agranulocytosis

**Cimetidine:** inhibition of clomipramine metabolism and increased toxicity risk

**Clonidine:** potential for increase in blood pressure

**Meperidine, pentazocine, dextromethorphan, and serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine, paroxetine):** increase risk for serotonin syndrome

**Monoamine oxidase (MAO) inhibitors (e.g., selegiline or amitraz):** should not be used concomitantly or within 14 days before or after clomipramine

**Phenobarbital:** increases levels of phenobarbital

**Rifampin:** potential for decrease in clomipramine levels

**Sympathomimetic agents:** increase risk of cardiac effects

## MONITORING
- Efficacy and adverse effects
- Liver function tests and heart rate and rhythm (ECG): baseline and annual monitoring, particularly in older animals and animals receiving clomipramine long-term

## Clonazepam

**Trade/brand name:** *Klonopin®* (US), *Klonopin® Wafers* (US), *Rivotril®* (CA, UK), generic (Rx)
**Classification:** Tranquilizer, CNS depressant, Benzodiazepine

### INDICATIONS

Management of psychogenic or compulsive dermatoses mostly associated with anxiety. Clonazepam is used primarily as an anticonvulsant therapy for epilepsy in dogs.

**Dogs:** Self-mutilations, acral lick dermatitis, excessive tail or nail biting/chewing, excessive anal or foot licking, flank sucking, tail dock neuroma.

**Cats:** Psychogenic self-induced alopecia, tail sucking, excessive nail or foot biting/chewing, hyperesthesia syndrome.

### CONTRAINDICATIONS

Patients with known hypersensitivity to clonazepam or other benzodiazepines. Use cautiously in debilitated or geriatric animals, in patients in coma or shock, with CNS depression, narrow-angle glaucoma, severe respiratory disease, marked muscle weakness, and hepatic or renal impairment. Caution in aggressive patients and working animals. Avoid in pregnant or lactating animals. It may be teratogenic. Clonazepam should not be discontinued abruptly. Benzodiazepines have been reported to exacerbate myasthenia gravis in humans.

### MECHANISM OF ACTION

Clonazepam possesses sedative, hypnotic, anticonvulsant, muscle-relaxant, and anxiolytic properties. Exact mechanism of action is unknown. Postulated mechanisms include: potentiation of the effects of GABA, an inhibitory neurotransmitter, by binding to specific benzodiazepine receptors; antagonism of serotonin; and diminished release or turnover of acetylcholine in the CNS system.

### DOSAGES

**Dogs:** 0.05–0.25 mg/kg PO q12–24h

**Cats:** 0.025–0.2 mg/kg PO q12–24h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 0.5 mg, 1 mg, 2 mg; *Klonopin®*, *Rivotril®*, generic
- Disintegrating oral tablets: 0.125 mg, 0.25 mg, 0.5 mg, 1 mg, 2 mg; *Klonopin® Wafers*, generic

### SIDE EFFECTS

There is very limited information regarding adverse effects of clonazepam in dogs and cats. Chronic administration may lead to dependence, and withdrawal syndrome if discontinued.

**Dogs**
- Common: variable and individual sedation effects, transient ataxia
- Rare: paradoxical excitement, tolerance to the drug

**Cats**
- Common: sedation, transient ataxia
- Rare: paradoxical excitement, acute hepatic necrosis (avoid long-term use)

**Note:** In humans, reported side effects include increased salivation, respiratory tract hypersecretion, gastrointestinal (e.g., vomiting, diarrhea, constipation), transient elevations in liver enzymes, and hematologic effects (e.g., anemia, leukopenia, thrombocytopenia).

### DRUG INTERACTIONS

**Antacids:** may affect clonazepam absorption. This can be managed by separating the medications by 2 hours

**CNS depressant drugs (e.g., barbiturates, narcotics, anesthetics):** may increase clonazepam serum levels and additive effects may occur

**Fluoxetine:** may increase clonazepam serum levels

**Hepatic metabolized drugs (amiodarone, cimetidine, chloramphenicol, clarithromycin, cyclosporine, diltiazem, erythromycin, isoniazid, ketoconazole, itraconazole):** clonazepam metabolism may be reduced and excessive sedation may occur

**Omeprazole, propanolol, valproic acid:** may decrease metabolism of benzodiazepines and cause excessive sedation

**Phenobarbital, phenytoin, propantheline:** may decrease clonazepam serum levels

**Rifampin:** may induce hepatic microsomal enzyme activity and decrease clonazepam efficacy

### MONITORING
- Efficacy and adverse effects
- Therapeutic blood levels if needed (it has been reported as 0.015–0.07 mcg/mL)
- Cats: liver function tests
- If cats develop inappetence, lethargy, ataxia or vomiting, medication needs to be discontinued

## Colchicine

**Trade/brand name:** Colchicine generic (US, CA, UK) (Rx)
**Classification:** Anti-inflammatory

### INDICATIONS

There is limited experience in veterinary medicine. True efficacy is unknown. It has been useful for the treatment of humans with leukocytoclastic vasculitis,

epidermolysis bullosa acquisita, linear IgA bullous dermatoses, dermatitis herpetiformis, Sweet syndrome, scleroderma, relapsing polychondritis, and dermatomyositis, among other conditions.

**Dogs:** It has been anecdotally reported for the treatment of canine cutaneous amyloidosis, familial shar-pei fever, shar-pei acute neutrophilic vasculitis or amyloidosis, epidermolysis bullosa acquisita, and hepatocutaneous syndrome.

**Cats:** Its use for dermatological conditions in cats has not been reported.

### CONTRAINDICATIONS

Colchicine is contraindicated in patients with serious renal disease and gastrointestinal or cardiac dysfunction. Caution in patients in early stages of these disorders and in geriatric or debilitated patients. Do not administer to breeding or pregnant animals (teratogenic and may reduce spermatogenesis). Caution in nursing animals.

### MECHANISM OF ACTION

Colchicine is best known for its antigout activity in humans; however, its precise mode of action has not been determined. It is an alkaloid that binds to microtubular proteins and alters a variety of basic cellular functions such as mitosis, chemotaxis and cell adhesion. It inhibits the following: secretion of immunoglobulins, mononuclear cells and neutrophil migration, lysosomal degranulation, IL-1 production, human leukocyte antigen (HLA)-DR expression, histamine release, synthesis of collagen by stimulating the activity of collagenases. Moreover, colchicine appears to alter neuromuscular function and to block the synthesis and secretion of serum amyloid A by hepatocytes, thereby preventing amyloid formation and deposition. It has also been shown to inhibit the expression of leukocyte vascular endothelial growth factor in dogs.

### DOSAGES

**Dogs**

- General dose: 0.01–0.03 mg/kg PO q24h
- Familial shar-pei fever: 0.03 mg/kg PO q24h for 2 weeks, and if no gastrointestinal problems occur the dose can be increased to twice daily. It must be given early in the course of the disease to be effective. Prophylactic use is controversial.
- Canine epidermolysis bullosa acquisita: 0.03 mg/kg PO q12h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 0.5 mg, 0.6 mg, 1 mg; generic

### SIDE EFFECTS

There is limited experience in veterinary medicine.

**Dogs**

- Common: nausea, anorexia, vomiting, diarrhea. Because these symptoms may be early signs of toxicity, it is recommended to discontinue therapy should they occur
- Rare: abdominal pain, malabsorption, increased alkaline phosphatase and alanine transferase serum levels, hair loss, bone marrow suppression (prolonged administration), renal damage, neuromuscular side effects. Overdoses can be fatal

### DRUG INTERACTIONS

**Antineoplastics and other bone marrow suppressant drugs (e.g., macrolides, chloramphenicol, flucytosine, amphotericin B):** additive myelosuppression

**Cyclosporine:** potential for increased risk of hepatic, renal, and neuromuscular toxicity

**Non-steroidal anti-inflammatory drugs (NSAIDs), especially phenylbutazone:** increased risk of thrombocytopenia, leucopenia, or bone marrow suppression

**Sympathomimetic agents and CNS depressants:** potential enhancement of activity of these drugs

### MONITORING

- Efficacy and adverse effects
- CBC should be monitored on a regular basis

## Corticotropin (ACTH)

**Trade/brand name:** *Acth*® (US, CA), *Acthar*® (US, CA), *Acthar*® *Gel*(US, CA), *Acthar*® *Hp* (US, CA) (Rx)
**Classification:** Hormone (ACTH)

### INDICATIONS

**Dogs and cats:** Diagnosis of spontaneous or iatrogenic hyperadrenocorticism and monitoring of the response to mitotane and trilostane therapy in spontaneous canine hyperadrenocorticism and alopecia X.

### CONTRAINDICATIONS

ACTH gel should not be used in patients hypersensitive to porcine proteins. Caution in pregnant animals. Do not administer the repository form (gel) IV. Patients should not receive prednisone, prednisolone, methylprednisolone, hydrocortisone, or cortisone on test day. ACTH administration may suppress intradermal test reactions; therefore, ideally, intradermal test and ACTH stimulation tests should not be performed on the same day.

### MECHANISM OF ACTION

ACTH stimulates the adrenal cortex (particularly the zona fasciculata) to secrete glucocorticoids (primarily cortisol).

### DOSAGES

Avoid use of compounded ACTH products, as compounded formulations may not be equivalent.

**ACTH stimulation test**

**Dogs:** 2.2 IU/kg IM with serum cortisol measured before and at 2 hours post injection

**Cats:** 2.2 IU/kg IM with serum cortisol measured before and at 1 and 2 hours post injection

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products:** This list is not complete as there are many different brands in different presentations available

- Solution for injection: 40 units/vial (*Acth®*), 25 units/mL (*Acthar®*), 40 units/mL (*Acthar® Hp*) (available in US); 25 IU/vial (*Acth® 25*), 40 IU/vial (*Acth® 40*), 80 IU/mL (*Acthar® Hp*) (available in CA)
- Gel form for injection: 40 units/mL, 80 units/mL; *Acth Gel®*, *Cortrophin Gel®*, *Cortigel®* (available in US); *Acthar Gel®* (available in CA)
- Lyophilized powder for injection: 25 IU/vial and 40 IU/vial; *Acthar®* (available in CA)

### SIDE EFFECTS

**Dogs and cats:** When used for diagnostic purposes, it is unlikely to cause side effects.

- Rare: prolonged use may result in fluid and electrolyte disturbances and other adverse effects

### DRUG INTERACTIONS

**Anticholinesterases (e.g., pyridostigmine):** ACTH may antagonize effects in patients with myasthenia gravis

**Diuretics:** ACTH may increase electrolyte loss

**Chronic use with any of the following drugs: barbiturates, phenytoin, rifampin, cyclophosphamide, estrogens, ulcerogenic drugs (e.g., NSAIDs), potassium-depleting drugs (e.g., amphotericin B), and oral anticoagulants:** several potential interactions may occur

### MONITORING

- Cortisol concentrations

## Cosyntropin

**Trade/brand name:** *Cortrosyn®* (US, CA), *Synacthen®* (CA); corticotropin; tetracosactrin; tetracosactide (Rx)
**Classification:** Hormone (ACTH analog)

### INDICATIONS

**Dogs and cats:** Diagnosis of spontaneous or iatrogenic hyperadrenocorticism and monitoring of the response to mitotane and trilostane therapy in spontaneous canine hyperadrenocorticism or alopecia X.

**Note:** Cosyntropin is considered by many dermatologists the agent of choice for the ACTH stimulation test in dogs and cats.

### CONTRAINDICATIONS

Patients with known hypersensitivity to cosyntropin or ACTH (possible cross-reactivity). Patients should not receive prednisone, prednisolone, methylprednisolone, hydrocortisone, or cortisone on test day. ACTH administration may suppress intradermal test reactions; therefore, ideally, intradermal test and ACTH stimulation tests should not be performed on the same day.

### MECHANISM OF ACTION

Cosyntropin is a synthetic corticotropin (ACTH) that acts similarly to endogenous corticotropin, stimulating the adrenal cortex to synthesize and release cortisol and sex hormones. Cosyntropin is not as immunogenic as endogenous corticotropin.

### DOSAGES

ACTH stimulation test

**Dogs:** 5 mcg/kg (maximum dose per dog: 250 mcg) IV or IM with serum cortisol measured before and at 1 hour post injection

**Cats:** 125 mcg per cat IV or IM with serum cortisol measured before and at 30 and 60 minutes post injection

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Powder for injection (lyophilized): 250 mcg/vial; *Cortrosyn*®, *Synacthen*®

### SIDE EFFECTS

**Dogs and cats:** When used for diagnostic purposes, it is unlikely to cause side effects.

- Rare: short-term use may induce hypersensitivity reactions

### DRUG INTERACTIONS

**Anticholinesterases (e.g., pyridostigmine):** ACTH may antagonize effects in patients with myasthenia gravis

**Diuretics:** ACTH may increase electrolyte loss

**Chronic use with any of the following drugs: barbiturates, phenytoin, rifampin, cyclophosphamide, estrogens, ulcerogenic drugs (e.g., aspirin, NSAIDs), potassium-depleting drugs (e.g., amphotericin B), and oral anticoagulants**: several potential interactions may occur

### MONITORING

- Cortisol concentrations

## Cyclophosphamide

**Trade/brand name:** *Cytoxan*® (US, CA), *Endoxana*® (US, UK), *Neosar*® (US), generic (Rx)
**Classification:** Immunomodulatory (immunosuppressive), Antineoplastic

### INDICATIONS

**Dogs and cats:** Most commonly used for the treatment of neoplastic diseases including lymphoreticular neoplasms (lymphomas), sarcomas, carcinomas, transmissible venereal tumors, and mast cell tumors. Also used as a rescue drug for refractory cases of immune-mediated diseases including pemphigus complex, cutaneous vasculitis, systemic lupus erythematosus, and bullous pemphigoid.

### CONTRAINDICATIONS

Cyclophosphamide should not be used in patients hypersensitive to the drug. Do not use in pregnant animals (teratogenic and embryotoxic). Caution in patients with leukopenia, thrombocytopenia, previous radiotherapy, or impaired hepatic or renal function, and in patients at risk for infections. Tablets should not be split or crushed, as the active ingredient is not uniformly dispersed throughout, and exposed drug represents a greater biosafety hazard than the cut surface.

### MECHANISM OF ACTION

Cyclophosphamide is a nitrogen mustard derivative and a non-specific cell-cycle inhibitor. Its metabolites (phosphoramide mustard and acrolein) act as alkylating agents interfering with DNA synthesis and function. Cyclophosphamide has potent immunosuppressive activity, impairing both humoral and cell-mediated immune systems.

### DOSAGE

It is usually used in combination with other drugs such as glucocorticoids or vincristine. Clinical response may take 1–4 weeks.

**Dogs**

- Antineoplastic: 50 mg/m$^2$ (approximately 2.2 mg/kg) PO q48h or q24h for 4 consecutive days per week. Alternative protocol for neoplasms: 100–300 m$^2$ IV q21 days. Recently, low-dose continuous (metronomic) cyclophosphamide has been applied to the treatment of various malignancies in dogs at 10 mg/m$^2$ PO q24h
- Immunosuppressive: 200–250 mg/m$^2$ (1.5–25 mg/kg) PO q48h or IV single dose. Undesirable for long-term use (>3–4 months), short-term use only in severe refractory cases

**Cats:** 6.25–12.5 mg per cat PO q24h 4 days per week

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 25 mg, 50 mg; *Cytoxan*®, generic
- Powder for injection: 100 mg, 200 mg, 500 mg, 1 g, and 2 g vials; *Cytoxan*® *Lyophilized*, *Neosar*®, *Endoxana*®

### SIDE EFFECTS

**Dogs and cats**

- Common: myelosuppression (nadir usually occurring 7–14 days after starting therapy, and may require up to 4 weeks for recovery), gastroenterocolitis (anorexia, nausea, vomiting, diarrhea), infertility, inhibition of hair regrowth or alopecia (especially in canine breeds with continuous hair growth such as

poodles and old English sheepdogs), altered wound healing, and sterile hemorrhagic cystitis (cats are less susceptible than dogs). Sterile hemorrhagic cystitis warrants discontinuation of this chemotherapy agent
- Rare: hepatotoxicity, nephrotoxicity, cardiotoxicity with high doses, pulmonary infiltrates and fibrosis, depression, immune-suppression with hyponatremia and leukemia. Cats may lose their whiskers

### DRUG INTERACTIONS

**Allopurinol, thiazide diuretics:** increase risk of myelosuppression

**Barbiturates (e.g., phenobarbital):** increase cyclophosphamide toxicity due to an increased rate of conversion of its metabolites

**Cardiotoxic drugs (e.g., doxorubicin):** increase risk of cardiotoxicity

**Chloramphenicol, glucocorticoids, imipramine, phenothiazines, potassium iodide, or vitamin A:** may inhibit cyclophosphamide metabolism

**Cisplatin:** synergistic effect

**Digoxin:** absorption of digoxin may be reduced

**Insulin:** insulin requirements are altered by concurrent cyclophosphamide therapy

**Succinylcholine:** metabolism may be reduced by cyclophosphamide

### MONITORING

- Efficacy and adverse effects
- CBC and urinalysis: baseline, after 10–14 days of treatment, then monthly

## Cyclosporine

**Trade/brand name:** *Atopica*® (US, UK), *Neoral*® (US, UK, CA), *Gengraf*® (US), generic (Rx)
**Classification:** Anti-inflammatory, Immunomodulatory (immunosuppressive)

### INDICATIONS

**Dogs:** Approved for atopic dermatitis. Extra-label indications include: perianal fistulas, sebaceous adenitis, sterile nodular panniculitis, neutrophilic dermatosis resembling pyoderma gangrenosum, Wells syndrome (eosinophilic dermatitis with edema), Sweet syndrome (neutrophilic dermatitis), alopecia areata, vasculitis, ulcerative dermatoses of the nasal philtrum, dermatomyositis, contact allergy, chronic pedal furunculosis, metatarsal sinus tracts, sterile granuloma/pyogranuloma complex, refractory cases of juvenile sterile granulomatous dermatitis and lymphadenitis (juvenile cellutitis), reactive histiocytic disorders, proliferative otitis externa, idiopathic keratinization disorders (primary seborrhea in springer spaniel, cairn terrier and West Highland white terrier, and follicular hyperkeratosis of cocker spaniels), autoimmune diseases such as pemphigus foliaceus (controversial

results), cutaneous lupus erythematosus, systemic lupus, vesicular cutaneous lupus erythematosus, exfoliative cutaneous lupus erythematosus, erythema multiforme, and uveodermatological syndrome.

**Cats:** Extra-label indications include atopic dermatitis, eosinophilic granuloma complex, urticaria pigmentosa, idiopathic sterile granulomatous diseases, plasmacytic stomatitis and pododermatitis, vasculitis, sebaceous adenitis, idiopathic facial dermatitis, feline acquired alopecia (pseudopelade), pemphigus erythematosus, and pemphigus foliaceus.

**Note:** Cyclosporine may also be used as a glucocorticoid-sparing agent.

### CONTRAINDICATIONS

Patients hypersensitive to cyclosporine. Patients with malignant neoplasia. Caution in patients with pre-existing infections, diabetes mellitus, or hepatic or renal disease, and in pregnant animals. Avoid use in reproducing animals. Avoid use of live modified or attenuated vaccines during treatment or within a 2-week interval before or after treatment, as the effect of cyclosporine on the immune response to modified live vaccines is unknown (killed vaccines should be used instead). Safety has not been established in dogs less than 6 months of age or less than 4 lb (1.8 kg) body weight. One study showed that administration of oral cyclosporine at 5 mg/kg/day for 30 days did not interfere with intradermal test results; however, drug withdrawal may be recommended for at least 4 weeks prior to intradermal testing if cyclosporine has been administered for longer than 30 days (Goldman *et al*. 2010). The effect of cyclosporine on allergy serum test results has not been investigated; therefore, at least 4 weeks withdrawal period may be recommended prior to testing.

### MECHANISM OF ACTION

Cyclosporine binds to a specific cellular receptor on calcineurin and inhibits the T-cell receptor-activated signal transduction pathway, therefore blocking the gene transcription of T-cell cytokines, especially IL-2, which is essential for T-cell proliferation. This inhibition makes cyclosporine a potent inhibitor of cell-mediated immunity and a lesser inhibitor of humoral immunity. It selectively depresses the induction and proliferation of cytotoxic T cells, antibody production by helper-T-cell-dependent B cells, the proliferation of activated T cells, and the activation of mononuclear phagocytes and helper T cells. Cyclosporine has also shown to have a wide variety of anti-inflammatory effects on leukocytes other than lymphocytes, and on other types of cells, including mast cells, eosinophils, Langerhans cells, endothelial cells, and keratinocytes. It has also been documented to have a cytostatic effect on epidermal keratinocytes.

### DOSAGE

Cyclosporine appears to be most consistently absorbed when given without food (at least 2 hours before and after a meal); however, one study showed that administration of cyclosporine with food does not interfere with clinical response (Thelen *et al*. 2006). In addition, administration with food may reduce gastrointestinal side effects.

#### Dogs

- Atopic dermatitis: may be used as a sole agent at 5 mg/kg (3.3–6.7 mg/kg) PO q24h or combined with ketoconazole to reduce cost in large dogs

(cyclosporine at 2.5–3 mg/kg PO q24h and ketoconazole at 5–10 mg/kg PO q24h). It may take 4–6 weeks to achieve a satisfactory clinical benefit

- Perianal fistulas: variable cyclosporine doses have been reported (1–10 mg/kg PO q12–24h with or without ketoconazole) with variable success. The most effective therapeutic dosing regimen has not been clearly established; however, clinical resolution appears to be faster with higher doses such as 5–10 mg/kg q12h. The authors normally use cyclosporine as a sole agent at 5–7 mg/kg PO q24h or combined with ketoconazole to reduce cost (cyclosporine at 2.5–5 mg/kg PO q24h and ketoconazole at 5–10 mg/kg PO q24h). Clinical response may be seen after 4–6 weeks of therapy
- Sebaceous adenitis: 5 mg/kg PO q24h. Clinical response may be seen after 4–6 weeks of therapy. Ketoconazole at 5–10 mg/kg q24h may be added to the therapy to reduce cyclosporine dose by half and consequently reduce cost. Topical therapy using 25 mL of cyclosporine (*Neoral*® oral solution, 100 mg/mL) mixed with 225 mL of sterile water (total volume of 250 mL) was used daily followed by an emollient spray in 20 dogs with sebaceous adenitis, with some cases showing hair regrowth after 6 weeks of treatment (Paterson 2004). Once hair had regrown (typically 8–12 weeks), the frequency of application was reduced to once or twice weekly. Additionally, anecdotal evidence recommends mixing four 100 mg capsules of cyclosporine (400 mg total) in 100 mL of baby oil and thoroughly applying the mixture to the skin and hair coat. After 1 hour, shampoo the dog with a degreasing product (e.g., benzoyl-peroxide-based shampoo). Repeat the procedure twice weekly. After clinical improvement is noticed (typically 30–40 days), try reducing the frequency of administration to weekly or every other week
- Sterile nodular panniculitis, neutrophilic dermatoses resembling pyoderma gangrenosum, alopecia areata, chronic pedal furunculosis, metatarsal sinus tracts, cutaneous histiocytosis, dermatomyositis, proliferative chronic otitis, idiopathic keratinization disorders: 5 mg/kg PO q24h. Clinical response may be seen after 1–2 months of therapy. Ketoconazole at 5–10 mg/kg q24h may be added to the therapy to reduce cyclosporine dose by half and consequently reduce cost.
- Pemphigus foliaceus: cyclosporine has been used for this condition with variable results. Higher doses such as 15–25 mg/kg PO q24h or 5–10 mg/kg PO q24h combined with 5–10 mg/kg PO q24h of ketoconazole may need to be used. Cyclosporine in conjunction with ketoconazole and azathioprine has also been reported with good success in three refractory cases of pemphigus foliaceus (Rosenkrantz and Aniya 2007)
- Cutaneous discoid lupus erythematosus: 30 mg/kg PO q24h was used in one dog and good response was noted after 6 weeks of therapy; however, the medication was discontinued after 24 weeks as the dog developed severe gingival hyperplasia and a proliferative lymphoplasmatoid dermatitis (Rosenkrantz *et al*. 1989). The authors have treated cases of discoid lupus erythematosus refractory to other therapies with 5 mg/kg PO q24h, with good results
- Vesicular cutaneous lupus erythematosus: 4 mg/kg PO q24h in association with 4 mg/kg PO q24h of ketoconazole was reported to be successful in one case, with remission maintained at 2 mg/kg PO q24h of cyclosporine alone (Font *et al*. 2006)
- Exfoliative cutaneous lupus erythematosus: 2.5–10 mg/kg PO q24h with or without ketoconazole at 5–7 mg/kg PO q24h was reported to improve cutaneous lesions and joint pain but did not stop disease progression (Mauldin *et al*. 2010)

- Refractory cases of juvenile sterile granulomatous dermatitis and lymphadenitis (juvenile cellutitis): 10 mg/kg PO q24h was reported to be efficacious in one case refractory to glucocorticoid therapy (Santoro and Campbell 2011). Once clinical remission is achieved, slow tapering of the dose is recommended

**Cats**

- Atopic dermatitis, eosinophilic granuloma complex: 5–10 mg/kg PO q24h. It may take 4–8 weeks to achieve a satisfactory clinical benefit
- Sebaceous adenitis: 5 mg/kg PO q24h. Clinical response may take 1–3 months
- Idiopathic granulomatous folliculitis and furunculosis: 5 mg/kg PO q24h. Clinical response may take 1–2 months
- Urticaria pigmentosa: 7.5 mg/kg PO q24h. Clinical response may take up to 1 month
- Pemphigus foliaceus: 8–10 mg/kg PO q24h

**Note:** A recent prospective study showed that administration of oral cyclosporine at a median dose of 5.2 mg/kg/day (range: 4.4–6.9 mg/kg/day) provides comparable efficacy relative to chlorambucil for the management of feline pemphigus foliaceus, while providing superior glucocorticoid-sparing effect (Irwin *et al*. 2011).

**Maintenance therapy:** Once significant clinical response is seen, the dose may be tapered by decreasing cyclosporine daily dose to 50% of the initial dose, or by decreasing the frequency of dosing to every other day followed by dosing three times a week, until a minimum frequency for adequate therapeutic maintenance is reached. Tapering the dose by decreasing the frequency of administration or reducing daily dosage appears to yield similar responses. During the tapering phase, relapses of clinical signs may occur. Ketoconazole dose is maintained, but the frequency should be reduced along with cyclosporine.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs only.

- Oral capsules: 10 mg, 25 mg, 50 mg, 100 mg; *Atopica*®

**Human-labeled products**

- Oral capsules (microemulsion or modified): 25 mg, 100 mg; *Neoral*®, *Gengraf*®, generic
- Oral solution (microemulsion or modified): 100 mg/mL in 50 mL vial; *Neoral*®, generic

## SIDE EFFECTS

**Dogs**

- Common: transient or persistent gastrointestinal signs (vomiting, diarrhea and anorexia), lethargy, gingival hyperplasia (observed mostly with chronic use), lymphadenopathy, urinary tract infection
- Rare: psoriasiform lichenoid-like dermatosis, viral papillomatosis, hepatotoxicity, nephrotoxicity and bone marrow suppression (unlikely with current recommended doses), hypertrichosis, excessive shedding, bacterial or fungal infections, corneal opacity, neurotoxicity (presented as tremors and reported with high doses), neoplastic diseases (particularly with long-term use and in combination with other immunosuppressants such as, glucocorticoids). A recent uncontrolled study

showed that oral administration of cyclosporine to dogs with atopic dermatitis at 5 mg/kg/day for 6 weeks had a negative impact in glucose homeostasis (unknown mechanism) (Kovalik *et al*. 2011); however, the clinical significance of these findings is unclear. To date, the authors have not seen development or worsening of diabetes in dogs or cats receiving long-term cyclosporine therapy. Clinical pathology changes generally not associated with clinical signs: elevated creatinine, hyperglobulinemia, hyperphosphatemia, hyperproteinemia, hypercholesterolemia, hypoalbuminemia, hypocalcemia, and elevated BUN. Other even less common changes include hypernatremia, hyperkalemia, elevated ALP, elevated ALT, hypercalcemia, and hyperchloremia

**Cats:** There is limited information on use in cats

- Common: gastrointestinal signs (vomiting, diarrhea and/or anorexia), weight loss and hypersalivation. These signs may be transient.
- Rare: gingival hyperplasia (observed mostly with chronic use), hypertrichosis, bacterial or fungal infection, systemic toxoplasmosis (possibly fatal), asymptomatic or symptomatic urinary tract infection, hepatotoxicity and nephrotoxicity (very unlikely with current dose recommendations for dermatological diseases), neoplasia (particularly in combination with other immunosuppressants such as steroids)

## DRUG INTERACTIONS

Cyclosporine should be used cautiously with drugs that affect the CYP enzyme system.

**Allopurinol, amiodarone, azole antifungals (e.g., ketoconazole, itraconazole, fluconazole), bromocriptine, chloroquine, cimetidine, cisapride, corticosteroids, danazol, grapefruit juice/powder, losartan, valsartan, macrolide antibiotics (e.g., erythromycin, clarithromycin), metoclopramide, omeprazole, sertraline:** increase cyclosporine serum levels, with potential risk of cyclosporine toxicity

**Calcium channel blockers (e.g., verapamil, diltiazem):** increase severity of gingival hyperplasia and increase cyclosporine serum levels, with potential risk of toxicity

**Carbamazepine, nafcillin, octreotide, phenobarbital, phenytoin, rifampin, sulfadimidine, triclopidine, trimethoprim sulfamethoxazole, St. John's wort:** decrease cyclosporine serum levels, with potential reduction in efficacy

**Digoxin:** increases digoxin serum levels, with potential toxicity

**Ketoconazole and other similar antifungals:** substantial reduction in cyclosporine metabolism in dogs and cats allows use of this interaction to reduce cyclosporine dose and result in cost reduction of treatment. Monitoring of cyclosporine serum levels may be required

**Macrocyclic lactones (e.g., ivermectin, milbemycin) or other P-glycoprotein substrates:** decreased efflux of these drugs from blood–brain barrier cells and potential risk of CNS toxicity

**Methotrexate:** potential increase in methotrexate serum levels

**Nephrotoxic drugs (e.g., acyclovir, cimetidine, diclofenac, ranitidine, amphotericin B, aminoglycosides, colchicine, erythromycin, vancomycin, trimethoprim sulfamethoxazole, NSAIDs):** possible additive nephrotoxicity

**Spironolactone and other potassium-sparing diuretics:** increase risk of hyperkalemia

**Vaccinations:** decrease vaccine effectiveness; avoid use of live attenuated vaccines

### MONITORING

- Efficacy and adverse effects
- Therapeutic drug monitoring (particularly when response is poor or adverse effects occur): a trough sample is usually recommended at either 12 or 24 hours after the last dose; however, a 2-hour blood sample value might correlate better with clinical results than a trough sample. In cats, levels are twice as high at 2 hours as at 12 hours. The most adequate and safest therapeutic range has not been determined in dogs and cats. It is speculated that an adequate level should be within 200–400 ng/mL for anti-inflammatory doses, and within 100–500 ng/mL and 250–1000 ng/mL for immunosuppressive doses in dogs and cats, respectively. Different methodologies may lead to different results. The therapeutic level should be measured at least 2 weeks after initiation of therapy, as cyclosporine levels tend to be more stable at that time.
- Chemistry profile, urinalysis and urine culture. The authors perform these tests at baseline and every 6–12 months during treatment, in addition to CBC at baseline and every 12 months

## Cyproheptadine Hydrochloride

**Trade/brand name:** *Periactin*® (US, CA, UK), generic (Rx)
**Classification:** Antihistamine (first-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic skin conditions including urticaria and insect-bite hypersensitivity. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of oral type 1 antihistamines for treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010).

**Note:** The response to cyproheptadine in dogs and cats, as with other antihistamines, is individualized and unpredictable. Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Do not use in animals allergic to cyproheptadine. Caution in patients with hyperthyroidism, cardiovascular disease, hypertension, glaucoma, prostatic hypertrophy, pyeloduodenal, or bladder neck obstruction. Cyproheptadine will interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Cyproheptadine is a histamine $H_1$-receptor antagonist with anti-allergic properties inhibiting histamine-induced wheal and flare responses. It also has anticholinergic, antiserotonergic, and calcium channel blocking actions.

### DOSAGES

**Dogs**
- Antihistamine: 0.5–2 mg/kg PO q8–12h

**Cats**
- Antihistamine: 2–4 mg per cat PO q12–24h
- Feline asthma: 1–2 mg per cat PO q12h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 4 mg; *Periactin*®, generic
- Oral syrup: 2 mg/5 mL in 473 mL btl; generic

### SIDE EFFECTS

**Dogs**
- Common: CNS depression (lethargy, sedation), dry mouth
- Rare: diarrhea, vomiting, anorexia, polyphagia (at higher dosages)

**Cats**
- Common: CNS depression (lethargy, sedation), dry mouth
- Rare: paradoxical excitement, diarrhea, vomiting, anorexia, polyphagia, hemolytic anemia

**Note:** Sedative effects of antihistamines may diminish with time.

### DRUG INTERACTIONS

**Cholinergics:** decrease efficacy of cyproheptadine

**Other CNS depressant drugs (e.g., barbiturates, tranquilizers):** increase sedation

**Selective serotonin reuptake inhibitors (SSRIs) (e.g., sertraline, fluoxetine, paroxetine):** potential for decrease in efficacy of these drugs

### MONITORING
- Efficacy and adverse effects

## Dapsone

**Trade/brand name:** *Avlosulfon*® (CA), generic (RX)
**Classification:** Anti-inflammatory, Antibacterial (sulfone)

### INDICATIONS

**Dogs:** Skin and soft tissue infections caused by mycobacteria (*Mycobacterium leprae*, *M. lepraemurium*), subcorneal pustular dermatosis, linear IgA dermatosis,

dermatitis herpetiformis, pemphigus complex, dermatomyositis, neutrophilic dermatitis (Sweet syndrome), cutaneous vasculitis including post-vaccination alopecia/vasculitis, and brown recluse spider (*Loxosceles*) bites (as adjunctive treatment).

### CONTRAINDICATIONS

Avoid use in cats, because of increased incidences of neurotoxicity and hemolytic anemia. Do not use in animals allergic to dapsone or other sulfone drugs or sulfonamides. It should not be used in patients with blood dyscrasias such as anemia. Caution in patients with hepatic disease (may need to reduce dose). Its safety in pregnant animals has not been evaluated.

### MECHANISM OF ACTION

Dapsone or diaminodiphenylsulfone is a sulfone with bacteriostatic and bactericidal activities. It has similar actions to that of sulfonamides, affecting primarily folic acid synthesis in susceptible organisms. Dapsone also has anti-inflammatory properties by decreasing neutrophil chemotaxis, complement activation, antibody production, and lysosomal enzyme synthesis.

### DOSAGES

**Dogs:** Rarely, dogs may become resistant to dapsone. The combination of dapsone with other drugs, such as glucocorticoids, may be synergistic, and it is often used as adjunctive therapy to treat non-infectious disorders. Clinical response may require 4–6 weeks.

- Mycobacteriosis: 1.1 mg/kg PO q6h until remission, then 0.3 mg/kg PO q8–12h after recovery. Dapsone should be combined with other antimicrobial drugs such as rifampin (10–20 mg/kg PO q24h) or clofazimine (4–8 mg/kg PO q24h) to avoid resistance
- Subcorneal pustular dermatosis, linear IgA dermatosis, pemphigus complex, cutaneous leukocytoclastic vasculitis: 1 mg/kg PO q8h until remission (usually 1–4 weeks) and then tapered to 1 mg/kg q12–24h or twice weekly as maintenance
- Brown recluse spider bite: 1 mg/kg PO q8h for 10 days
- Dermatomyositis: 1 mg/kg PO q8–12h until remission (usually 1–4 weeks) and then tapered to 1 mg/kg q12–24h or twice weekly as maintenance

**Cats:** Avoid use in cats.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 25 mg, 100 mg; *Avlosulfon*® (100 mg only), generic

### SIDE EFFECTS

There is limited experience in veterinary medicine. Potential toxicity can be serious. Gastrointestinal signs may be reduced by administering dapsone with food.

**Dogs**

- Common: mild non-regenerative anemia, mild leucopenia, and mild to moderate elevations of serum alanine aminotransferase may be expected during induction, but, if the animal remains clinically normal, therapy does not need to be discontinued; the levels should return to normal when dosage is reduced for maintenance

- Rare: gastrointestinal signs (vomiting, diarrhea, anorexia), hepatotoxicity, hemolytic anemia, fatal thrombocytopenia and leukopenia, neuropathies, pruritic erythematous maculopapular cutaneous eruptions, photosensitivity, and potential carcinogenic effect

**Cats:** Cats are more susceptible to dapsone toxicity. Fatal hemolytic anemia and neurotoxicity reported.

### DRUG INTERACTIONS

**Activated charcoal, antacids, para-aminobenzoic acid (PABA), rifampin:** potential decrease in dapsone serum levels

**Probenecid, folic acid antagonists, trimethoprim:** potential increase in dapsone serum levels, and potentiate toxicity

**Pyrimethamine, sulfonamides:** potentiate hematologic reactions

### MONITORING

- Efficacy and adverse effects
- CBC, chemistry profile and urinalysis: every 2–3 weeks during induction therapy (first 4 months) and then every 3–4 months
- Periodic liver function tests

## Dexamethasone

**Trade/brand name:** *Decadron®* (US, CA, UK), *Dexamethasone Intensol®* (US), *Hexadrol® Phosphate* (US, CA), generic (Rx)
**Classification:** Anti-inflammatory (glucocorticoid), Immunomodulatory (immunosuppressive), Hormone

### INDICATIONS

**Dogs and cats:** Alternative anti-inflammatory therapy for allergic diseases such as atopic dermatitis, and immunosuppressive therapy for autoimmune diseases such as pemphigus complex (particularly in cases that do not respond to or do not tolerate the conventional prednisone/prednisolone therapy). Also used to diagnose (low-dose dexamethasone suppression test) or localize (low-dose or high-dose dexamethasone suppression test) spontaneous hyperadrenocorticism.

### CONTRAINDICATIONS

Do not use in pregnant animals. Systemic glucocorticoids are generally contraindicated in patients with renal disease, diabetes mellitus, and infectious diseases. Avoid long-term daily or every-other-day use. Use dexamethasone cautiously in cats with any cardiovascular disorders that alter the compensatory mechanisms for increased plasma volume to avoid congestive heart failure (Ployngam *et al*. 2006). Dexamethasone, as any other glucocorticoid, should be discontinued slowly in animals receiving chronic therapy. Dexamethasone will interfere with intradermal and allergy serum test reactivity; therefore, drug withdrawal is usually recommended for at least 4 weeks prior to allergy testing for oral administration

and 8 weeks for injectable administration. Injectable dexamethasone is considered unsuitable for management of chronic dermatologic diseases due to potential severe effect on the HPA-axis.

### MECHANISM OF ACTION

The mechanism of action of glucocorticoids is very complex, but basically they alter the transcription of DNA, leading to alterations in cellular metabolism, thereby causing inhibition of inflammatory cells and suppression of many inflammatory mediators.

### DOSAGES

**Dogs**

- Anti-inflammatory: 0.07–0.16 mg/kg PO q24h or divided q12h
- Immunosuppressive: 0.3–0.9 mg/kg PO q24h or divided q12h

**Note:** Initial dose should be maintained until clinical remission is achieved for up to 7 days, then the dose should be tapered to q48h. If clinical symptoms are still well controlled after 5–7 days, dose should be tapered further to q72h for maintenance. When used long-term, drug should be discontinued gradually.

- Dexamethasone suppression test: for low-dose and high-dose dexamethasone suppression test administer 0.01–0.015 mg/kg and 0.1 mg/kg IV, respectively, and collect cortisol samples at 0, 4, and 8 hours post administration

**Cats**

- Anti-inflammatory: 0.125–1 mg/kg PO q24h or divided q12h
- Immunosuppressive: 1 mg/kg PO q12–24h

**Note:** Initial dose should be maintained until clinical remission is achieved for up to 7 days, then the dose should be tapered to q48h. If clinical symptoms are still well controlled after 5–7 days, dose should be tapered to q72h for maintenance.

- Dexamethasone suppression test: for low-dose and high-dose dexamethasone suppression test administer 0.1 mg/kg and 1 mg/kg IV, respectively, and collect cortisol samples at 0, 4, and 8 hours post administration. Normal cortisol concentration after suppression test should be <30–40 nmol/L (1.1–1.3 mcg/dL)

### FORMULATIONS

**Veterinary-labeled products:** Available in injectable form only and approved for dogs and cats. However, injectable forms are not recommended for management of dermatological diseases in dogs and cats.

**Human-labeled products**

- Oral tablets: 0.25 mg, 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, 6 mg; *Decadron®*, generic
- Oral solution: 0.5 mg/5 mL in 100 mL, 237 mL, 500 mL, 1 mg/mL (concentrate) in 30 mL dropper; *Dexamethasone Intensol®*, generic
- Injection (as sodium phosphate): 4 mg/mL in 1, 5, 10 and 30 mL vials; *Hexadrol® Phosphate*, generic. Used in the diagnosis of hyperadrenocorticism

### SIDE EFFECTS

Side effects are mostly associated with long-term administration, especially if administered at high dosages or on a daily regimen. Glucocorticoids can retard growth in young animals. Adverse side effects are generally manifested as hyperadrenocorticism clinical signs.

**Dogs**
- Common: polyuria, polydipsia and polyphagia
- Uncommon: weight gain, panting, vomiting, diarrhea, gastrointestinal ulceration, elevated liver enzymes (mainly alkaline phosphatase), pancreatitis, lipidemias, diabetes mellitus, muscle wasting, dull and dry hair coat, alopecia, atrophic/thin skin, calcinosis cutis, behavioral changes (depression, lethargy, hyperactivity, aggression, viciousness)
- Rare: anorexia, weight loss and severe muscle wasting (most commonly seen with long-term daily immunosuppressive doses)

**Cats:** Cats tend to develop fewer side effects than dogs; however, cats are more predisposed to diabetes mellitus than dogs.
- Rare: polyuria, polydipsia, polyphagia, weight gain, vomiting, diarrhea, depression. Congestive heart failure has been reported in cats treated with corticosteroids (Smith *et al*. 2004)

**Note:** Adverse effects associated with immunosuppressive dosages are more common and potentially more severe. Discontinuation of the drug and alternate therapy may be necessary. Glucocorticoids should not be discontinued abruptly after long-term use. Laboratory alterations may include hypercholesterolemia, glucosuria, hypokalemia, decrease of thyroid serum hormones levels (tT3, tT4, fT4, TSH), increased activity of alkaline phosphatase (other liver enzymes may also be elevated with long-term use), neutrophilia, monocytosis, and lymphopenia.

## DRUG INTERACTIONS

**Amphotericin B, potassium depleting diuretics (e.g., spironolactone):** hypokalemia

**Anticholinesterase agents (e.g., neostigmine, pyridostigmine):** in patients with myasthenia gravis may cause profound muscle weakness. Anticholinesterase drug should be discontinued at least 24h prior to dexamethasone administration

**Aspirin, diazepam:** reduction in the serum levels of these drugs

**Azole antifungals (e.g., ketoconazole) and macrolide antibiotics (e.g., erythromycin, clarithromycin):** may increase dexamethasone serum levels; ketoconazole may induce adrenal insufficiency when glucocorticoids are withdrawn by inhibiting adrenal corticosteroid synthesis

**Barbiturates, phenytoin, rifampin:** may decrease dexamethasone serum levels

**Cyclophosphamide:** potential inhibition of hepatic metabolism of cyclophosphamide; dosage adjustments may be required

**Cyclosporine:** potential increase in serum levels of cyclosporine and dexamethasone, by mutual inhibition of hepatic metabolism; clinical significance is unknown

**Ephedrine:** potential decrease in dexamethasone serum levels and interference with dexamethasone suppression tests

**Indomethacin:** potential false-negative results in dexamethasone suppression tests

**Insulin:** insulin requirements may increase

**Mitotane:** may alter dexamethasone metabolism

**Non-steroidal anti-inflammatory drugs (NSAIDs):** increase risk of gastrointestinal ulceration. NSAIDs should be discontinued at least 48h prior to administration of dexamethasone

**Vaccines:** patients receiving immunosuppressive dosages of glucocorticoids should not receive live-attenuated-virus vaccines, as virus replication may be increased; a reduced immune response may occur after vaccine, toxoid, or bacterin administration

### MONITORING

- Efficacy and adverse effects
- Growth and development in young animals
- For immunosuppressive dosage, chemistry profile, CBC, urinalysis, and urine culture should be performed at baseline, then every 2–4 weeks until maintenance dosage is achieved. The authors recommend chemistry profile, urinalysis, and urine culture at least once a year for dogs on maintenance glucocorticoid therapy. These tests may need to be performed more often in more debilitated patients
- ACTH stimulation test, if indicated

## Diazepam

**Trade/brand name:** *Valium*® (US, UK), *Diazepam Intensol*® (US), *Atensine*® (UK), generic (Rx)
**Classification:** Tranquilizer, CNS depressant, Benzodiazepine

### INDICATIONS

Management of psychogenic or compulsive dermatoses mostly associated with anxiety.

**Dogs:** Self-mutilations, acral lick dermatitis, excessive tail or nail biting/chewing, excessive anal or foot licking, flank sucking, tail dock neuroma.

**Cats:** Excessive grooming or psychogenic self-induced alopecia, tail sucking, excessive nail or foot biting/chewing, hyperesthesia syndrome.

### CONTRAINDICATIONS

Patients with known hypersensitivity to diazepam. Avoid in debilitated or geriatric animals, in patients in coma or shock, in those with CNS or respiratory depression, severe muscle weakness, hepatic or renal impairment, and in cats exposed to chlorpyrifos. Avoid in pregnant or lactating animals. It may be teratogenic. Caution in aggressive patients and working animals.

### MECHANISM OF ACTION

The exact mechanism of action of diazepam is unknown. Postulated mechanisms include potentiation of the effects of GABA, an inhibitory neurotransmitter, by binding to specific benzodiazepine receptors; antagonism of serotonin; and reduction in the release or turnover of acetylcholine in the CNS.

## DOSAGES

Diazepam may be used in combination with tricyclic antidepressants for the management of more severe behavioral abnormalities.

**Dogs:** 0.5–2.2 mg/kg PO q12–24h or as needed

**Cats:** 0.2–0.5 mg/kg PO q12–24h

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 2 mg, 5 mg, 10 mg; *Valium*®, *Atensine*®, generic
- Oral solution: 1 mg/mL in 30 mL dropper, and 5 mg and 10 mg patient cups; *Diazepam Intensol*®, generic

## SIDE EFFECTS

Chronic administration of diazepam may lead to dependence and withdrawal syndrome if discontinued.

**Dogs**

- Common: variable degree of sedation, muscle weakness, ataxia, polyphagia, paradoxical CNS excitement, aggression or unusual behavior
- Rare: tolerance to the drug

**Cats**

- Common: sedation, muscle weakness, ataxia, polyphagia, changes in behavior (irritability, depression, aberrant demeanor)
- Rare: anorexia, lethargy, increase in ALT/AST, hyperbilirubinemia, idiosyncratic fatal hepatic necrosis (avoid long-term use), tolerance to the drug

**Note:** Neutropenia has been reported as a serious side effect in humans.

## DRUG INTERACTIONS

**Amitriptyline and other antihistamines:** may increase diazepam serum levels and potential for enhanced sedative effect

**Antacids, mineral oil:** may decrease oral diazepam absorption. This can be managed by separating the medications by 2 hours

**Cimetidine, erythromycin, omeprazole, propranolol, valproic acid:** may decrease metabolism of benzodiazepines and excessive sedation

**CNS depressant drugs (e.g., barbiturates, narcotics, anesthetics), antifungals (e.g., itraconazole, ketoconazole), quinidine:** may increase diazepam serum levels

**Dexamethasone, phenobarbital, phenytoin:** may decrease diazepam serum levels

**Digoxin:** may increase digoxin serum levels

**Pancuronium, succinylcholine:** increase in duration and intensity of respiratory depression

**Rifampin:** may induce hepatic microsomal enzyme activity and decrease diazepam's efficacy

### MONITORING

- Efficacy and adverse effects
- If cat develops inappetence, lethargy, ataxia or vomiting, medication needs to be discontinued
- Liver function serum tests (especially ALT and AST) in cats: baseline and within 5 days of initiation of treatment

## Dicloxacillin Sodium

**Trade/brand name:** *Dynapen*® (US), generic (Rx)
**Classification:** Antibacterial (beta-lactam)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including superficial and deep pyodermas, wounds and abscesses caused by susceptible Gram-positive bacteria, particularly *Staphylococcus*. Not effective against methicillin-resistant *Staphylococcus* strains, mycobacteria, fungi, mycoplasma, rickettsia, and virus. Because there are no clinical efficacy studies available, and because other drugs are available to treat staphylococcus skin infections in dogs and cats, dicloxacillin is not commonly used. Moreover, in dogs oral absorption is low and may not be suitable for therapy.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to penicillins. Caution in patients with documented hypersensitivity to other beta-lactam antibiotics (e.g., cephalosporins, carbapenems, cefamycins). Avoid use in pregnant or lactating animals as its safety has not been determined.

### MECHANISM OF ACTION

Like cloxacillin and oxacillin, dicloxacillin is a beta-lactam antibiotic that inhibits bacterial cell wall synthesis by binding to penicillin binding proteins, leading to cell lysis and death of the organism.

### DOSAGES

Absorption in dogs is better on an empty stomach.

**Dogs and cats:** 20–30 mg/kg PO q8h
Duration of treatment: 1–2 weeks past resolution of clinical signs.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 125 mg, 250 mg, 500 mg; *Dynapen*®, generic

### SIDE EFFECTS

Penicillins usually have minimal toxicity associated with their use.

**Dogs**
- Common: vomiting, diarrhea, anorexia
- Rare: neurotoxicity (e.g., ataxia associated with very high doses or very prolonged use), elevated liver enzymes, tachypnea, dyspnea, edema, tachycardia, idiosyncratic hypersensitivity reactions manifested as cutaneous rashes, fever, anemia, lymphadenopathy, eosinophilia, neutropenia, agranulocytosis, thrombocytopenia, anaphylaxis

**Cats**
- Common: vomiting, diarrhea, anorexia
- Rare: idiosyncratic hypersensitivity reactions manifested as cutaneous rashes, fever, anemia, lymphadenopathy, eosinophilia, neutropenia, agranulocytosis, thrombocytopenia, anaphylaxis

### DRUG INTERACTIONS

**Aminoglycosides:** in-vitro evidence of synergism against *Staphylococcus aureus* strains

**Cyclosporine:** may reduce cyclosporine serum levels

**Probenecid:** increases serum levels of dicloxacillin

**Tetracyclines:** potential antagonism; do not use together

**Warfarin:** may decrease warfarin efficacy

### MONITORING
- Efficacy and adverse effects

## Difloxacin Hydrochloride

**Trade/brand name**: *Dicural*® (US, UK) (Rx)
**Classification:** Antibacterial (third-generation fluoroquinolone)

### INDICATIONS

**Dogs:** Skin and soft tissue infections including superficial and deep pyodermas, wounds and abscesses caused by susceptible Gram-negative and Gram-positive bacilli and cocci, including most species and strains of *Klebsiella*, *Staphylococcus*, *Escherichia coli*, *Enterobacter*, *Campylobacter*, *Shigella*, *Proteus*, and *Pasteurella*. Some strains of *Pseudomonas aeruginosa*, and most *Enterococcus*, are resistant. Like other fluoroquinolones, difloxacin has weak activity against most anaerobes and is not a good choice when treating known or suspected anaerobic infections.

**Cats:** No information available.

**Note:** The authors do not recommend the use of fluoroquinolones as first-line therapy for pyoderma. Fluoroquinolones should be considered primarily for chronic deep pyodermas associated with extensive scar tissue, because of their excellent tissue penetration. Antibiotic selection, however, should be based on culture and susceptibility results.

### CONTRAINDICATIONS

Contraindicated in dogs known to be hypersensitive to difloxacin or other fluoroquinolones and in immature, growing animals, because of potential arthropathies (during the rapid growth phase between 2–8 months in small and medium-sized breeds and up to 18 months in large and giant breeds). Caution in animals with known or suspected CNS disorders (e.g., seizure disorders), because of potential CNS stimulation and seizures. Avoid use in breeding, pregnant, or lactating dogs, as safety has not been determined. Avoid use in cats, as complete safety has not been established.

### MECHANISM OF ACTION

Difloxacin is a concentration-dependent bactericidal agent that inhibits bacterial DNA gyrase enzyme (a type II topoisomerase), preventing bacterial DNA synthesis and consequently bacterial replication.

### DOSAGES

**Dogs:** 5–10 mg/kg PO q24h
Duration of treatment: Manufacturer recommends treating for 2–3 days beyond the cessation of clinical signs to a maximum of 30 days therapy. The authors recommend treating cutaneous infections for 1–2 weeks past resolution of clinical signs.

**Cats:** no dosing information available

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs.
- Oral tablets: 11.4 mg, 45.4 mg; 136 mg; *Dicural*®

**Human-labeled products: None**

### SIDE EFFECTS

**Dogs**
- Common: self-limiting gastrointestinal effects such as nausea, vomiting, diarrhea, anorexia, and arthropathy in young animals
- Rare: high concentrations may cause CNS toxicity, especially in animals with renal failure

**Cats:** Safety in cats has not been reported.

### DRUG INTERACTIONS

**Aminoglycosides, third-generation cephalosporins agents, and extended-spectrum penicillins:** potential synergism against some bacteria (particularly *Pseudomonas aeruginosa* or other Enterobacteriaceae)

**Antacids, dairy products containing cations ($Mg^{++}$, $Al^{+++}$, $Ca^{++}$):** may prevent difloxacin absorption

**Clindamycin:** in-vitro synergy reported against strains of *Peptostreptococcus*, *Lactobacillus*, and *Bacteroides fragilis*

**Cyclosporine:** fluoroquinolones may exacerbate the nephrotoxicity of cyclosporine

**Nitrofurantoin:** may antagonize the antimicrobial activity of the fluoroquinolones, and their concomitant use is not recommended

**Probenecid:** may block tubular secretion of difloxacin and may increase its serum level and half-life

**Sucralfate:** may inhibit absorption of difloxacin; separate doses of these drugs by at least 2 hours

**Theophylline:** may increase theophylline serum levels

### MONITORING

- Efficacy and adverse effects

## Diphenhydramine Hydrochloride

**Trade/brand name:** *Benadryl*® (US, CA), *Benadryl Allergy*® (US, CA), *Dreemon*® (UK), *Medinex*® (UK), *Nytol*® (UK), many different brands and generics available
**Classification:** Antihistamine (first-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic conditions including urticaria, angioedema, and insect-bite hypersensitivity. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of oral type 1 antihistamines for treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010). It may also be used as adjunctive therapy for mast cell tumors.

**Note:** It is one of the most common antihistamines used in dogs for control of pruritic conditions. The response to diphenhydramine in dogs and cats, as with other antihistamines, is individualized and unpredictable. Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Do not use in animals allergic to diphenhydramine. Caution in patients with hyperthyroidism, cardiovascular disease, hypertension, glaucoma, prostatic hypertrophy, pyeloduodenal or bladder neck obstruction. Caution in patients with hepatic disease, and in pregnant and lactating animals. Diphenhydramine will interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Diphenhydramine is a histamine $H_1$-receptor antagonist with anti-allergic properties inhibiting histamine-induced wheal and flare responses. It has substantial anticholinergic and sedative effects.

### DOSAGES

**Dogs and cats:** 2–4 mg/kg PO q8–12h

### FORMULATIONS

**Veterinary-labeled products:** None for systemic administration.

**Human-labeled products**

- Oral tablets: 25 mg, 50 mg; *Aller-Dryl®*, *Allermax®*, *Allerg-G-Time®*, *Anti-Hist®*, *Banophen®*, *Benadryl®*, *Benadryl Allergy®*, *Dreemon®*, *Genahist®*, *Histaprin®*, *Medinex®*, *Nytol®*, *Q-dryl®*, generic
- Oral tablets: 12.5 mg; *Benadryl Children's Allergy®*
- Oral capsules: 25 mg, 50 mg; *Benadryl®*, *Benadryl Allergy®*, *Anti-Hist®*, *Diphen®*, *Diphenyl®*, *Genahist®*, *Geridryl®*, generic
- Oral liquid, solution, elixir or syrup: 12.5 mg/5 mL in 30, 118, 120, 236, 237, and 473 mL, and in 3.8 L, and 25 mg/5 mL in 118 mL btl; *Allermax®*, *Benadryl Children's Allergy®*, *Genhist®*, generic

**Note:** Many formulations are available combining diphenhydramine with decongestants, analgesics, and/or antitussives, and those are not recommended, because of potential unpredictable side effects.

### SIDE EFFECTS

**Dogs and cats**

- Common: CNS depression (lethargy, somnolence) and anticholinergic effects (dry mouth, urinary retention)
- Rare: diarrhea, vomiting, anorexia, paradoxical excitement (cats)

**Note:** Sedative effects of antihistamines may diminish with time. Liquid formulation has bitter taste.

### DRUG INTERACTIONS

**Anticholinergic drugs (e.g., tricyclic antidepressants):** diphenhydramine may potentiate anticholinergic effects

**Anticoagulants (e.g., heparin, warfarin):** counteraction of anticoagulation effects

**Epinephrine:** potential enhancement of epinephrine effects

**Monoamine oxidase (MAO) inhibitors (e.g., amitriptyline, amitraz):** may potentiate anticholinergic effects

**Other CNS depressant drugs:** increase sedation

### MONITORING

- Efficacy and adverse effects

## Doramectin

**Trade/brand name:** *Dectomax®* (US), *Doramec®* (US)
**Classification:** Antiparasitic (macrocyclic lactone)

### INDICATIONS

**Dogs:** Generalized demodicosis, sarcoptic mange.

**Cats:** Generalized follicular demodicosis (*Demodex cati*), notoedric mange.

**Note:** The authors do not use doramectin as first-line therapy for demodicosis, but as an alternative for dogs and cats that cannot tolerate ivermectin, except for ivermectin-sensitive canine breeds, where doramectin should be avoided.

Ideally, client informed consent should be obtained prior to initiation of treatment, as the treatment of these conditions with doramectin is extra-label.

## CONTRAINDICATIONS

The manufacturer recommends not using doramectin in animal species other than cattle and swine, because of potential severe adverse reactions. Use in dogs and cats is extra-label. Canine breeds susceptible to ABCB1-1 (MDR1) allele mutation such as collies, Border collies, Shetland sheepdogs, Australian shepherds, long-haired whippets, old English sheepdog, German shepherds (especially white German shepherds), silken windhound, McNab and herding-breed crosses should not receive doramectin, because of potential high risk of toxicity. Susceptible breeds should be tested for the mutant ABCB1-1 (MDR1) gene prior to considering treatment with systemic avermectin drugs. Do not use without up-to-date negative heartworm test, or in patients with heartworm disease.

## MECHANISM OF ACTION

Doramectin, similar to other macrocyclic lactones, is neurotoxic to parasites by increasing membrane permeability to chloride ions and potentiating the effects of the inhibitory neurotransmitter GABA, leading to paralysis and death of the parasite.

## DOSAGES

### Dogs

- Demodicosis
  - 600 mcg/kg (0.6 mg/kg) SC or PO once weekly
  - 300 mcg/kg (0.3 mg/kg) PO twice weekly may decrease side effects

  Duration of treatment: for 4 weeks past two consecutive negative skin scrapings 4–6 weeks apart
- Sarcoptic mange: 200–400 mcg/kg (0.2–0.3 mg/kg) SC once weekly for 3–4 treatments

### Cats

- Follicular demodicosis (*Demodex cati*): 400–600 mcg/kg (04–0.6 mg/kg) SC once weekly for 4 weeks past two consecutive negative skin scrapings 4–6 weeks apart
- Notoedric mange (*Notoedris cati*): 200–300 mcg/kg (0.2–0.3 mg/kg) SC single dose or once weekly for 2–3 treatments

## FORMULATIONS

**Veterinary-labeled products:** Approved only for cattle and swine.

- Doramectin injectable solution 1%: 10 mg/mL in 100, 250, and 500 mL multi-dose vials; *Dectomax*®, *Doramec*®

**Human-labeled products:** None

## SIDE EFFECTS

### Dogs and cats

- Uncommon: hypersalivation, mydriasis, blindness, lethargy, tremors, ataxia and pain or swelling at the injection site
- Rare: coma, death (particularly in sensitive breeds)

**Note:** Side effects in some dogs may not be seen for days to weeks after beginning of therapy. Cats appear less sensitive to avermectin's side effects than dogs.

### DRUG INTERACTIONS

**Drugs that may inhibit P-glycoprotein at the blood–brain barrier (e.g., bromocriptine, carvedilol, chlorpromazine, cyclosporine, erythromycin, fluoxetine, grapefruit juice, itraconazole, ketoconazole, methadone, paroxetine, pentazocine, quinidine, St. John's wort, tamoxifen, verapamil):** caution with concomitant use because of potential additive neurotoxicity

### MONITORING

- Efficacy and adverse effects
- Check heartworm status prior to administration

## Doxepin Hydrochloride

**Trade/brand name:** *Sinequan*® (US, CA, UK), *Sinepin*® (UK), generic (Rx)
**Classification:** Behavior modifying drug (tricyclic antidepressant), Antihistamine (first-generation)

### INDICATIONS

Management of behavior disorders, neuropathic pain, and psychogenic dermatoses. Similar to other antihistamines, its efficacy for management of atopic dermatitis is questionable (Olivry *et al.* 2010).

**Dogs:** Tail biting, flank sucking, anal licking, acral lick dermatitis, neuropathic pain and pruritus, atopic dermatitis.

**Cats:** Psychogenic alopecia and dermatitis, tail sucking, excessive grooming, hyperesthesia syndrome, neuropathic pain and pruritus, atopic dermatitis.

**Note:** The response to doxepin in dogs and cats, as with other antihistamines, is individualized and unpredictable. Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Hypersensitivity to tricyclic antidepressants. Should not be used with monoamine oxidase (MAO) inhibitors. Caution in patients with urinary retention or glaucoma, or in epileptic patients, as it may lower seizure threshold. Doxepin may interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Doxepin increases neurotransmitter levels of serotonin and norepinephrine by inhibiting their uptake at presynaptic nerve terminals. Doxepin has antihistamine properties by blocking $H_1$ and H2 receptors, and also has anticholinergic and alpha-1-adrenergic blocking activities.

### DOSAGES

Several weeks may be required before efficacy is noted.

**Dogs**
- Psychogenic dermatoses: 3–5 mg/kg PO q12h (maximum dose 50 mg per dog)
- Atopic dermatitis: 0.5–1 mg/kg PO q12h. Start with lower dose and gradually increase by 1 mg/kg every 2 weeks up to the maximum dose as needed

**Cats**
- Psychogenic dermatoses, atopic dermatitis: 0.5–1 mg/kg PO q12–24h. Start with lower dose and gradually increase up to the maximum dose as needed. Allow 3–4 weeks for initial trial

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral capsules: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg; *Sinequan®*, *Sinepin®*, generic
- Oral solution: 10 mg/mL in 118 mL; *Sinequan®*, generic

### SIDE EFFECTS

**Dogs and cats**
- Rare: ventricular arrhythmias (particularly with overdoses), hyperexcitability, gastrointestinal effects (diarrhea, vomiting), lethargy/sedation, increased appetite

### DRUG INTERACTIONS

**Anticholinergic agents:** potential for additive effects

**Antihistamines:** potential for increase in sedation

**Cimetidine:** potential for inhibition of doxepin metabolism and increase risk of toxicity

**CNS depressants:** potential for additive effects

**Meperidine, pentazocine, dextromethorphan, monoamine oxidase (MAO) inhibitors (e.g., selegiline and amitraz), or SSRIs (e.g., fluoxetine, paroxetine, sertraline):** increase risk of serotonin syndrome

**Sympathomimetic agents:** increase risk of cardiac effects

### MONITORING
- Efficacy and adverse effects

## Doxycycline

**Trade/brand name:** *Adoxa®* (US), *Doryx®* (US, CA), *Monodox®* (US); *Periostat®* (US, CA, UK), *Vibramycin®* (US, UK, CA); *Vibra-Tabs®* (US, CA); generic (Rx)
**Classification:** Antibacterial (tetracycline), Anti-inflammatory

## INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including superficial and deep pyodermas, wounds, and abscesses caused by susceptible Gram-positive bacteria such as some strains of *Staphylococcus* (including methicillin-resistant strains), *Streptococcus*, *Actinomyces*, *Bacillus anthracis*, *Clostridium perfringens*, *C. tetani*, *Listeria monocytogenes*, *Nocardia*, and Gram-negative bacteria including *Bordetella*, *Brucella*, *Bartonella*, *Haemophilus*, *Pasteurella multocida*, *Shigella*, *Ehrlichia*, and *Yersinia pestis*. It is also effective against most *Mycoplasma*, spirochetes, *Chlamydia*, *Rickettsia*, and *Mycobacterium*. Doxycycline, as sole therapy or in combination with niacinamide, can be also used for mild cases of immune-mediated dermatoses, such as discoid lupus erythematosus, pemphigus erythematosus, pemphigus foliaceus, vasculitis, sterile pyogranuloma, dermatomyositis, lupoid onychodystrophy, facial dermatitis of Persian and Himalayan cats, feline plasmacytic pododermatitis, and feline eosinophilic granuloma complex.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy if used for treatment of bacterial skin infections.

## CONTRAINDICATIONS

Do not use in animals hypersensitive to tetracyclines. Avoid use in pregnant animals, as tetracycline can retard fetal skeletal development and discolor deciduous teeth. Avoid in young animals, and avoid or reduce dose in animals with severe liver disease, esophagitis, or dysphagia. Unlike either oxytetracyclines or tetracyclines, doxycycline can be used in patients with renal impairment.

## MECHANISM OF ACTION

Like other tetracyclines, doxycycline is a bacteriostatic agent that inhibits protein synthesis by reversibly binding to 30S ribosomal subunits of susceptible organisms, thereby preventing binding to those ribosomes of aminoacyl-transfer RNA. Tetracyclines also are believed to reversibly bind to 50S ribosomes and, additionally, alter cytoplasmic membrane permeability in susceptible organisms. The immunomodulatory mechanism of action of doxycycline when combined with niacinamide for the management of immune-mediated disorders is not completely understood, but suppression of leukocyte chemotaxis secondary to complement activation by antibody–antigen complexes and protease release from leukocytes are possible mechanisms.

## DOSAGES

### Dogs and cats

- Sterile inflammatory dermatoses, immune-mediated dermatoses, bacterial skin infection: 5 mg/kg PO q12h or 10 mg PO q24h

**Note:** Duration of treatment for pyoderma: 1–2 weeks past resolution of clinical signs. For the treatment of immune-mediated skin diseases, doxycycline should be tried for at least 4–6 weeks prior to assessing its efficacy. When combined with niacinamide, the usual dose of niacinamide is 250 mg PO q8h for dogs ≤ 10 kg and 500 mg PO q8h for dogs >10 kg. Administer with food if gastrointestinal signs occur. Administer doxycycline to cats with water or moist food to avoid esophageal stricture.

## FORMULATIONS

**Veterinary-labeled products:** None in the US

**Human-labeled products**
- Oral tablets and capsules (as hyclate): 20 mg, 50 mg, 100 mg; *Vibramycin®*, *Periostat®*, *Vibra-Tabs®*, generic
- Oral tablets and capsules (as monohydrate): 50 mg, 75 mg, 100 mg; *Monodox®*, *Adoxa®*
- Coated pellets (as hyclate): 75 mg, 100 mg; *Doryx®*
- Powder for oral suspension (as the monohydrate): 5 mg/mL after reconstitution in 60 mL btl; *Vibramycin®*
- Oral syrup (as the calcium salt): 10 mg/mL in 473 mL; *Vibramycin®*

### SIDE EFFECTS

**Dogs and cats**
- Common: nausea, vomiting, diarrhea, anorexia (administration with food may reduce incidence of these signs)
- Rare: esophageal strictures in cats (give water or moist food to administer). Long-term use may result in overgrowth (superinfections) of non-susceptible bacteria or fungi. In humans, doxycycline (or other tetracyclines) has also been associated with photosensitivity reactions and, rarely, hepatotoxicity or blood dyscrasias

### DRUG INTERACTIONS

**Anticoagulant (e.g., warfarin):** tetracyclines may depress plasma prothrombin activity – may need dosage adjustment

**Digoxin:** possible increase in the bioavailability of digoxin and digoxin toxicity. These effects may persist for months after discontinuation of the tetracycline

**Divalent or trivalent cations (e.g., oral antacids, saline cathartics, aluminum, calcium, magnesium, zinc or bismuth cations):** decrease absorption of doxycycline. All oral tetracyclines must be given at least 1–2 hours before or after the cation-containing product

**Insulin:** may reduce insulin requirements in diabetic patients

**Methoxyflurane:** increases nephrotoxic effects of methoxyflurane

**Oral iron products, oral sodium bicarbonate, kaolin, pectin, or bismuth subsalicylate:** decrease tetracycline absorption. Administration of iron salts should be preferably 3 hours before or 2 hours after doxycycline

**Penicillins, cephalosporins, aminoglycosides:** possible interference with bactericidal activity of these drugs

**Theophylline:** gastrointestinal side effects may be increased if administered concurrently

### MONITORING
- Efficacy and adverse effects

## Enrofloxacin

**Trade/brand name:** *Baytril®* (US, CA, UK), generic (Rx)
**Classification:** Antibacterial (second-generation fluoroquinolone)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including superficial and deep pyodermas, wounds, and abscesses caused by susceptible Gram-negative bacilli and cocci, including most species and strains of *Pseudomonas aeruginosa*, *Proteus*, *Staphylococcus* (including penicillinase-producing and methicillin-resistant strains), *Klebsiella*, *Escherichia coli*, and *Enterobacter*. Also effective against *Campylobacter*, *Shigella*, *Salmonella*, *Aeromonas*, *Haemophilus*, *Yersinia*, *Serratia*, *Vibrio*, *Brucella*, *Chlamydia*, *Mycoplasma*, and atypical mycobacterial infection. Systemic enrofloxacin, concurrently with topical therapy, may also be of benefit for treatment of chronic infections of the ear canal, particularly otitis media, caused by susceptible organisms such as *Pseudomonas*; however, tissue concentration is not known for the external or middle ear and this indication is controversial with unpredictable efficacy.

**Note:** The authors do not recommend the use of fluoroquinolones as first-line therapy for pyoderma. Fluoroquinolones should be considered primarily for chronic deep pyodermas associated with extensive scar tissue, because of their excellent tissue penetration. Antibiotic selection, however, should be based on culture and susceptibility results.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to fluoroquinolones. Contraindicated in young growing animals because of possible cartilage abnormalities. Enrofloxacin is not recommended for cats less than 8 weeks of age; dogs less than 1 year of age and large-breed dogs less than 18 months of age. Caution in dehydrated patients and patients with seizure disorders, and in those with hepatic or renal impairment. Should not be used by humans (may cause hallucinations, vivid dreams, and headache). Do not use doses higher than 5 mg/kg/day in cats. Avoid use in breeding, pregnant, or lactating cats, as safety has not been determined.

### MECHANISM OF ACTION

Enrofloxacin is a bactericidal agent with broad-spectrum activity that inhibits bacterial DNA-gyrase (type II topoisomerase), thereby preventing DNA supercoiling and DNA synthesis. Fluoroquinolones have been reported to have anti-inflammatory properties including inhibition of TNF-alpha synthesis and suppression of induced leukotriene production by neutrophils, lymphocytes, monocytes, and basophils.

### DOSAGES

Administer on an empty stomach, unless vomiting occurs.

**Dogs**

- General dose: 5 mg/kg PO q24h
- Bacterial skin infections and chronic otitis externa/media associated with *Pseudomonas*: 10–20 mg/kg PO q12–24h for 1–2 weeks past resolution of clinical signs
- Atypical mycobacteriosis: 5–15 mg/kg PO q24h

**Cats**

- General dose: 5 mg/kg PO q24h for 1–2 weeks past resolution of clinical signs

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats

- Oral tablets: 22.7 mg, 68 mg; *Baytril®*
- Oral chewable tablets: 22.7 mg, 68 mg, 136 mg; *Baytril®*

**Human-labeled products:** None

## SIDE EFFECTS

**Dogs**
- Common: vomiting, diarrhea, anorexia, elevated liver enzymes
- Rare: cartilage abnormalities in young animals, ataxia, seizures, depression, lethargy, aggression, vocalization, anxiety

**Cats**
- Rare: vomiting, diarrhea, anorexia, elevated liver enzymes, ataxia, seizures, depression/lethargy, vocalization, aggression, ocular toxicity (mydriasis, retinal degeneration, and permanent blindness – mostly associated with doses higher than 15 mg/kg)

## DRUG INTERACTIONS

**Antacids containing cations (e.g., magnesium, aluminum, calcium):** may bind to enrofloxacin and prevent its absorption

**Antibiotics (e.g., aminoglycosides, third-generation cephalosporins agents, and extended-spectrum penicillins):** synergism may occur, but is not predictable, against some bacteria (particularly *Pseudomonas aeruginosa* or other Enterobacteriaceae)

**Bronchodilators (theophylline, aminophylline):** may increase blood levels of these drugs

**Cimetidine:** use carefully, because cimetidine has been shown to interfere with the metabolism of fluoroquinolones

**Cyclosporine:** nephrotoxicity may be exacerbated and cyclosporine metabolism may be reduced by fluoroquinolones

**Flunixin:** may increase AUC (area under the curve) and elimination half-life of enrofloxacin and vice-versa; the interaction of other NSAIDs and enrofloxacin is unknown

**Glyburide:** possible severe hypoglycemia

**Iron, zinc (oral):** decrease enrofloxacin absorption; doses should be separated by at least 2 hours

**Methotrexate:** potential for increase in methotrexate levels with resultant toxicity

**Nitrofurantoin:** may antagonize antimicrobial activity of the fluorquinolones; concomitant use is not recommended

**Phenytoin:** enrofloxacin may alter phenytoin levels

**Probenecid:** blocks tubular secretion of enrofloxacin and may increase its blood level and half-life

**Sucralfate:** may inhibit absorption of enrofloxacin, separate doses of these drugs by at least 2 hours

**Warfarin:** potential for increase in warfarin effects

### MONITORING

- Efficacy and adverse effects
- In cats, monitor for mydriasis and/or retinal changes

## Erythromycin

**Trade/brand name:** *E.E.S. Granules*® (US), *EryPed Drops*® (US), *E-Mycin*® (US, CA), *Ery-Tab*® (US), *Eryc*® (US, CA), *Erythroped*® (UK), many brands and generics available (Rx)
**Classification:** Antibacterial (macrolide)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections including superficial and deep pyodermas, wounds, and abscesses caused by susceptible Gram-positive cocci, including *Staphylococcus* and *Streptococcus*, Gram-positive bacilli including *Bacillus anthracis*, *Corynebacterium*, *Clostridium*, (not *C. difficile*), *Listeria*, and *Erysipelothrix*, some strains of Gram-negative bacilli, including *Haemophilus*, *Pasteurella*, and *Brucella*. Some strains of *Actinomyces*, *Mycoplasma*, *Chlamydia*, *Ureaplasma*, and *Rickettsia* are also inhibited by erythromycin. Usually, it has good efficacy against staphylococcal pyoderma, but resistance is common. It may be used as a second-line therapy for pyodermas.

**Note:** Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to erythromycin or its class. In humans, the estolate form has been rarely associated with the development of cholestatic hepatitis. This effect has not apparently been reported in animals, but the estolate form should probably be avoided in patients with pre-existing liver dysfunction.

### MECHANISM OF ACTION

Erythromycin is usually a bacteriostatic agent, but in high concentrations or against highly susceptible organisms it may be bactericidal. Macrolides are believed to act by binding to the 50S ribosomal subunit of susceptible bacteria, thereby inhibiting peptide bond formation.

### DOSAGES

Administer erythromycin on an empty stomach unless gastrointestinal signs occur.

**Dogs and cats**

- General dose: 10–20 mg/kg PO q8–12h
- Bacterial skin infections: 10–15 mg/kg PO q8h or 15–25 mg/kg PO q12h until 1–2 weeks after complete resolution of clinical signs

### FORMULATIONS

**Veterinary-labeled products:** None approved for dogs and cats

**Human-labeled products**

Several forms of erythromycin for oral administration are available. There is no scientific data to suggest that one form is better absorbed than the other.

- Enteric-coated oral tablets: 250 mg, 333 and 500 mg; *Ery-Tab®*, *E-Mycin®*, *E-Base®*
- Film-coated oral tablets: 250 mg, 500 mg; *Erythromycin Filmtabs®*, *PCE Dispertab®*, *Erythrocin Stearate®*
- Oral tablets with polymer-coated particles: 333 mg and 500 mg; *PCE Dispertab®*
- Delayed-release oral capsules: 250 mg; *Eryc®*, generic
- Estolate oral suspension: 125 mg/5 mL in 480 mL and 250 mg/5 mL in 480 mL, generic
- Stearate film-coated oral tablets: 250 mg, 500 mg; *Erythrocin Stearate®*, generic
- Ethylsuccinate oral tablets: 400 mg (as ethylsuccinate); *E.E.S. 400®*, generic
- Ethylsuccinate oral powder for suspension: 200 mg (as per 5 mL when reconstituted in 60, 100, and 200 mL); *E.E.S. Granules®*, EryPed® 200 and 400
- Ethylsuccinate oral suspension: 200 mg/5 mL in 100 and 480 mL; *EES 200®*, generic
- Ethylsuccinate oral suspension: 400 mg/5 mL in 100 and 480 mL; *EES 400®*, generic
- Ethylsuccinate oral suspension: 100 mg/2.5 mL in 50 mL; *EryPed Drops®*

## SIDE EFFECTS

**Dogs and cats**

- Common: vomiting
- Rare: nausea, anorexia, diarrhea, abdominal pain, liver dysfunction and/or abnormal liver function tests, increased risk of cholestasis and hepatotoxicity (mostly with estolate), allergic reactions (urticaria, mild skin eruptions, anaphylaxis)

## DRUG INTERACTIONS

Erythromycin, like other macrolides, is known to inhibit the cytochrome P450 enzymes and may decrease the metabolism of other coadministered drugs, such as: **alfentanil, bromocriptine, buspirone, carbamazepine, cyclosporine, disopyramide, methylprednisolone, midazolam, alprazolam, triazolam, quinidine, sildenafil, systemic tacrolimus, and theophylline.**

**Azole antifungals (ketoconazole, itraconazole, fluconazole):** potential for increase in erythromycin serum levels

**Bactericidal antimicrobials (e.g., penicillins):** potential for antagonism of penicillins

**Cisapride:** potential for increase in the metabolism of cisapride

**Digoxin:** potential for increase in digoxin serum levels with resultant digoxin toxicity; veterinary significance of this interaction is unknown

**Diltiazem, verapamil:** potential for increase in erythromycin serum levels

**Ergot alkaloids:** possible ergot toxicity

**Kaolin, pectin, bismuth:** decrease gastrointestinal absorption of erythromycin

**Lincosamides (e.g., clindamycin, lincomycin) and chloramphenicol:** avoid concurrent use with erythromycin, because of competitive protein binding and in-vitro evidence of antagonism

**Methylprednisolone:** potential for inhibition of methylprednisolone metabolism

**Omeprazole:** potential for increase in serum levels of one another

**Sulfonamides, rifampin:** potential synergism

**Terfenadine:** may predispose to severe and life-threatening cardiac arrhythmias in humans

**Theophylline:** decreases clearance of theophylline and potential toxicity

**Warfarin:** prolongs prothrombin times and bleeding

### MONITORING

- Efficacy and adverse effects
- Periodic liver function tests if patient receiving erythromycin estolate long-term

## Essential Fatty Acids

**Trade/brand name:** *Actis Omega Dog*® (US), *Actis Omega Cat*® (US), *Allerderm EFA-Caps*® (US), *Free Form Snip Tips*® (US); *Omegaderm*® (US); many brands available
**Classification:** Anti-inflammatory, Nutritional supplement

### INDICATIONS

**Dogs and cats:** Pruritic and/or inflammatory conditions such as atopic dermatitis, sebaceous adenitis, and symmetrical onychodystrophy, and keratinization disorders such as seborrhea and ichthyosis. They are unlikely to provide significant benefit if administered as sole therapy. Essential fatty acids may work as glucocorticoid-sparing agents and can also be used to improve coat quality and ameliorate dry skin.

### CONTRAINDICATIONS

Caution in patients with coagulation disorders or receiving anticoagulant medications, as fatty acids may affect bleeding time. Caution in patients with non-insulin-dependent diabetes, as omega-3 fatty acids have impaired insulin secretion with resultant increased glucose levels in humans with type 2 diabetes. Caution in patients with history of pancreatitis or protracted diarrhea. Safety in pregnant animals has not been established.

### MECHANISM OF ACTION

The exact mechanism of action of essential fatty acids is not well known. However, by competing with arachidonic acid for the enzymes lipoxygenase and cyclooxygenase, they decrease the synthesis of inflammatory leukotrienes and prostaglandins in the body, thereby potentially reducing inflammation and pruritus.

### DOSAGES

**Dogs and cats:** There is no current evidence of superiority of any essential fatty acid formulation, combination, dosage, or ratio to improve skin barrier and coat quality or to reach anti-inflammatory effects in dogs with atopic dermatitis or other inflammatory skin disorders. Specific dosage recommendations will vary

according to each commercially available product (see the label directions for specific dose recommendations).

- The recommended dose, by most dermatologists, as adjunctive therapy for inflammatory disorders such as atopic dermatitis, is usually based on eicosapentanoic acid (EPA) and docosapentanoic acid (DHA), both omega-3: EPA = 180 mg/4.5 kg (10 lb)/day and DHA = 120 mg/4.5 kg (10 lb)/day. The dose is then calculated based on the amount of EPA and DHA in a given commercial product. The duration of treatment may vary with each treated condition, however; it may take up to 8–12 weeks for clinical improvement to be seen
- Omega-6 or combination (omega-3/omega-6) products are typically recommended for keratinization disorders or when skin barrier restoration is desirable, and the dose will vary according to the manufacturer, but the authors typically at least double the labeled dose

## FORMULATIONS

**Note:** Different omega-3 and omega-6 sources are available. This list is not complete.

### Veterinary-labeled products

- *Allerderm EFA-Caps®* (for dogs and cats). *Each Flavor-Gel®* capsule contains omega-3 (EPA: 80 mg, DHA: 50 mg) and omega-6 (LA: 30 mg, GLA: 18 mg) fatty acids and vitamins. Available in btl of 60 caps
- Allerderm *EFA-Caps®* HP (for dogs). *Each Flavor-Gel®* capsule contains omega-3 (EPA: 120 mg, DHA: 80 mg) and omega-6 (LA: 50 mg, GLA: 38 mg) fatty acids, and vitamins A (800 IU), D (25 IU) and E (11 IU). Available in btl of 60 and 250 caps
- Allerderm *EFA Z® Plus* (for dogs and cats). Each pump (1 mL) contains omega-3 (EP: 120 mg, DHA: 80 mg) and omega-6 (LA: 50 mg, DHA: 38 mg) fatty acids, vitamins A (136 IU), E (1.9 IU), along with zinc and some other vitamins. Available in a pump or pour dispensing 8 oz btl (vanilla flavor)
- *Free Form Snip Tips®* (for small dogs and cats). Each capsule contains omega-3 fatty acids (EPA: 262 mg, DHA: 172 mg), and vitamin E (1 IU). Available in btl of 60 and 250 caps (porcine source). Free Form Snip Tips (for medium to large dogs). Each capsule contains omega-3 fatty acids (EPA: 515 mg, DHA: 338 mg), and vitamin E (2 IU). Available in btl of 60 caps (porcine source)
- *Omegaderm®* EZ-Dose Packets (for dogs and cats). Each 4 mL sachet contains 5 : 1 ratio of omega-6 (LA: 364 mg/mL, GLA: 7.6 mg/mL) to omega-3 (EPA: 44.8 mg/mL, DHA: 30 mg/mL) fatty acids, vitamins A (114.8 mg/mL), E (3.8 mg/mL), in addition to B6, biotin and zinc. Available in 28 packages of 4 mL (small dogs and cats) and 8 mL (medium and large dogs)
- *Actis Omega Dog®*. Each pump (1 mL) contains omega-3 (EPA: 135 mg, DHA: 90 mg, ALA: 0.2 mg) and omega-6 (LA: 22 mg, GLA: 52 mg) fatty acids, vitamins A (165 IU) and E (33.9 IU) and natural antioxidants (3.6 mg). Available in 4.5 oz btl
- *Actis Omega Cat®*. Each pump (1 mL) contains omega-3 (EPA: 30.9 mg, DHA: 20.6 mg, ALA: 2.55) and omega-6 (LA: 307 mg, GLA: 92.6 mg) fatty acids, vitamins A (123 IU) and E (26.5 IU) and natural antioxidants (3.6 mg). Available in 1.5 oz btl
- *Aller-G3® Capsules* (for small dogs). Each capsule contains omega-3 fatty acids (EPA: 110 mg, DHA: 73 mg), and vitamins A (220 IU), D3 (50 IU) and E (2 IU)

- *Aller-G3® Capsules* (for medium dogs). Each capsule contains omega-3 fatty acids (EPA: 180 mg, DHA: 120 mg), and vitamins A (400 IU), D3 (100 IU) and E (4 IU). Available in btl of 60 and 250 caps
- *Aller-G3® Capsules* (for large and giant dogs). Each capsule contains omega-3 fatty acids (EPA: 360 mg, DHA: 240 mg), and vitamins A (400 IU), D3 (100 IU) and E (4 IU). Available in btl of 60 and 250 caps
- *Aller-G3® Liquid* (for dogs and cats). Each 1 mL contains omega-3 fatty acids (EPA: 180 mg, DHA: 120 mg), and vitamins A (300 IU), D3 (50 IU) and E (4 IU). Available in 8 oz btl
- *Welactin® Canine Liquid*. Each 1 teaspoon (5 mL) contains omega-3 fatty acids (EPA: 775 mg, DHA: 525 mg). Available in 8 and 16 oz btl
- *Welactin® Canine Soft Gel Caps*. Each capsule contains omega-3 fatty acids (EPA: 165 mg, DHA: 105 mg). Available in btl of 120 caps
- *Welactin® Feline Soft Gel Twist Caps*. Each capsule contains omega-3 fatty acids (EPA: 150 mg, DHA: 100 mg). Available in btl of 60 caps
- *EicosaCaps®* (for dogs and cats ≤40 lb). Each capsule contains omega-3 fatty acids (EPA: 15.79 mg, DHA: 10.52 mg) and omega 6 (borage oil), vitamins C (50 mg) and E (10 IU), zinc (2000 mcg) and garlic. Available btl of 60 caps
- *EicosaCaps® L* (for dogs and cats of 41–70 lb). Each capsule contains omega-3 fatty acids (EPA: 47.34 mg, DHA: 31.56 mg) and omega 6 (borage oil), vitamins C (100 mg) and E (10 IU), zinc (4000 mcg) and garlic. Available in btl of 60 caps
- *EicosaDerm® Liquid* (for dogs and cats). Each pump (2 mL) contains omega-3 fatty acids (EPA: 360 mg, DHA: 240 mg) and vitamin E (10 IU). Available in btl of 8 and 32 oz

**Human-labeled products:** Many products are available

### SIDE EFFECTS

**Dogs and cats**
- Uncommon: gastrointestinal side effects (vomiting, diarrhea, flatulence) may occur with high dosages
- Rare: lethargy, increase in pruritus and bleeding time and decrease in platelet aggregation (avoid use in patients with coagulopathies)

### DRUG INTERACTIONS

**Anticoagulants (e.g., aspirin, heparin, warfarin):** potential effect on bleeding time

### MONITORING
- Efficacy and adverse effects

## Ethambutol

**Trade/brand name:** *Etibi®* (CA), *Myambutol®* (US, CA) (Rx)
**Classification:** Antibacterial (antimycobacterial)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections such as leprosy, opportunistic mycobacteriosis, or localized atypical mycobacterial infections caused by

*Mycobacterium* spp. including *M. tuberculosis*, *M. avium complex* (MAC), *M. bovis*, and *M. genavense*.

**Note:** Usually used in combination with other antimycobacterial drugs such as rifampin, enrofloxacin, and azithromycin to avoid resistance. Ideally, bacterial culture and sensitivity should be performed prior to beginning therapy.

### CONTRAINDICATIONS

Hypersensitivity to ethambutol. Caution in patients with marked renal impairment (dosage may need to be reduced). In humans, ethambutol is contraindicated in patients with ocular disorders including optic neuritis. Teratogenesis has been reported in laboratory animals during pregnancy.

### MECHANISM OF ACTION

Ethambutol is a bacteriostatic agent with antimycobacterial properties. Its exact mechanism of action is unknown, but it diffuses into the mycobacterial cells and interferes with RNA synthesis, inhibiting intracellular metabolism and multiplication, leading to cell death. Resistance can occur.

### DOSAGE

Ethambutol is often used as adjunctive therapy in combination with other recommended antimycobacterial drugs.

**Dogs**

- General dose: 10–15 mg/kg PO q24h or 25 mg/kg q72h for 3–6 months. May be combined with one (or both) of the following antibiotics: enrofloxacin (5–15 mg/kg PO q24h), rifampin (10–20 mg/kg PO q12–24h)

**Cats**

- General dose: 10–20 mg/kg PO q24h for 3–6 months. May be combined with clarithromycin (62.5 mg per cat PO q12h), azithromycin (5–10 mg/kg PO q12–24h) or rifampin (10–15 mg/kg PO q24h)

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 100 mg, 400 mg; *Etibi®*, *Miambutol®*

### SIDE EFFECTS

**Dogs and cats:** Side effects are not well documented in dogs and cats. Non-dose-related degenerative changes in the CNS, dose-related myocardial toxicity, and depigmentation of the tapetum lucidum of the eyes have been reported in dogs receiving long-term treatment. However, doses as high as 400 mg/kg/day for 4 weeks in dogs were associated with no significant changes in electroretinogram or visual evoked potential. In humans, ocular abnormalities such as reversible optic neuritis causing decreased visual acuity, abdominal pain, anorexia, vomiting, CNS signs, and thrombocytopenia have been reported. In addition, ethambutol-induced peripheral neuropathy has been reported in rabbits.

### DRUG INTERACTIONS

**Aluminum-containing antacids:** potential for reduction in absorption of ethambutol, with reduced efficacy

### MONITORING

- Efficacy and adverse effects
- Ocular and renal functions with long-term therapy: baseline and monthly monitoring

## Famciclovir

**Trade/brand name:** *Famvir®* (US, CA, UK), generic (Rx)
**Classification:** Antiviral

### INDICATIONS

There is limited experience in veterinary medicine. Its true efficacy is unknown.

**Cats:** Feline herpes virus 1 (FHV-1) ulcerative facial and nasal dermatitis and stomatitis (herpetic dermatitis); FHV-1 rhinotracheitis (oral and cutaneous ulcers); FHV-1 keratoconjunctivitis; herpes-virus-induced exfoliative erythema multiforme.

### CONTRAINDICATIONS

Patients with known hypersensitivity to antivirals. Caution in patients with renal dysfunction.

### MECHANISM OF ACTION

Famciclovir is converted to penciclovir, which inhibits herpes viral DNA polymerase via competition with deoxyguanosine triphosphate; thereby, it selectively inhibits herpes virus DNA synthesis.

### DOSAGES

**Cats:** Appropriate systemic doses have not been determined and are mostly anecdotal. Famciclovir is often used in combination with interferon or lysine and it has not been evaluated for long-term therapy (>30 days). Higher doses seem to produce a faster response, with some cats only responding to high doses; however, treatment can be very expensive.

- FHV-1 rhinotracheitis (traditional dose): 31.25 mg per cat (one-quarter of a 125 mg tablet) PO q12h for 2 weeks
- FHV-1 infections, herpetic dermatitis
  - Dose based on pharmacokinetics in cats: 90 mg/kg PO q8h (this dose may be cost-prohibitive)
  - Most recently proposed starting dose (less expensive): for adult cats (weighing 3.5–5 kg): 125 mg per cat PO q12h; for kittens: 25–40 mg/kg q8–12h. If needed, dose can be increased for better response

**Note:** The duration of therapy has not been determined, but generally should be for 2 weeks for acute disease, and until resolution of clinical signs in chronic cases.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Film-coated oral tablets: 125 mg, 250 mg, 500 mg; *Famvir®*, generic

### SIDE EFFECTS

**Cats:** Adverse effects are not well documented in cats, but it appears to be well tolerated. The only side effect reported in a very small number of cats receiving high doses of famciclovir is transient (reversible) loss of renal concentrating ability.

**Note:** In humans famciclovir is generally safe, but it can cause nausea, vomiting, diarrhea, headache, pruritus, cutaneous rash, urticaria, neutropenia, and renal failure.

### DRUG INTERACTIONS

**Cimetidine, probenecid, theophylline:** potential for increase in famciclovir serum levels

**Digoxin:** slight increase in digoxin serum levels

### MONITORING

- Efficacy and adverse effects
- Renal function tests (specific gravity, BUN, serum creatinine) and CBC with chronic use

## Fexofenadine Hydrochloride

**Trade/brand name:** *Allegra*® (US, CA), generic (Rx)
**Classification:** Antihistamine (second-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic skin conditions including urticaria and insect-bite hypersensitivity. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of first- and second-generation antihistamines for treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010).

**Note:** For management of allergic skin diseases, the response to fexofenadine in dogs and cats, as with other antihistamines, is individualized and unpredictable.

Fexofenadine does not appear to be more effective than first-generation antihistamines. Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Do not use in animals hypersensitive to fexofenadine. Dosage adjustment is recommended in humans with severe renal or hepatic impairment. Avoid use in pregnant and lactating animals. Fexofenadine may interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Fexofenadine is the active metabolite of terfenadine, with selective histamine $H_1$-receptor antagonism and anti-allergic properties inhibiting histamine-induced wheal and flare responses. It possesses minimal anticholinergic or antiserotonergic effects.

### DOSAGES

There is limited clinical experience in dogs and cats.

**Dogs:** 2–5 mg/kg PO q12–24h. A much higher dose (18 mg/kg PO q12–24h) has been reported to be efficacious and safe

**Cats:** 10–15 mg per cat PO q12–24h

**Note:** Fexofenadine is labeled as once-daily dosage for humans and may have the advantage of once-daily administration in dogs and cats as well. Higher doses appear to be more effective.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 30 mg, 60 mg, 180 mg; *Allegra*®, generic

**Note:** Allegra-D contains pseudoephedrine; its use should be therefore avoided in dogs and cats.

### SIDE EFFECTS

Fexofenadine has a low incidence of sedation compared to conventional antihistamines commonly used in dogs and cats. Nevertheless, there is limited clinical experience with this drug in dogs and cats, and side effects are not well reported.

**Dogs:** no evidence of toxicosis has been reported in dogs receiving oral fexofenadine doses up to 2 g/kg. Sedation at high doses may occur

**Cats:** no adverse effects were reported with doses of 10.2 to 20 mg/kg of fexofenadine

**Note:** Headache, throat irritation, viral infection, nausea, dysmenorrhoea, drowsiness, dyspepsia and fatigue have been reported in humans.

### DRUG INTERACTIONS

**Antacids:** decrease serum levels of fexofenadine
**Erythromycin, ketoconazole:** increase serum levels of fexofenadine

### MONITORING

- Efficacy and adverse effects

## Fluconazole

**Trade/brand name:** *Diflucan*® (US, CA, UK), generic (Rx)
**Classification:** Antifungal (triazole)

### INDICATIONS

**Dogs and cats:** A variety of systemic mycoses including blastomycosis, histoplasmosis, sporotrichosis, cryptococcosis, and coccidioidomycosis. It may also be useful for the treatment of candidiasis, dermatophytosis (not as efficacious as other azoles),

onychomycosis, *Malassezia* dermatitis, and otitis media associated with fungal infection (use of systemic antifungal for otitis media is controversial). Fluconazole is more useful in treating CNS or ocular infections than other azoles. Fluconazole does not have appreciable effects (unlike ketoconazole) on hormone synthesis.

### CONTRAINDICATIONS

Hypersensitivity to fluconazole or other azoles. Caution in animals with impaired renal or hepatic function. Use with caution in pregnant animals.

### MECHANISM OF ACTION

Fluconazole is a fungistatic triazole agent that inhibits ergosterol synthesis in the fungal cell membrane and alters the permeability, allowing leakage of intracellular components. It inhibits fungal cytochrome P450 sterol C14 alpha-demethylation.

### DOSAGES

Fluconazole may be given with or without food.

**Dogs**

- Systemic mycosis: 5–10 mg/kg PO q12–24h. Duration of treatment may vary according to the fungal organism involved. Generally, treatment should continue until at least 1–2 months after complete resolution of clinical signs
- Candidiasis: 2.5–5 mg/kg PO q12–24h for 56–84 days
- Dermatophytosis, onychomycosis: 5–10 mg/kg PO q24h until two consecutive negative cultures
- *Malassezia* dermatitis: 5–10 mg/kg PO q24h until at least 1 week after complete resolution of clinical signs
- Otitis media: 5–10 mg/kg PO q24h until complete resolution of clinical signs or after negative culture

**Cats**

- Systemic mycosis: 50 mg per cat PO q12–24h. In most cases it is administered once daily. Duration of treatment may vary according to the fungal organism involved. Generally, treatment should continue until at least 1–2 months after complete resolution of clinical signs. Controlled clinical studies using fluconazole for systemic diseases in cats are lacking, and thus its efficacy has yet to be determined for these diseases
- Candidiasis: 2.5–5 mg/kg or 50 mg per cat PO q24h for 30 days. Dose is extrapolated from dogs
- Dermatophytosis, onychomycosis: 5 mg/kg PO q24h until 2 consecutive negative cultures
- *Malassezia* dermatitis: 5 mg/kg PO q24h until at least 1 week after complete resolution of clinical signs
- Otitis media: 5–10 mg/kg PO q24h until complete resolution of clinical signs or after negative culture

**Note:** Pulse-therapy administration protocols such as every other day, 2–3 days per week, 1 week on/1 week off, first 7–10 days of every month, or once weekly may be used for treatment of dermatophytosis, onychomycosis, and *Malassezia* dermatitis, as fluconazole has extended residual levels in the body including the skin and nails (demonstrated in human medicine). These protocols were not evaluated through clinical trials in dogs and cats.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 50 mg, 100 mg, 150 mg and 200 mg; *Diflucan®*, generic
- Powder for oral suspension: 10 mg/mL, 40 mg/mL (when reconstituted) in 35 mL; *Diflucan®*

### SIDE EFFECTS

**Dogs and cats:** There is limited clinical experience in dogs and cats. However, it appears to be safe. In subacute toxicity studies in dogs, a dose of 30 mg/kg caused slight increases in plasma transaminase activity. Fluconazole appears to present few side effects, including hepatotoxicity, compared to ketoconazole and itraconazole. However; inappetence, increase in liver enzymes and hepatotoxicity may occur. In humans, side effects have been reported to be limited to occasional headaches and gastrointestinal effects such as anorexia, nausea, vomiting, and diarrhea. Additionally, increase in liver enzymes and hepatotoxicity, exfoliative skin disorders, Stevens–Johnson syndrome, toxic epidermal necrolysis, alopecia, angioedema, seizures, hypokalemia, hypercholesterolemia, neutropenia, and thrombocytopenia have also been rarely reported in humans.

### DRUG INTERACTIONS

**Aminophylline, buspirone, cisapride, cyclophosphamide, cyclosporine, fentanyl, glipizide, glyburide, midazolam, NSAIDs, rifabutin, theophylline:** increase in serum levels of these drugs

**Amphotericin B:** potential antagonism against *Candida* or *Aspergillus*. The clinical implication of this interaction is unknown

**Diuretics, thiazides:** increase in fluconazole serum levels

**Other azoles (e.g., ketoconazole, itraconazole):** may inhibit the metabolism of these drugs with potential toxicity

**Rifampin:** may reduce fluconazole serum levels

**Terfenadine:** may lead to toxicity of this drug

**Tricyclic antidepressants (e.g., clomipramine, amitriptyline):** may exacerbate the effects of these drugs

**Vincristine, vinblastine:** may inhibit the metabolism of these drugs

**Warfarin, other coumarin anticoagulants:** may increase serum levels of these drugs and increase prothrombin time

### MONITORING
- Efficacy and adverse effects
- Occasional liver function tests with long-term use

## Flucytosine

**Trade/brand name:** *Ancobon®* (US), *Ancotil®* (CA, UK) (Rx)
**Classification:** Antifungal (pyrimidine)

### INDICATIONS

**Dogs and cats:** May be used for cutaneous and systemic cryptococcosis, candidiasis, and some cases of phaeohyphomycosis. Because it penetrates relatively well into the CNS, it has been used most commonly for the treatment of CNS cryptococcosis, particularly in combination with amphotericin B or ketoconazole, mostly due to occurrence of rapid resistance.

### CONTRAINDICATIONS

Hypersensitivity to flucytosine. Extreme caution in animals with impaired renal or hepatic function (may need to monitor flucytosine serum levels), pre-existing bone marrow suppression, hematologic diseases, and in those receiving other bone marrow suppressant drugs. Avoid use in pregnant animals, as flucytosine is teratogenic.

### MECHANISM OF ACTION

Flucytosine is a fungistatic or fungicidal agent (depending on fungal species and strains) that penetrates the fungal cell wall and is converted into fluorouracil, which acts as an antimetabolite by competing with uracil, thereby interfering with pyrimidine metabolism and eventually RNA and protein synthesis.

### DOSAGES

Flucytosine is usually combined with amphotericin B or an azole, as flucytosine monotherapy may not be effective and resistance commonly develops.

**Dogs and cats (oral dose):** 25–50 mg/kg PO q6h or 50–75 mg/kg PO q8h for at least 6 weeks or until no clinical evidence of the disease. Treatment may require up to 12 months

**Dogs (injectable dose):** 25–35 mg/kg IV q8h

**Cats (injectable dose):** 25–50 mg/kg IV q6h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 250 mg and 500 mg; *Ancobon®*
- Injectable solution: 10 mg/mL; *Ancotil®* (available in CA and UK)

### SIDE EFFECTS

**Dogs and cats**

- Common: gastrointestinal side effects (nausea, anorexia, vomiting, diarrhea)
- Uncommon: dose-dependent bone marrow suppression (anemia, leukopenia, thrombocytopenia) that may occur within days of onset of treatment, fixed cutaneous eruptions on the scrotum and nasal planum in dogs, oral ulceration and increase in hepatic enzymes or hepatotoxicity
- Rare: severe drug reactions may develop in dogs within 10–14 days of treatment; aberrant behavior with seizures and toxic epidermal necrolysis have been reported in cats

### DRUG INTERACTIONS

**Aminoglycosides, amphotericin B:** potential nephrotoxicity

**Amphotericin B:** in-vitro synergism against *Cryptococcus* and *Candida*

**Bone marrow suppressants, carboplatin, cisplatin, cytotoxic drugs, interferon alpha and beta:** increase in bone marrow suppression

**Ketoconazole:** potential toxicity, particularly in cats

### MONITORING

- Efficacy and adverse effects
- Renal function: at least twice weekly (if also using amphotericin B)
- CBC (platelet count) and hepatic enzymes: at least monthly

## Fluoxetine Hydrochloride

**Trade/brand name:** *Prozac*® (US, CA, UK), *Reconcile*® (US, UK), generic (Rx)
**Classification:** Behavior modifying drug (selective serotonin reuptake inhibitor)

### INDICATIONS

Management of behavior disorders such as psychogenic dermatoses.

**Dogs:** Tail biting, flank sucking, anal licking, acral lick dermatitis.

**Cats:** Psychogenic alopecia and dermatitis, tail sucking, excessive grooming, hyperesthesia syndrome

**Note:** Fluoxetine is most effective when combined with a behavior modification program.

### CONTRAINDICATIONS

Hypersensitivity to fluoxetine, other SSRIs, or monoamine oxidase (MAO) inhibitors. Should not be used in dogs with epilepsy or history of seizures or in combination with drugs that lower the seizure threshold (e.g., acepromazine, chlorpromazine). Fluoxetine dose adjustment may be needed in patients with severe hepatic impairment. Caution in animals with diabetes mellitus, as it may alter blood glucose. Caution in animals predisposed to aggression. Avoid use in breeding, pregnant, and lactating animals, as safety has not been determined.

### MECHANISM OF ACTION

Fluoxetine and its primary metabolite, norfluoxetine, selectively inhibit serotonin reuptake in the brain and downregulate 5-$HT_1$ receptors, resulting in potentiation of serotonin pharmacologic activity (antidepressive activity and rising in motor activity thresholds). Fluoxetine also has minor dopamine and norepinephrine reuptake inhibition properties.

### DOSAGES

**Dogs:** 1–2 mg/kg PO q24h

**Cats:** 0.5–2 mg/kg PO q24h

**Note:** The dose may be gradually increased to the highest recommended dose. Lag phase of 4–6 weeks.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs
- Chewable oral tablets: 8 mg, 16 mg, 32 mg, 64 mg; *Reconcile*®

**Human-labeled products**
- Oral tablets: 10 mg, 20 mg; *Prozac*®, generic
- Delayed-release oral capsules: 10 mg, 20 mg, 40 mg, 90 mg; *Prozac*® *Pulvules* and *Prozac*® Weekly, generic
- Oral solution: 4 mg/mL in 120 mL and 473 mL btl; *Prozac*®, generic

## SIDE EFFECTS

Fluoxetine is relatively safe for dogs and cats, with few side effects, mostly behavioral and gastrointestinal.

**Dogs**
- Common: lethargy, anorexia (may be transient), vomiting, diarrhea, tremors, anxiety, irritability, aggressive behavior, insomnia/hyperactivity, panting, vocalization, mydriasis, nystagmus, ataxia (these signs are most commonly seen with high doses)
- Rare: seizures

**Cats**
- Common: anorexia, vomiting, diarrhea, tremors, anxiety, vocalization, irritability, sleep disturbances, mydriasis, changes in elimination patterns

## DRUG INTERACTIONS

Because fluoxetine is highly metabolized by the liver, it may be subject to the effects of cytochrome P450 inhibitors.

**Anticoagulants (e.g., aspirin, warfarin):** increase in bleeding risk

**Anticonvulsants (e.g., phenothiazines):** fluoxetine may antagonize the effects of these drugs

**Buspirone, isoniazide pentazocine:** increase risk for serotonin syndrome

**Cyproheptadine:** may decrease or reverse the effects of SSRIs

**Diazepam, alprazolam, phenytoin:** potential increase in serum levels of these drugs

**Diuretics:** increase hyponatremia risk

**Insulin:** may alter insulin requirements

**Monoamine oxidase (MAO) inhibitors (e.g., amitraz, selegiline):** high risk for serotonin syndrome; use is contraindicated. May need a 5-week washout period after discontinuing fluoxetine and, a 2-week washout period if first discontinuing the MAO inhibitor

**Propranolol, metoprolol, trazodone:** may increase serum levels of these drugs

**Tricyclic antidepressants (e.g., clomipramine, amitriptyline):** may increase serum levels of these drugs with potential for increase in risk for serotonin syndrome – concurrent use is contraindicated

## MONITORING

- Efficacy and adverse effects

# Gabapentin

**Trade/brand name:** *Gabarone®* (US), *Neurontin®* (US, CA, UK), generic (Rx)
**Classification:** Neuropathic (analgesic)

## INDICATIONS

**Dogs and cats:** Management of neuropathic pain or pruritus and paresthesia. May be used in cases of idiopathic chronic pruritus unresponsive to conventional therapy, chronic otitis commonly associated with neuropathic or inflammatory pain, burn and nerve injury, canine acral lick dermatitis, feline idiopathic ulcerative dermatosis, and feline hyperesthesia syndrome. There is limited information regarding the use of this drug for dermatological conditions in dogs and cats. In humans, it has also been used for the treatment of brachioradial pruritus, cutaneous dysesthesia, neurotic excoriation, and delusional parasitosis.

## CONTRAINDICATIONS

Hypersensitivity to gabapentin. Caution in patients with renal impairment and behavior abnormalities. Avoid use of available human oral solution (Neurontin) in dogs as it contains xylitol, which has been reported to cause hypoglycemia and hepatotoxicity at doses greater than 0.1 g/kg. However, the use of 15 mg/kg of the solution appears safe. Nonetheless, there is limited information on its safety. In cats, xylitol toxicity does not appear to be a concern, but the solution should also be used with caution in cats. Avoid use in pregnant animals. Avoid abrupt withdrawal of drug.

## MECHANISM OF ACTION

Gabapentin is an analog of the neurotransmitter GABA, but it does not interact with its receptors, inhibit GABA uptake or degradation, or convert into GABA. Gabapentin has analgesic and anticonvulsant properties; however, its exact mechanism of action is unknown. It has been suggested that it increases the synaptic levels of GABA in the CNS, most likely by increasing the synthesis of GABA. In addition, it has been demonstrated to bind to voltage-sensitive calcium channels in neuronal tissue and inhibit depolarization. It has been shown to relieve hyperalgesia in skin that has been hypersensitized to pain.

## DOSAGES

**Dogs and cats:** 1–10 mg/kg PO q24h. Start at the lower end of the dose range and gradually increase dose to effect

**Note:** Therapeutic serum level is reported to range from 4 to 16 mg/mL; however, serum levels are not necessarily monitored.

### Dogs

- Idiopathic pruritus unresponsive to conventional therapy: 11–15 mg/kg PO q8–12h. Clinical improvement should occur within 1–2 weeks of treatment. If partial or no improvement, gabapentin dose can be increased up to 50% of initial daily dose for another 1–2 weeks

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral film-coated tablets and capsules: 100 mg, 200 mg, 300 mg, 400 mg, 600 mg, 800 mg; *Gabarone®*, *Neurontin®*, generic
- Oral solution: 250 mg/5 mL (50 mg/mL) in 470 and 473 mL; *Neurontin®* (contain xylitol – use with caution in dogs)

### SIDE EFFECTS

**Dogs and cats:** Gabapentin seems to be a safe drug with few reported side effects.
- Common: drowsiness and fatigue
- Rare: ataxia

**Note:** In humans, the most common side effects associated with gabapentin are dizziness, somnolence, gastrointestinal side effects, ataxia, visual disturbances, and peripheral edema. Cutaneous leukocytoclastic vasculitis, skin vesicular eruptions, and hypersensitivity syndrome have also been reported in humans.

### DRUG INTERACTIONS

**Antacids:** may decrease gabapentin bioavailability; antacids should be administered at least 2 hours away from gabapentin

**Hydrocodone:** may increase the AUC (area under the curve) of gabapentin and increase its efficacy and/or adverse effects. Gabapentin may reduce hydrocodone AUC and potentially reduce its efficacy

**Morphine:** may increase gabapentin serum levels

### MONITORING
- Efficacy and adverse effects

## Griseofulvin

**Trade/brand name:** *Fulvicin P/G®* (US, CA), Microsize: *Fulvicin U/F®* (US, CA), *Grifulvin V®* (US); Ultramicrosize: *Gris-PEG®* (US), *Grisovin®* (UK) (Rx)
**Classification:** Antifungal

### INDICATIONS

**Dogs and cats:** Dermatophytic fungal infections of the skin, hair, and claws caused by *Microsporum* and *Trychophyton*. Accurate diagnosis of the infecting organism is essential prior to treatment. It is not clinically useful against other pathogenic fungi or bacteria. Due to its immunomodulatory properties, it may also be effective for the treatment of some non-infectious, inflammatory dermatoses such as canine juvenile cellulitis. The use of griseofulvin for the treatment of inflammatory dermatoses is anecdotal, and the potential severe side effects may outweigh its benefits. Since the advent of azoles, the authors have not used

griseofulvin in dogs and cats because of potential concerning side effects, particularly in cats.

### CONTRAINDICATIONS

Hypersensitivity to griseofulvin. Caution in animals with impaired hepatic function. Do not use in pregnant animals, because of its teratogenic effects, and in breeding or lactating animals. Caution with administration in cats. Due to potential exacerbation of bone marrow effects, griseofulvin should not be used in cats with viral infections such as FIV and FeLV.

### MECHANISM OF ACTION

Griseofulvin, a fungistatic agent, inhibits mitosis by interacting with microtubules and disrupting the mitotic spindle. It also has anti-inflammatory and immunomodulatory properties and it is known to suppress delayed-type hypersensitivity reactions.

### DOSAGES

A wide range of doses has been reported. Dosing is different for microsize and ultramicrosize forms. Doses listed here represent the commonly used ones. Oral absorption is improved if given with a fatty meal.

**Dogs**

- Dermatophytosis, onychomycosis
  - Microsize: 25 mg/kg PO q12h or 50 mg/kg PO q24h. Dose may be increased in refractory cases (50–60 mg/kg PO q12h)
  - Ultramicrosize: 5–10 mg/kg PO q24h or divided to give twice daily. Duration of treatment: treat until 2 consecutive negative cultures are obtained at 1–3 week intervals
- Juvenile sterile granulomatous dermatitis and lymphadenitis (juvenile cellulitis): in one study, six dogs with juvenile cellulitis were treated with microsize griseofulvin at 14.2–34 mg/kg PO q12h and in all cases the clinical signs resolved within 3 weeks (Shibata and Nagata 2004)

**Cats**

- Dermatophytosis, onychomycosis
  - Microsize: 25 mg/kg PO q12h. Dose may be increased in refractory cases (50–60 mg/kg PO q12h)
  - Ultramicrosize: 5–10 mg/kg PO q24h. Duration of treatment: treat until 2 consecutive negative cultures are obtained at 1–3 week intervals

### FORMULATIONS

**Veterinary-labeled products:** Approved for horses

- Powder for oral suspension (microsize): 2.5 g in 15 g sachets; *Fulvicin U/F® Powder*

**Human-labeled products**

- Oral tablets (microsize): 250 mg, 500 mg; *Grifulvin V®*, *Fulvicin U/F®*, *Grisactin®*
- Oral capsules (microsize): 250 mg; *Grisactin®*
- Oral suspension (microsize): 125 mg/5 mL in 120 mL; *Grifulvin V®*
- Oral tablets (ultramicrosize): 125 mg, 165 mg, 250 mg, 330 mg; *Fulvicin P/G®*, *Gris-PEG®*, *Grisactin® Ultra*, generic

### SIDE EFFECTS

**Dogs and cats**

- Common: nausea (disagreeable taste), anorexia, vomiting, diarrhea
- Uncommon/rare: teratogenicity, anemia, leukopenia, thrombocytopenia, depression, ataxia, hepatotoxicity, maculopapular and exfoliative eruptions, photosensitivity, pruritus, erythema multiforme, toxic epidermal necrolysis

**Note:** Cats, particularly kittens, are more susceptible to side effects (especially teratogenicity and bone marrow suppression) than dogs. Bone marrow effects resolve in cats when treatment is discontinued; however, irreversible idiosyncratic pancytopenia has been reported.

### DRUG INTERACTIONS

Griseofulvin is an enhancer of cytochrome P450 enzymes. Therefore, drugs involved in cytochrome P450 metabolism may be metabolized and cleared faster if given with griseofulvin.

**Aspirin, cyclosporine, theophylline:** potential decrease in serum levels of these drugs

**Phenobarbital and other barbiturates:** decrease griseofulvin serum levels; may need to adjust griseofulvin dose with concurrent use

**Warfarin or other coumarin anticoagulants:** griseofulvin may reduce the anticoagulant effect of these drugs; anticoagulant adjustment may be needed

### MONITORING

- Efficacy and adverse effects
- Fungal culture
- CBC: at baseline and at 2–3 week intervals (mainly cats)
- Liver enzymes (if indicated)

## Hydroxychloroquine Sulfate

**Trade/brand name:** *Plaquenil*® (US, CA, UK), *Quineprox*® (US, CA, UK) (Rx)
**Classification:** Anti-inflammatory, Antimalarial

### INDICATIONS

**Dogs:** There is limited experience in veterinary medicine, with only a few reports on dermatological diseases. One study showed that hydroxychloroquine helped prevent progression of clinical signs associated with exfoliative cutaneous lupus erythematosus in 2/3 German short-haired pointer dogs (Mauldin *et al*. 2010). A recent report showed successful treatment (along with intermittent use of 0.1% tacrolimus, 0.1% predinicarbate cream, and restriction of sun exposure) of a new variant of canine chronic cutaneous lupus erythematosus presented as multi-focal lesions along the trunk, neck, and extremities in a Chinese crested dog (Oberkirchner *et al*. 2011). Hydroxychloroquine may also be used as an alternative therapy for other variants of canine lupus erythematous such as systemic lupus erythematosus and vesicular cutaneous lupus erythematosus.

**Note:** In humans, combination therapy with immunosuppressive agents (particularly methotrexate) has been demonstrated to enhance response to therapy of systemic and cutaneous lupus erythematosus cases.

**Cats:** No reports on dermatological use.

### CONTRAINDICATIONS

Hypersensitivity to the drug or other aminoquinoline compounds. In humans, hydroxychloroquine should not be used in combination with drugs with a tendency to produce dermatitis, as dermatologic reactions may occur. It is also contraindicated in patients with risks of hemolysis, risk factors for irreversible retinopathy, muscle weakness, severe blood disorders, liver disease, concurrent administration with known hepatotoxic drugs, and porphyria, as the drug may exacerbate these conditions. Caution is recommended with high doses or long-term therapy and in patients with known glucose-6-phosphate dehydrogenase deficiency. It should be avoided during pregnancy, as the drug is known to cross the placenta in humans. Due to a previous report of acute cardiotoxicity in anesthetized dogs receiving repeated intravenous high doses of hydroxychloroquine, and anecdotal reports of cardiotoxicity in humans, caution is warranted when administering this drug to dogs with cardiologic abnormalities.

### MECHANISM OF ACTION

Hydroxychloroquine is an aminoquinoline known to possess antimalarial and immunomodulatory activities. The exact immunomodulatory mechanism is unknown; however, it is thought to inhibit neutrophil phagocytosis and superoxide production, chemotaxis, and toll-like receptor (TLR)-9 stimulation.

### DOSAGES

**Dogs:** 5–10 mg/kg PO q24h

**Note:** In humans, hydroxychloroquine is usually taken with food or milk to prevent gastrointestinal side effects.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 200 mg; *Plaquenil®*, *Quineprox®*

### SIDE EFFECTS

Despite a few reports demonstrating that the drug appears to be well tolerated in dogs, the authors recommend caution when using this drug, as there is currently limited experience in veterinary medicine.

**Dogs:** In one study all three treated dogs receiving 5–10 mg/kg/day orally did not show any adverse effects (electrocardiograms, ophthalmologic examinations, CBCs, and chemistry profiles were normal compared to baseline throughout the trial) (Mauldin *et al*. 2010). The hydroxychloroquine serum concentrations, measured at the end of the study, were within the human therapeutic range (2.4–4 mg/mL). One dog treated with hydroxychloroquine at 5 mg/kg/day also did not show any adverse effects (Oberkirchner *et al*. 2011). Acute cardiotoxicity has been reported in anesthetized dogs receiving repeated intravenous high doses of hydroxychloroquine.

**Note:** Many adverse reactions have been reported in humans; however, they have been reported less commonly with hydroxychloroquine than with other antimalarial drugs such as chloroquine. Side effects reported include: CNS (irritability,

dizziness, vertigo, ataxia, convulsions, nerve deafness, nystagmus); neuromuscular (myopathy or neuromyopathy, weakness and muscle atrophy); dermatological (bleaching of hair, alopecia, pruritus, photosensitivity, exfoliative dermatitis and skin eruptions); hematological (various blood dyscrasias such as aplastic anemia and thrombocytopenia); gastrointestinal (anorexia, nausea, vomiting, diarrhea, isolated cases of hepatotoxicity); allergic (urticaria, angioedema and bronchospasm); miscellaneous (weight loss, exacerbation or precipitation of porphyria); cardiologic (rare cases of cardiomyopathy reported with high daily doses); ocular (blurred vision, decreased visual acuity, transient corneal edema, decreased corneal sensitivity, photophobia, corneal deposits, retinal edema, atrophy, abnormal pigmentation). Patients with retinal changes may be asymptomatic. Retinopathy appears to be dose-related and occurs most commonly with daily long-term therapy, and it may progress despite discontinuation of the drug.

### DRUG INTERACTIONS

There is limited experience in veterinary medicine.

**Aurothioglucose:** increases risk of blood dyscrasias; in humans, concurrent use with antimalarial drugs is contraindicated

**Digoxin:** increases digoxin serum concentrations

**Hepatotoxic drugs:** additive toxicity

**Metoprolol:** increases metoprolol plasma levels

### MONITORING

- Efficacy
- Despite apparent safety in dogs, the authors recommend monitoring for adverse effects at baseline and regularly during therapy with the following: ophthalmic and cardiac exams, CBC, chemistry profile and ECG (if administering the drug to dogs with cardiologic abnormalities)

## Hydroxyzine Hydrochloride/Palmoate

**Trade/brand name:** *Atarax*® (US, CA, UK), *Vistaril*® (US), *Ulcerex*® (UK), generic (Rx)
**Classification:** Piperazine antihistamine (first-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic skin conditions including urticaria and insect-bite hypersensitivity. Despite the widespread use of antihistamines to treat canine atopic dermatitis, currently there is no conclusive evidence of efficacy of oral type 1 antihistamines for treatment of chronic and acute flares of canine atopic dermatitis (Olivry *et al*. 2010).

**Note:** For management of allergic skin diseases, the response to hydroxyzine in dogs and cats, as with other antihistamines, is individualized and unpredictable. A better result may be achieved with the combination of hydroxyzine and chlorpheniramine than with hydroxyzine used as sole therapy, as this treatment

modality has been reported to be efficacious in ameliorating the clinical signs of canine atopic dermatitis (Olivry *et al*. 2010). Antihistamines should be given as preventative therapy, on a daily basis, to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Do not use in animals allergic to hydroxyzine. Caution in patients with prostatic hypertrophy, bladder neck obstruction, severe cardiac failure, angle-closure glaucoma, pyeloduodenal obstruction, or hepatic disease. Caution in pregnant and lactating animals. Hydroxyzine may interfere with the intradermal test reactivity. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Hydroxyzine is a histamine $H_1$-receptor antagonist with anti-allergic properties inhibiting histamine-induced wheal and flare responses. It also has anticholinergic, sedative, tranquilizing, antispasmodic, local anesthetic, mild bronchodilative, and antiemetic activities.

### DOSAGES

**Dogs and cats:** 2 mg/kg PO q12h

**Note:** A pharmacological study in dogs suggested that increasing either hydroxyzine dosage or frequency of administration would not result in histamine inhibition superior to that obtained with twice-daily administration at 2 mg/kg (Bizikova *et al*. 2008).

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets (hydrochloride): 10 mg, 25 mg, 50 mg, 100 mg; *Atarax*®, generic
- Oral solution (hydrochloride): 10 mg/5 mL in 16, 118, 120, and 473 mL vials; *Atarax*®, generic
- Oral capsules (palmoate; equivalent to hydrochloride): 25 mg, 50 mg, 100 mg; *Vistaril*®, generic
- Oral suspension (palmoate; equivalent to hydrochloride): 25 mg/5 mL in 120 and 473 mL vials; *Vistaril*®

### SIDE EFFECTS

**Dogs**

- Common: sedation, anticholinergic effects (e.g., dry mouth, decreased GI secretions)
- Uncommon: paradoxical hyperactivity, decreased appetite, hypotension, fine rapid tremors, whole body tremors, seizures (may reduce seizure threshold)

**Cats**

- Common: sedation
- Rare: polydipsia, depression, behavioral changes

### DRUG INTERACTIONS

**Anticholinergic agents:** additive anticholinergic effects

**Epinephrine:** inhibition or reversion of the vasopressor effects of epinephrine; use norepinephrine or metaraminol instead

**Monoamine oxidase (MAO) inhibitors (e.g., amitraz, selegiline, furazolidone):** increase anticholinergic effects such as sedation

**Other CNS depressant drugs (e.g., barbiturates, tranquilizers, phenothiazines, tramadol):** additive CNS depression

### MONITORING

- Efficacy and adverse effects

## Immunoglobulin, Human Intravenous (hIVIG)

**Trade/brand name:** *Carimune*® (US), *Gammagard*® (US), *Gamimune N*® (US, CA), *Octagam*® (US), generic (Rx)
**Classification:** Immunomodulatory (immunosuppressive)

### INDICATIONS

**Dogs and cats:** At this time, there is insufficient evidence to recommend the widespread use of hIVIG for autoimmune skin diseases and cutaneous drug reactions in dogs and cats. However, it might be warranted to use it for severe cases of pemphigus foliaceus, pemphigus vulgaris, and epidermolysis bullosa acquisita that are refractory to conventional therapy. It may also be of benefit in severe cases of vasculitis, drug reactions such as erythema multiforme, Stevens–Johnson syndrome, and toxic epidermal necrolysis. In dogs, hIVIG has been most commonly used for the treatment of immune-mediated hemolytic anemia and immune-mediated thrombocytopenia. It is important to take into consideration the high cost of therapy and the potential induction of antihuman IgG autoantibodies.

### CONTRAINDICATIONS

Due to the relatively high oncotic pressure of hIVIG, it should be used with caution in patients with cardiac and renal diseases, and the concomitant administration of colloids should be avoided. Multiple doses should be avoided, as safety associated with repeated administrations has not been determined.

### MECHANISM OF ACTION

hIVIG is prepared from pooled plasma from healthy human donors and contains primarily intact IgG, with traces of IgA, IgM, CD4, CD8, and human leukocyte antigen (HLA) molecules. Transfusion of these pooled immunoglobulins has been shown to correct immune dysregulation. Proposed mechanisms of action include functional blockade of Fc receptors on macrophages and effector cells, inhibition of cell activation and cytokine synthesis, neutralization of circulating autoantibodies and immune complexes, downregulation of autoantibody production, blockade of complement activity and microbial activity, interference with T and B cell function and increase in colloid osmotic pressure. By blocking Fas/Fas ligand (CD95/CD95L) interactions, hIVIG is also thought to prevent keratinocyte apoptosis.

### DOSAGES

There is limited clinical experience in dogs and cats. The dose range below is based on anecdotal reports on treatment of different dermatological diseases.

**Dogs and cats:** 0.5–1.5 g/kg IV in 5–6% sterile saline solution infused over 4–12 hours

**Note:** Dosages less than 0.5 g/kg may not be efficacious; however, there may be no differences in response among 0.5 g/kg and higher doses. Infusions may be repeated on 2 consecutive days or after flare-ups, however, with caution. Animals may start showing improvement 1–4 days after starting therapy. Azathioprine and/or glucocorticoids should be started after 1–3 days of hIVIG as immunomodulating agents to prevent relapses after the hIVIG has been completely metabolized. These drugs may be tapered and discontinued after several months of therapy without disease relapses. Food, fluids, and all medications should be withheld during treatment with hIVIG to diminish the likelihood of adverse reactions.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Human immunoglobulin liquid
  - 3 g, 6 g, 12 g vials; *Carimune*®, generic
  - 5 g vials; *Octagam*®, *Gammagard*®, generic
  - 5 g and 10 g vials; *Gamimune N*®, generic

### SIDE EFFECTS

Despite the fact that use of hIVIG appears safe, there is limited clinical experience in dogs and cats and it should be administered with caution.

**Dogs and cats**

- Rare: vomiting, induction of antihuman IgG autoantibodies with allergic reaction or immune complex formation

### DRUG INTERACTIONS

None known. However, food, fluids, and all medications should be withheld during treatment with hIVIG to diminish the likelihood of adverse interactions.

### MONITORING

- Efficacy
- Patients must be closely monitored for any adverse side effects throughout the infusion period
- Baseline: chemistry profile, CBC, urinalysis, blood pressure, temperature, heart rate, and respiratory rate. Blood pressure, temperature, heart rate, and respiratory rate should also be monitored during infusion

## Interferon Alpha, Recombinant Human

**Trade/brand name:** *Alferon-N*® (US), *Intron-A*® (US, CA, UK), *Roferon-A*® (US, CA, UK), *Viraferon*® (UK) (Rx)
**Classification:** Immunomodulatory (immunostimulant)

## INDICATIONS

Used to stimulate the immune system.

**Cats:** Dermatological conditions associated with viral infections such as herpetic dermatitis, FeLV and FIV dermatitis, and papillomatosis. It may also be of benefit in cases of eosinophilic granuloma complex such as indolent ulcer; however, such indication has not been substantiated by controlled studies.

**Dogs:** Dermatological conditions associated with viral infections such as severe oral and cutaneous papillomatosis. It may also be of some benefit in cases of cutaneous T-cell lymphoma (Tzannes *et al*. 2008) and idiopathic recurrent superficial pyoderma in dogs (transient benefit) (Thompson *et al*. 2004); however, such indications have not been substantiated by controlled studies.

## CONTRAINDICATIONS

Do not use in patients hypersensitive to the drug, and do not vaccinate dogs and cats receiving interferon. With parental use, caution in patients with pre-existing autoimmune disease, severe cardiac disease, pulmonary disease, uncontrolled diabetes, herpes infections, or CNS disorders. Safety during pregnancy or lactation has not been established.

## MECHANISM OF ACTION

Interferon alpha is a cytokine with antiviral and immunomodulating actions likely due to its effects on the synthesis of RNA, DNA, and cellular proteins. Its antiproliferative and antineoplastic activities might also be related to the effects on the synthesis of RNA, DNA, and cellular proteins, but this is not known. Interferon alpha was also shown to inhibit the release of granule proteins from human eosinophils.

## DOSAGES

There is limited clinical experience in dogs and cats. Oral absorption may be poor.

### Dogs

- Cutaneus T-cell lymphoma: 1.5–2 million units (MU)/$m^2$ SC of alpha-2a, 3 times weekly
- Idiopathic recurrent superficial pyoderma (anecdotal): 1000 IU/mL PO q24h of alpha-2b
- Papillomatosis (anecdotal): 20,000 IU PO q24h. Each vial contains 10 million IU of interferon alpha-2b; dilute in sterile saline (ideally, in 0.1% bovine serum albumin) to a final concentration of 100,000 IU/mL; if not administered immediately, prepare aliquots of 0.2 mL (20,000 IU) and freeze at –70 °C.

### Cats

- Viral infections: 30 units per cat PO q24h on alternate weeks. Repeat protocol if necessary
- Eosinophilic ulcer/indolent ulcer (anecdotal): 60–300 units per cat PO or SC q24h for 30 consecutive days or on alternate weeks

**Note:** Users should consult the manufacturer for recommendation on reconstitution and storage and for any further advice as needed.

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Interferon alpha-2a injection: 3 million IU/0.5 mL syringe, 6 million IU/0.5 mL syringe, 9 million IU/0.5 mL syringe; *Roferon-A®*
- Interferon alpha-2b powder for injection: 5 million IU/vial, 10 million IU/vial, 18 million IU/vial, 25 million IU/vial, 50 million IU/vial in vials with 1, 2 or 5 mL diluent/vial; *Intron-A®*
- Interferon alpha-2b injection: 3 million IU/dose, 5 million IU/dose, 5 million IU/dose, 10 million IU/dose in multidose pens; *Intron-A®*
- Interferon alpha-2b solution for injection: 3 million IU/vial, 5 million IU/vial, 10 million IU/vial, 18 million IU/vial, 25 million IU/vial in vials, Pak-3, -5, -10 (vials and syringes) and in multidose vials 22.8 million IU/3.8 mL/vial or 32 million IU/3.2 mL/vial; *Intron-A®*
- Interferon alpha-N3 injection: 5 million IU/mL in 1 mL vials; *Alferon-N®*

### SIDE EFFECTS

There is limited clinical experience in dogs and cats.

**Dogs and cats**

- Uncommon
  - Oral administration: vomiting and nausea
  - Parenteral administration: malaise, fever, allergic reactions, myelotoxicity, myalgia, development of antihuman IgG autoantibodies after 7–8 weeks of treatment with allergic reaction or immune complex formation. Slight temporary decrease in white blood cells, platelets, and red blood cells, and rise in the concentration of alanine aminotransferase may be observed. Cats may show transient fatigue

### DRUG INTERACTIONS

**Acyclovir, zidovudine:** potential additive or synergistic antiviral effects. Veterinary significance of this potential interaction is unclear

**Other vaccine/immunomodulatory agents:** do not mix with interferon alpha

### MONITORING

- Efficacy and adverse effects

## Interferon Gamma, Recombinant Canine

**Trade/brand name:** *Interdog®* (Japan) (Rx)
**Classification:** Immunomodulatory (immunostimulant)

### INDICATIONS

**Dogs:** Canine recombinant interferon gamma (KT-100) is labeled in Japan for the treatment of atopic dermatitis.

### CONTRAINDICATIONS

Do not use in patients hypersensitive to the drug, and do not vaccinate animals receiving interferon. Caution in patients with pre-existing autoimmune disease,

severe cardiac disease, pulmonary disease, uncontrolled diabetes, herpes infections, or CNS disorders. Safety during pregnancy or lactation has not been established.

### MECHANISM OF ACTION

Interferon gamma is a cytokine that plays an important role as an immune modulator. The mechanism by which interferon gamma acts to decrease skin inflammation in atopic dermatitis is unknown; however, in humans it is suggested to shift the Th2-cytokine dominance towards Th1 dominance. In dogs with atopic dermatitis, interferon gamma was shown to decrease IL-4: interferon-gamma mRNA ratio in peripheral blood mononuclear cells, to significantly decrease the serum total IgE levels, and to decrease the number of mast cells in the dermis, suggesting that in atopic dogs interferon gamma may act by modulating the Th2/Th1 cytokine balance and by reducing serum total IgE production.

### DOSAGES

There is limited clinical experience in dogs with interferon gamma for dermatological diseases. Canine recombinant interferon gamma should be administered under the prescription and instruction of a veterinarian.

**Dogs**

- Atopic dermatitis: The following treatment protocol was obtained from a recent open, randomized clinical trial comparing two doses of recombinant canine interferon-gamma for the treatment of atopic dermatitis (Yasukawa *et al*. 2010)
    - 5000 or 10,000 units/kg administered SC q24h three times a week for 4 weeks then once weekly for 4 additional weeks. Significant improvement may be seen during the first 4 weeks of therapy. Overall, both doses appear to be efficacious, with the efficacy rate apparently being higher with 10,000 units/kg than with 5000 units/kg, suggesting that the response to interferon gamma might be dose-dependent. Some dogs may stay in remission without recurrence of allergic symptoms and may not require additional treatment.

**Note:** Users should consult the manufacturer for recommendation on reconstitution and storage and for any further advice as needed.

### FORMULATIONS

**Veterinary-labeled products:** None approved in the US

- Injectable solution: 60,000 units/vial; *Interdog*® (available in Japan)

**Human-labeled products:** None

### SIDE EFFECTS

There is limited clinical experience in dogs; however, side effects appear to be minimal.

**Dogs:** soft stool, facial swelling, and pain at the site of injection have been reported. Laboratory abnormalities were not reported in conducted studies

### DRUG INTERACTIONS

**Acyclovir, zidovudine:** potential additive or synergistic antiviral effects. Significance of this potential interaction is unclear

**Hepatotoxic or myelosuppressive drugs:** avoid concurrent use with interferon gamma

**Other vaccine/immunomodulatory agents:** do not mix with interferon gamma

### MONITORING
- Efficacy and adverse effects

## Interferon Omega, Recombinant Feline

**Trade/brand name:** *Virbagen Omega*® (UK) (Rx)
**Classification:** Immunomodulatory (immunostimulant)

### INDICATIONS
Used to stimulate the immune system.

**Dogs:** Dermatological conditions associated with viral infections such as severe oral and cutaneous papillomatosis. A randomized, double-blind controlled clinical trial showed that recombinant feline interferon omega may have some clinical benefit in the long-term management of canine atopic dermatitis (Carlotti *et al*. 2009). It may also be of some benefit in cases of cutaneous T-cell lymphoma.

**Cats:** Dermatological conditions associated with viral infections such as herpetic dermatitis, FeLV and FIV dermatitis, and papillomatosis. It may also be of benefit in severe refractory cases of acne, gingivostomatitis (associated with feline calicivirus infection), and indolent ulcer.

### CONTRAINDICATIONS
Do not use in patients hypersensitive to the drug, and do not vaccinate dogs and cats receiving interferon. Caution in patients with pre-existing autoimmune disease, severe cardiac disease, pulmonary disease, uncontrolled diabetes, or CNS disorders. Safety during pregnancy or lactation has not been established.

### MECHANISM OF ACTION
Interferon omega is a type I interferon that has a similar mechanism of action to interferon alpha. Type I interferons have antiviral, antiproliferative, and immunomodulatory effects. In addition, they induce apoptosis of virus-infected cells and promote CD8+ cytotoxic T cells and natural killer cell responses by enhancing the expression of major histocompatibility class I (MHC-I) molecules. Type I interferons also induce a form of nitric oxide synthase, which plays a role in immune responses to infections.

### DOSAGES
There is limited clinical experience in dogs and cats with interferon omega for dermatological diseases.

**Dogs**
- General: 2.5 million units (MU)/kg IV q24h for 3 days
- Atopic dermatitis: 1–5 MU (0.1–0.5 mL) per injection according to body weight (5–15 kg: 1 MU; 15–25 kg: 2 MU; 25–45 kg: 3.33 MU; >45 kg: 5 MU) SC 3 times weekly for a total of 10 injections for the first 6 months period, then 1 injection per month for maintenance

**Cats**

- General: 1.5 MU/kg IV or SC q24–48h for up to 5 days, then reduce according to clinical response to twice weekly and then once weekly
- Acne (anecdotal): 1 MU/kg SC once a week for 3 weeks
- Herpes dermatitis: the following protocol was extracted from a paper published in *Veterinary Dermatology* (Gutzwiller *et al*. 2007): 1.5 MU/kg administered on days 0 and 2 (the first dose is divided, to be given half intralesionally and half subcutaneously), on day 9 repeat the same dose (1.5 MU/kg) given subcutaneously, then on days 19, 21, and 23 give half dose (0.75 MU/kg) intralesionally and half dose subcutaneously
- Gingivostomatitis (anecdotal): 1 MU/kg SC q48h for 5 doses

**Note:** Users should consult the manufacturer for recommendation on reconstitution and storage and for any further advice as needed.

## FORMULATIONS

**Veterinary-labeled products:** None approved in the US

- Feline recombinant interferon omega (*Virbagen Omega*®) is labeled in EU for dogs with parvovirus infection and for cats with FeLV and/or FIV infections.
- Injectable solution: 5 or 10 million units (MU)/vial; *Virbagen Omega*® (available in UK)

**Human-labeled products:** None

## SIDE EFFECTS

There is limited clinical experience in dogs and cats.

**Dogs**

- Uncommon: hyperthermia, vomiting (3–6 hours post injection), slight temporary decrease in white blood cells, platelets, and red blood cells, and rise in the concentration of alanine aminotransferase, development of antibodies if treatment is prolonged (beyond labeled dosage period) or repeated, pruritus (reported duration: 3 days) after injection

**Cats**

- Uncommon: hyperthermia, vomiting (3–6 hours post injection), soft feces/mild diarrhea and transient fatigue, slight temporary decrease in white blood cells, platelets, and red blood cells, and rise in the concentration of alanine aminotransferase. Increased incidence and severity of adverse effects may occur with intravenous administration

**Note:** Complications associated with long-term maintenance use in dogs and cats are not known at this time.

## DRUG INTERACTIONS

**Acyclovir, zidovudine:** potential additive or synergistic antiviral effects; significance of this potential interaction is unclear

**Hepatotoxic or myelosuppressive drugs:** avoid concurrent use with interferon omega

**Other vaccine/immunomodulatory agents:** do not mix with interferon omega

### MONITORING
- Efficacy and adverse effects
- CBC and hepatic function on a regular basis

## Iodide, Potassium

**Trade/brand name:** *SSKI*® (US), *Pima*® (US), generic (Rx)
**Classification:** Antifungal (inorganic halogen)

### INDICATIONS

**Dogs and cats:** Sporotrichosis. Historically, potassium iodide has been considered the drug of choice for sporotrichosis in dogs and cats; however, serious adverse effects associated with this agent led to its replacement with more effective and safer antifungal drugs such as the azoles (e.g., itraconazole).

### CONTRAINDICATIONS
Contraindicated in animals with iodide hypersensitivity, hyperthyroidism, renal failure, dehydration, and in pregnant or lactating animals. Do not use the injectable form in dogs or cats.

### MECHANISM OF ACTION
The exact mode of action of potassium iodide is unknown, as no fungicidal effects have been observed in vitro; however, action may result from enhancement of the immune response of the host by stimulating the halide-peroxide killing system of phagocytic cells, quenching toxic oxygen metabolites and inhibiting neutrophil chemotaxis.

### DOSAGES
Metallic taste is extremely unpleasant; give with food or a fatty liquid (whole milk, cream) to prevent nausea and vomiting.

**Dogs:** 40 mg/kg PO q8–12h for at least 60 days or 30 days beyond clinical resolution

**Cats:** 20 mg/kg PO q12–24h for at least 60 days or 30 days beyond clinical resolution

### FORMULATIONS

**Veterinary-labeled products:** None approved for dogs or cats

**Human-labeled products**
- Oral solution: 1 g KI/mL; 325 mg KI/5 mL in 24 mL, 30 mL, pint and gallon; *SSKI*®, generic
- Oral syrup (raspberry flavor): 62.5 mg KI/mL in pints and gallons; *Pima*®

### SIDE EFFECTS
Chronic use or overdose may cause signs of iodism. Cats are apparently more prone to iodide toxicity than dogs.

**Dogs**
- Uncommon: signs of iodide toxicity such as excessive tearing, hyperthermia, weakness, depression, decreased weight gain, coughing, anorexia, vomiting,

diarrhea. In addition, dogs may present with ocular and nasal discharge, scaly and dry hair coat

**Cats**

- Common: signs of iodide toxicity such as excessive tearing, hyperthermia, weakness, depression, decreased weight gain, coughing, anorexia, vomiting, and diarrhea. In addition, cats may present with cardiovascular failure, hypothermia, and twitching

### DRUG INTERACTIONS

**Antithyroid medications:** potential for decrease in the efficacy of antithyroid medications

**Other potassium-containing medications:** possible hyperkalemia
**Thyroid supplements:** potential for enhancement of the efficacy of thyroid supplements

### MONITORING

- Efficacy and iodism signs

## Isotretinoin

**Trade/brand name**: *Accutane*® (US, CA), *Amnesteem*® (US), *Claravis*® (US), *Isotrex*® (UK), *Sotret*® (US), generic (Rx)
**Classification**: Synthetic retinoid (second-generation)

### INDICATIONS

There is no scientific or clinical evidence to encourage the use of isotretinoin to treat most of these dermatoses.

**Dogs:** Sebaceous adenitis, vitamin-A responsive dermatosis, sebaceous gland hyperplasia and adenoma, solar dermatosis, actinic keratosis, squamous cell carcinoma, infundibular keratinizing acanthomas (multiple keratoacanthomas or intracutaneous cornifying epitheliomas), multiple epidermal inclusion cysts, ichthyosis, Schnauzer comedo syndrome, follicular dysplasias (e.g., color dilution alopecia), inflammatory linear verrucous epidermal nevus, idiopathic nasodigital hyperkeratosis and ear margin seborrhea, epitheliotropic lymphoma. A recent study also showed a potential benefit of retinoic acids (particularly 9-cis retinoic acid or Alitretinoin at 2 mg/kg/day PO) for the treatment of pituitary-dependent hyperadrenocorticism (Castillo *et al*. 2006); however, investigations have not been performed with isotretinoin.

**Cats:** Sebaceous adenitis, acne, epitheliotropic lymphoma.

### CONTRAINDICATIONS

Patients with severe renal or hepatic disease, hypersensitivity to isotretinoin, hypertriglyceridemia or other lipid abnormalities, unspayed or pregnant females and breeding males (teratogenic), households with pregnant women or women planning to become pregnant (drug should not be handled by pregnant women).

### MECHANISM OF ACTION

Regulation of epithelial cell proliferation and differentiation. It is believed that isotretinoin alters gene expression through nuclear retinoic acid receptors (RARs) and bind to DNA to cause transcription or transrepression changes in protein synthesis, leading to cellular differentiation and variable antiproliferative, anti-inflammatory, and immunomodulatory effects. It affects monocyte and lymphocyte function, which can cause changes in cellular immune responses. In addition, it reduces sebaceous gland size and activity, thereby reducing sebum production. It also may indirectly reduce bacterial populations in sebaceous pores.

### DOSAGES

Must be given with food to optimize absorption. May take several months before clinical response is seen, and chronic therapy is often needed (may be able to transit into every-other-day therapy).

**Dogs**

- General dose: 1–3 mg/kg PO q24h
- Sebaceous adenitis: 1 mg/kg PO q12–24h. Improvement should be seen within 6 weeks; at that time the frequency of administration can be reduced to every other day or the dose lowered to 0.5 mg/kg q24h
- Keratoacanthoma, ichthyosis, sebaceous gland hyperplasia and adenoma: 1–3 mg/kg PO q12–24h
- Schnauzer comedo syndrome: 1 mg/kg PO q24h or divided q12h
- Epitheliotropic lymphoma: 3–4 mg/kg PO q24h or divided q12h (palliative treatment)

**Cats**

- General dose: 1–3 mg/kg PO q24h
- Acne: 5 mg/kg PO q24h
- Epitheliotropic lymphoma: 10 mg per cat PO q24h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 10 mg, 20 mg, 30 mg, 40 mg; *Accutane®*, *Claravis®*, *Amnesteem®*, *Sotret®*

**Note:** Availability to veterinarians may be restricted due to concerns of teratogenic effects in humans.

### SIDE EFFECTS

There is limited experience in veterinary medicine. Incidence of side effects may be higher in cats. Laboratory abnormalities generally not associated with clinical signs, e.g., hypertriglyceridemia, hypercholesterolemia, and increased serum levels of platelets, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase, may be present.

**Dogs**

- Rare: keratoconjunctivitis sicca, anorexia, vomiting, diarrhea, abdominal distension, lassitude, hyperactivity, collapse, behavioral changes, joint pain/stiffness, pruritus, exfoliative dermatitis, erythema of feet and mucocutaneous junctions, polydipsia and swollen tongue

**Cats**
- Uncommon: anorexia with resultant weight loss, conjunctivitis, blepharospasm, periocular crusting and erythema, erythema, vomiting, diarrhea

**Note:** These side effects in dogs and cats are usually transient or resolve with discontinuation or decrease in dose of the drug. Long-term use may result in development of skeletal abnormalities, including cortical hyperostosis, periosteal calcification, and long bone demineralization. All retinoids are potent teratogens.

### DRUG INTERACTIONS

**Cyclosporine:** potential for increase in serum levels of cyclosporine

**Other retinoids (e.g., isotretinoin, tretinoin) or vitamin A:** potential additive toxic effects

**Tetracycline:** increases the risk for the occurrence of cerebral edema and increase in cerebrospinal fluid pressure

### MONITORING
- Efficacy and adverse effects
- Liver function tests: baseline, 1–2 months and later as necessary
- Dogs: Schirmer tear tests: baseline, 1–2 months and later as necessary
- Avoid excessive exposure to sunlight as the effects of UV light are enhanced by retinoids
- Intake of vitamin A supplements to avoid possible additive toxic effects
- Cats: monitor weight

## Itraconazole

**Trade/brand name:** *Sporanox®* (US, CA, UK), *Itrafungol®* (UK) (Rx)
**Classification**: Antifungal (third-generation azole, triazole)

### INDICATIONS

**Dogs and cats:** A variety of systemic mycoses including blastomycosis, histoplasmosis, sporotrichosis, cryptococcosis, and coccidioidomycosis. Itraconazole is also used for the treatment of dermatophytosis, onychomycosis, and *Malassezia* dermatitis. It may also be useful for treatment of aspergillosis, candidiasis, pythiosis, lagenidiosis, zygomycosis, phaeohyphomycosis, hyalohyphomycosis, and otitis externa caused by fungal organisms. Itraconazole is considered by many dermatologists the antifungal of choice for dermatophytosis in cats.

### CONTRAINDICATIONS

Hypersensitivity to itraconazole or other azoles. Caution in animals with impaired hepatic function or achlorhydria (or hypochlorhydria). Avoid use in patients with impaired ventricular function, as itraconazole has a negative inotropic effect and may lead to congestive heart failure. Avoid use in pregnant animals, as it may be teratogenic, and in nursing animals.

### MECHANISM OF ACTION

Itraconazole is a fungistatic triazole agent that inhibits ergosterol synthesis in the fungal cell membrane by inhibiting the fungal cytochrome P450 sterol C14 alpha-demethylase, altering membrane permeability and allowing leakage of intracellular components. In humans, itraconazole was shown to be incorporated into sebum and stratum corneum and to be detected in skin for 3–4 weeks after treatment. Itraconazole also has immunomodulatory effects, probably by suppressing T-lymphocyte proliferation. It does not have appreciable effects on hormone synthesis, unlike ketoconazole.

### DOSAGES

Itraconazole should be given with food for better absorption and bioavailability. Itraconazole solution is well absorbed in cats even without food.

#### Dogs

- Systemic mycosis, sporotrichosis: 5–10 mg/kg PO q24h. Duration of therapy: may vary according to the fungal organism involved. Generally, for at least 30–60 days after clinical recovery. Cryptococcosis, nasal aspergillosis: 5 mg/kg PO q12h for at least 60 days after clinical recovery
- Dermatophytosis, onychomycosis: 5–10 mg/kg PO q24h. Alternative pulse therapy protocol: 5–10 mg/kg PO q24h on an every other week schedule. Duration of therapy: until at least 2 consecutive negative cultures 1–2 weeks apart
- *Malassezia* dermatitis: 5 mg/kg PO q24h for 1 week after complete resolution of clinical signs
  **Note:** A controlled study showed that pulse therapy with itraconazole at 5 mg/kg PO q24h for 2 consecutive days per week seems to be as effective for canine *Malassezia* dermatitis as daily administration of ketoconazole at 10 mg/kg (Bensignor 2008), which may be due to the persistence of itraconazole in the stratum corneum for long periods after discontinuation of therapy.
- Pythiosis, lagenidiosis: 10 mg/kg PO q24h for 3–9 months after surgical resection
  **Note:** Medical therapy has traditionally been unrewarding for these conditions. However, the combination of itraconazole with terbinafine (5–10 mg/kg PO q24h) and aggressive surgical excision may be more beneficial.
- Zygomycosis, phaeohyphomycosis, hyalohyphomycosis: 5–15 mg/kg PO q24h for 3–9 months after clinical recovery or surgical resection

#### Cats

- Systemic mycosis: 5–10 mg/kg PO q24h or divided twice daily. In most cases, it is administered once daily. Duration of therapy: may vary according to the fungal organism involved. Generally, for at least 30–60 days after clinical recovery
- Dermatophytosis, onychomycosis: 5–10 mg/kg PO q24h. Pulse therapy: 5 mg/kg PO q24h on an every other week schedule. Alternative pulse therapy protocols: 5–10 mg/kg PO q24h on 2 consecutive days per week or 10 mg/kg PO q24h for 28 days, then on alternate weeks. Duration of therapy: until at least 2 consecutive negative cultures 1–2 weeks apart
- *Malassezia* dermatitis: 5 mg/kg PO q24h. Alternative pulse therapy protocol: 5 mg/kg PO q24h for 2 consecutive days per week. Duration of therapy: until 1 week after complete resolution of clinical signs

## FORMULATIONS

Compounded formulations are highly unstable and insoluble (unless compounded from commercially-available products) and should be avoided. Generic formulations should ideally not be used because of reported unpredictable absorption.

**Veterinary-labeled products:** None in the US

**Human-labeled products**

- Oral capsules: 100 mg; *Sporanox®*, *Itrafungol®* (UK only)
- Oral solution: 10 mg/mL in 150 mL; *Sporanox®*, *Itrafungol®* (UK only)

## SIDE EFFECTS

**Dogs**

- Common: anorexia (especially at higher doses), hepatotoxicity. Anorexia is often the symptomatic marker for toxicity, and it usually occurs in the second month of treatment
- Uncommon: 7.5% of dogs treated with itraconazole at ≥10 mg/kg/day may develop ulcerative dermatitis and cutaneous vasculitis (lymphedema and/or necrotizing lesions on one or more limbs) that may require dosage reduction to 5 mg/kg/day or discontinuation of the drug. Increase in blood urea nitrogen has also been reported
- Rare: serious erythema multiforme or toxic epidermal necrolysis reactions

**Cats**

- Common: adverse effects appear to be dose-related. Gastrointestinal side effects (anorexia, weight loss, vomiting), hepatotoxicity (increased ALT, jaundice), and depression. Increased liver enzymes in the absence of other signs do not necessarily mandate dosage reduction or drug discontinuation. Once ALT levels return to normal and other adverse effects have diminished, if necessary, the drug may be restarted at a lower dosage or longer dosing interval with intense monitoring

## DRUG INTERACTIONS

Itraconazole is a cytochrome P450 enzyme inhibitor, which may lead to several drug interactions. However, this inhibition is not as prominent as with ketoconazole.

**Amphotericin B:** potential antagonism against aspergillosis or candidiasis

**Antacids:** may reduce oral absorption of itraconazole (administer itraconazole at least 1 hour before or 2 hours after antacids)

**Antihistamines (e.g., terfenadine), benzodiazepines (e.g., diazepam), buspirone, busulfan, calcium channel blocking agents (e.g., verapamil), cisapride, corticosteroids, cyclosporine, cyclophosphamide, digoxin, fentanyl/alfentanil, hypoglycemics, midazolam, quinidine, sulfonylurea antidiabetic agents (e.g., glipizide, glyburide), vincristine/vinblastine:** itraconazole may increase serum levels of these drugs

**$H_2$ blockers (e.g., ranitidine, famotidine), proton-pump inhibitors (e.g., omeprazole):** increase in gastric pH may reduce itraconazole absorption

**Ivermectin:** itraconazole may increase the risk for neurotoxicity

**Macrolide antibiotics (e.g., erythromycin, clarithromycin):** potential for increase in itraconazole serum levels

**Phenobarbital, phenytoin, rifampin, griseofulvin:** may decrease itraconazole serum levels

**Warfarin, other coumarin anticoagulants:** may increase prothrombin time in patients receiving these drugs

### MONITORING

- Efficacy and adverse effects
- Routine liver function tests (monthly ALT) with long-term use

## Ivermectin

**Trade/brand name**: *Ivomec 1%®* (US, CA), *Ivermax 1%®* (US), *Eqvalan Liquid®* (US, CA), *Animec 1%®* (UK), *Bimectin 1%®* (UK) (Rx)
**Classification**: Antiparasitic (macrocyclic lactone)

### INDICATIONS

**Dogs:** Generalized demodicosis, sarcoptic mange, cheyletiellosis, otodectic acariosis, nasal mites (*Pneumonyssoides caninum*).

**Cats:** Cheyletiellosis, otodectic acariosis, notoedric mange, follicular demodicosis (*Demodex cati*).

**Note:** *Demodex gatoi* appears unresponsive to ivermectin, possibly because this mite parasitizes the skin surface, where the drug concentration may not be adequate to kill the mite. Ideally, client informed consent should be obtained prior to initiation of treatment, as the treatment of these conditions with ivermectin is extra-label.

### CONTRAINDICATIONS

Use in dogs and cats is extra-label. Canine breeds susceptible to ABCB1-1 (MDR1) allele mutation such as collies, Border collies, Shetland sheepdogs, Australian shepherds, long-haired whippets, old English sheepdog, German shepherds (especially white German shepherds), silken windhounds, McNab and herding-breed crosses should not receive ivermectin without testing for the ABCB1-1 gene mutation, because of the higher risk of toxicity. Do not use without up-to-date negative heartworm test, or in patients with heartworm disease.

### MECHANISM OF ACTION

Ivermectin, similar to other macrocyclic lactones, is neurotoxic to parasites by increasing membrane permeability to chloride ions and potentiating the effects of the inhibitory neurotransmitter GABA, leading to flaccid paralysis and death of the parasite. Mammals are generally protected from neurological effects of macrocyclic lactones.

### DOSAGES

If toxicicity is noticed, drug must be discontinued.

**Dogs**

- Generalized demodicosis: 300–600 mcg/kg (0.3–0.6 mg/kg) PO q24h until 4 weeks past two negative skin scrapings 4–6 weeks apart

**Note:** If needed, particularly in puppies, a gradual increase in dosage may be safer to use: starting at 50 mcg/kg (0.05 mg/kg) and increasing by 50 mcg/kg per day or starting at 100 mcg/kg (0.1 mg/kg) PO and increasing by 100 mcg/kg every 3–7 days until the final target dose is reached.

- Sarcoptic mange, cheyletiellosis: 200–400 mcg/kg (0.2–0.4 mg/kg) SC every 2 weeks. If diagnosis is confirmed (i.e., positive skin scrapings): administer 3 treatments. If treatment trial: administer two treatments and re-evaluate; if no response to treatment, reconsider the diagnosis; if response to treatment, give last dose

**Note:** An alternative protocol for sarcoptic mange is 200–400 mcg/kg (0.2–0.4 mg/kg) PO once weekly for four treatments.

- Otodectic acariosis: 300 mcg/kg (0.3 mg/kg) SC every 2 weeks or topical application of 0.5 mL (0.1 mg/mL) per ear for 1–2 treatments
- Nasal mites: 300 mcg/kg (0.3 mg/kg) SC every 1–2 weeks for 2–3 treatments

**Cats**

- Cheyletiellosis: 300 mcg/kg (0.3 mg/kg) SC every 2 weeks. If diagnosis is confirmed (i.e., positive skin scrapings), administer three treatments. If treatment trial, administer two treatments and re-evaluate; if no response to treatment, reconsider diagnosis; if response to treatment, give last dose
- Notoedric mange: 300 mcg/kg (0.3 mg/kg) SC every 2 weeks for 2–3 treatments
- Otodectic acariosis: 300 mcg/kg (0.3 mg/kg) SC every 2 weeks or topical application of 0.5 mL (0.1 mg/mL) per ear for 1–2 treatments
- Follicular demodicosis (*Demodex cati*): 200–400 mcg/kg (0.2–0.4 mg/kg) PO q24–48h until 4 weeks past two negative skin scrapings 4–6 weeks apart

**Note:** For sarcoptic mange, cheyletiellosis and otodectic acariosis, all in-contact animals should be treated concurrently with a suitable acaricide. For notoedric mange, all in-contact cats should be treated. The environment should ideally be cleaned and treated with an environmental acaricide.

## FORMULATIONS

**Veterinary-labeled products:** Approved for large animals only

- Injection: 10 mg/mL (1%) in 50, 200, and 500 mL btl; *Ivomec 1%®*, *Ivermax 1%®*, *Animec 1%®*, *Bimectin 1%®*
- Oral liquid: 10 mg/mL (1%) in 50 and 100 mL btl; *Eqvalan Liquid®*, *Ivercide Liquid for Horses®*

**Note:** *Ivomec 1%®* injectable is the most popular treatment for canine generalized demodicosis and sarcoptic mange among veterinary dermatologists. *Eqvalan 1%®* oral liquid for horses might be a more palatable alternative than Ivomec 1% injectable product, because of the high propylene glycol content of the latter. Both formulations appear to perform well.

**Human-labeled products:** None for use in dogs and cats

### SIDE EFFECTS

**Dogs and cats**

- Uncommon: hypersalivation, mydriasis, blindness, lethargy, weakness, tremors, ataxia, depression, behavior abnormalities, anorexia, vomiting and diarrhea (particularly with oral administration), pain or swelling at the injection site
- Rare: coma, death (particularly in sensitive breeds)

**Note:** Side effects in some dogs may not be seen for days to weeks after beginning of therapy. Cats appear less sensitive to avermectin side effects than dogs.

### DRUG INTERACTIONS

**Drugs that may inhibit P-glycoprotein (amiodarone, bromocriptine, carvedilol, clarithromycin, chlorpromazine, cyclosporine, diltiazem, erythromycin, fluoxetine, grapefruit juice, itraconazole, ketoconazole, methadone, paroxetine, pentazocine, quinidine, spironolactone, St. John's wort, tamoxifen, verapamil):** caution with concomitant use due to potential for increase in ivermectin neurotoxicity

**Benzodiazepines:** drug effects may be potentiated by ivermectin. Concurrent use not recommended in humans

### MONITORING

- Efficacy and adverse effects
- Check heartworm status prior to administration

## Ketoconazole

**Trade/brand name:** *Nizoral*® (US, CA, UK), generic (Rx)
**Classification:** Antifungal (first-generation azole, imidazole)

### INDICATIONS

**Dogs and cats:** *Malassezia* dermatitis, dermatophytosis, candidiasis, blastomycosis, coccidiomycosis, cryptococcosis, histoplasmosis, and leishmaniasis. It should not be used solely as first choice for systemic mycosis (mainly if CNS or eyes are involved) unless cost is an important factor. When combined with amphotericin B the efficacy rate to treat systemic mycosis is comparable with itraconazole alone. Ketoconazole is also used to treat canine hyperadrenocorticism and to reduce cyclosporine dose in dogs.

### CONTRAINDICATIONS

Known hypersensitivity to the drug and pregnancy (teratogenic and embryotoxic in laboratory animals). Caution in animals with liver disease or thrombocytopenia. Cats are very sensitive to the side effects of ketoconazole, and it should be used cautiously or avoided in this species. Avoid in breeding male dogs as ketoconazole may cause infertility by decreasing testosterone synthesis.

### MECHANISM OF ACTION

Ketoconazole interferes with the synthesis of ergosterol, an essential component of the fungal cell membrane, by inhibiting the cytochrome P450 lanesterol

C14-demethylase. It is fungistatic at commonly used doses. In mammals, ketoconazole inhibits cortisol synthesis by blocking the cytochrome P450 (CYP) enzyme 11 beta-hydroxylase (CYP11B1). It can also inhibit testosterone synthesis by blocking CYP enzymes. Ketoconazole effect in increasing cyclosporine blood levels results from the inhibition of the CYP enzyme CYP3A involved in the metabolism of cyclosporine. Ketoconazole also has anti-inflammatory and immunomodulatory effects such as inhibition of 5-lipoxygenase activity, neutrophil chemotaxis, and lymphocyte blastogenesis.

## DOSAGES

Always administer with food to improve absorption.

**Dogs**

- *Malassezia* dermatitis or otitis: 5–10 mg/kg PO q24h for 14–30 days and re-evaluate
- Systemic mycosis: 5–10 mg/kg PO q12h or 15–20 mg/kg q12h if ocular or CNS involvement. It is recommended to use in conjunction with amphotericin B for immediate efficacy. Treatment should be continued for at least 60 days past clinical resolution, and for cryptococcosis until the cryptococcal antigen titer is zero
- Dermatophytosis: 5–10 mg/kg PO q24h until two negative fungal cultures are obtained 2 weeks apart
- Hyperadrenocorticism: 10–15 mg/kg PO q12h administered long-term if improvement is noticed. Start with 10 mg/kg PO q12h for 7–14 days. Perform an ACTH stimulation test at 7–14 days, and if no response increase the dose to 15 mg/kg q12h. At least 20% of the cases fail to respond to this treatment regimen, and success is typically associated with high doses. A recent report showed that 90% (43/48) of dogs treated with ketoconazole at the dose of 5–25 mg/kg (median dose 12.5 mg/kg) PO q12h had evidence of clinical improvement (Lien and Huang 2008). Only 47% of the dogs had some improvement in dermatologic signs
- In conjunction with cyclosporine to reduce dose: 5–10 mg/kg PO q24h
- Leishmaniasis: 7–25 mg/kg PO q24h for 40 to 90 days

**Cats:** use very cautiously or avoid.

- *Malassezia* dermatitis: 5 mg/kg PO q24h for 14–30 days and re-evaluate. Dermatologists typically use itraconazole to treat feline *Malassezia* dermatitis because of better tolerance
- Dermatophytosis: 5 mg/kg PO q24h until two or three negative fungal cultures are obtained 2 weeks apart. Dermatologists typically use itraconazole or terbinafine to treat feline dermatophytosis because of better efficacy and tolerance
- Systemic mycosis: 10 mg/kg or 50 mg per cat PO q12–24h for at least 60 days past clinical resolution and for cryptococcosis until the cryptococcal antigen titer is zero

**Note:** Do not administer concurrently with antacids, anticholinergics (e.g., propantheline), omeprazole, or $H_2$ blockers (e.g., cimetidine, ranitidine), because these drugs will decrease ketoconazole absorption.

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 200 mg; *Nizoral*®, generic

## SIDE EFFECTS

### Dogs

- Common: anorexia, vomiting and/or diarrhea
- Uncommon: reversible lightening of hair coat (typically after 3–4 months of therapy), pruritus and alopecia. Hepatotoxicity or increase in liver enzymes may be idiosyncratic or dose-related
- Rare: cataract development (associated with long-term therapy) and thrombocytopenia

### Cats

- Common: anorexia, vomiting, diarrhea, hepatotoxicity or increase in liver enzyme
- Rare: cholangiohepatitis

## DRUG INTERACTIONS

**Antacids:** antacids reduce oral absorption of ketoconazole; give these drugs at least 1 hour before or 2 hours after administration of ketoconazole

**Antidepressants, tricyclic (e.g., amitriptyline, clomipramine):** the metabolism of these drugs may be reduced by ketoconazole and side effects increased

**Antihistamines:** antihistamines are substrates for CYP enzymes and ketoconazole should be used cautiously with antihistamines [can predispose to the cardiotoxicity of astemizole (*Hismanal*®) and terfenadine (*Seldane*®)]

**Benzodiazepines, buspirone, busulfan, digoxin:** blood levels may be increased by concurrent use with ketoconazole

**Cisapride, cyclosporine:** inhibition of metabolism of these drugs through inhibition of CYP enzymes increasing their plasma levels

**Ivermectin:** increase in serum concentration of ivermectin, possibly by inhibiting its elimination through interfering with P-glycoprotein transport function; risks for neurotoxicity will increase with concurrent use

**Macrolide antibiotics (clarithromycin, erythromycin):** may increase ketoconazole serum levels

**Methylprednisolone:** may extend methylprednisolone duration of activity

**Mitotane:** the adrenolytic effect of mitotane may be inhibited by ketoconazole's inhibition of CYP enzymes

**Phenytoin:** may reduce serum levels of ketoconazole by inducing CYP enzymes

**Rifampin:** may reduce serum levels of ketoconazole by inducing CYP enzymes

**Theophylline:** ketoconazole may reduce serum levels of theophylline

**Warfarin:** inhibition of warfarin metabolism through inhibition of CYP enzymes, increasing its plasma levels

## MONITORING

- Efficacy and adverse effects
- Liver enzymes should be monitored regularly with long-term treatment or in geriatric animals

## Leflunomide

**Trade/brand name:** *Arava*® (US, CA, UK) (Rx)
**Classification:** Immunomodulatory (immunosuppressive)

### INDICATIONS

**Dogs:** Systemic and cutaneous reactive histiocytosis.

**Cats:** Progressive histiocytosis.

### CONTRAINDICATIONS

Leflunomide hypersensitivity, pregnancy, bone marrow suppression, pre-existing infection, liver dysfunction, other immunosuppressive or hepatotoxic drugs, live virus vaccines.

### MECHANISM OF ACTION

Leflunomide reversibly inhibits the enzyme dihydroorotate dehydrogenase involved in de-novo pathway of pyrimidine synthesis, resulting in decreased DNA and RNA synthesis and inhibition of cell proliferation. Its antiproliferative effect involves T and B lymphocytes, smooth muscle cells, and fibroblasts. Leflunomide is metabolized to the active form A77 1726 by the intestinal mucosa.

### DOSAGES

Very limited available reports on the use of this drug in dogs and cats, and doses reported are anecdotal.

**Dogs:** 2–4 mg/kg PO over 24 hours to obtain a serum through level of 20 mcg/mL.

**Cats:** 2–4 mg/kg PO over 24 hours. Cats metabolize the drug much slower than dogs and may require half the oral dose to attain adequate blood levels.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 10 mg and 20 mg; *Arava*®, generic

### SIDE EFFECTS

**Dogs**: vomiting, anemia and lymphopenia. Gastrointestinal toxicity may occur at doses used in humans as a result of accumulation of the metabolite trimethyl-fluoroanaline

**Cats:** no information available

**Note:** Diarrhea, nausea, alopecia, cutaneous lupus erythematosus, toxic epidermal necrolysis (TEN), Stevens–Johnson syndrome, hypertension, hepatotoxicity, myelosuppression, peripheral neuropathy, and interstitial lung disease have been reported in humans.

### DRUG INTERACTIONS

**Activated charcoal:** can decrease the concentration of leflunomide active metabolite A77 1726

**Methotrexate:** may increase the risk of pancytopenia induced by methotrexate

**Phenytoin:** can increase phenytoin serum levels

**Rifampin:** can increase A77 1726 peak levels

**Warfarin:** may enhance the effect of warfarin

### MONITORING

- Efficacy and adverse effects
- Monitor liver enzymes, CBC, and trough levels (target 20 mcg/mL) during treatment

## Levamisole Hydrochloride

**Trade/brand name:** *Ergamisol®* (US, CA), generic (Rx)
**Classification:** Immunomodulatory (immunostimulant), Antiparasitic

### INDICATIONS

Used as an immunomodulatory.

**Dogs:** Idiopathic recurrent pyoderma, systemic lupus erythematosus.

**Cats:** Eosinophilic granuloma.

**Note:** In humans, it can be used as adjunctive therapy for malignant melanoma, with conflicting results.

### CONTRAINDICATIONS

Levamisole is not approved for lactating animals. Use cautiously in animals with high burdens of heartworm microfilaria, since reactions due to extensive microfilaria kill rate are possible. Avoid in severely debilitated animals or animals with severe renal or hepatic disease.

### MECHANISM OF ACTION

The immunomodulatory mechanism of action of levamisole is not well known; however, it is reported to restore the host defense by non-specific stimulation of T-cell-mediated immunity. Levamisole is also reported to stimulate monocyte and neutrophil phagocytosis and intracellular killing of bacteria. It is most effective in immune-compromised individuals, and it has minimal to no effect in immune-competent animals because stimulation above normal levels does not appear to occur.

### DOSAGES

It is important to be aware that the immunostimulatory dose range of levamisole is narrow and not well defined, and inappropriate dosage may cause immunosuppression rather than immunostimulation.

#### Dogs

- Idiopathic recurrent pyoderma: 2.2 mg/kg PO q48h (efficacy reported in 10% of cases) or 0.5–2 mg/kg PO 3 times/week; use in conjunction with appropriate antibiotic therapy

- Systemic lupus erythematosus: 2.5–5 mg/kg PO q48h in conjunction with prednisone at the initial dose of 0.5 to 1 mg/kg PO q12h. The prednisone is tapered off within 1–2 months and the levamisole is continued as maintenance therapy. This protocol was reported to show good response in 75 % of cases, with remissions of months to years

**Cats**
- Eosinophilic granuloma: 5 mg/kg PO three times/week

### FORMULATIONS

**Veterinary-labeled products:** Approved for large animals only

**Human-labeled products**
- Oral tablets: 50 mg; *Ergamisol*®, generic

### SIDE EFFECTS

**Dogs:** vomiting, diarrhea, anorexia, lethargy, salivation, muscular tremors, adverse cutaneous drug reaction, blood dyscrasias

**Cats:** hypersalivation, excitement, mydriasis, vomiting

### DRUG INTERACTIONS

**Aspirin:** may increase aspirin serum levels

**Chloramphenicol:** fatality may occur with concurrent use

**Cholinesterase-inhibiting drugs (e.g., organophosphate, neostigmine), nicotine-like compounds (e.g., pyrantel, morantel, diethylcarbamazine):** these drugs may enhance levamisole toxic effects

**Warfarin:** may increase warfarin bleeding effects

### MONITORING
- Efficacy and adverse effects.

## Levothyroxine Sodium

**Trade/brand name:** *Soloxine*® (US, CA), *Thyro-Tabs*® (US, CA), *Synthroid*® (US, CA), *Eltroxin*® (US, CA), *Levotec*® (CA), *Thyroxyl*® (UK) (Rx)
**Classification:** Hormone

### INDICATIONS

**Dogs and cats:** Treatment of hypothyroidism.

### CONTRAINDICATIONS

Use with caution in hypoadrenocorticism (increased metabolism of adrenal hormones may precipitate a hypoadrenocortical crisis), diabetes mellitus (increase in body metabolism may potentiate ketoacidosis by increasing ketone synthesis), congestive heart failure (increase in body metabolism may result in unnecessary stress on the heart).

### MECHANISM OF ACTION

Thyroid hormones influence various metabolic processes. They stimulate calorigenesis, enzyme and protein synthesis, and synthesis, mobilization, and degradation of carbohydrates and lipids. They are essential for the development of the neural and skeletal systems. Moreover, thyroid hormones have chronotropic and inotropic effects on the heart, stimulate erythropoiesis, increase bone formation and resorption, and influence the rate of secretion and degradation of all other hormones.

### DOSAGES

Administer levothyroxine ideally on an empty stomach, since food may reduce bioavailability by about 45%.

**Dogs:** Start therapy with a brand-name product at 0.02 mg/kg PO q12h (maximum 0.8 mg PO q12h). However, a recent study showed that levothyroxine *solution* administered *once daily* at the initial dose of 0.02 mg/kg controlled hypothyroidism in 85% of the treated dogs (Traon *et al*. 2009). Re-evaluate response in 4–8 weeks and readjust the dose based on improvement of symptoms, serum T4 concentration, and signs of thyrotoxicosis. Serum T4 concentration should be evaluated 4–6 hours after levothyroxine administration (peak level) if given twice daily, and it should be in the upper half of, or slightly above, the reference interval. If the dosing frequency is once daily, blood samples should be collected 24 hours after levothyroxine administration (through level), and the hormone concentration should be in the middle of the reference interval (>1.5 mcg/dL or 19.3 nmol/L).

**Note:** In animals with concurrent diseases, especially heart failure, start with 25% of the recommended dose and increase by 25% weekly if no complications are noted.

*For myxedema coma*: 4–5 mcg/kg IV q12h initially. After the animal is stabilized, oral administration can be considered.

**Cats:** Start therapy at 0.05–0.1 mg per cat PO q24h. Monitor response to therapy and adjust drug accordingly as described above for dogs.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs

- Oral tablets: 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, and 0.8 mg; *Levosyn®*, *Thyrosyn®*, *Thyroxine-L Tablets®*, *Thyrozine®*, *Thyrokare®*
- Oral tablets: 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg, and 1 mg; *Soloxine®*, *Thyro-Tabs®*
- Oral chewable tablets: 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, and 0.8 mg; *Nutrived® T-4 Chewable Tablets*, *Heska Thyromed Chewable Tablets®*, *Canine Thyroid Chewable Tablets®*
- Oral solution: 1 mg/mL in 30 mL btl; *Leventa®*

**Human-labeled products**

- Oral tablets: 0.025 mg, 0.05 mg, 0.075 mg, 0.088 mg, 0.1 mg, 0.112 mg, 0.125 mg, 0.137 mg, 0.15 mg, 0.175 mg, 0.2 mg, and 0.3 mg; *Eltroxin®*, *Synthroid®*, *Levothroid®*, *Levoxyl®*, *Thyro-Tabs®*, *Unithroid®*, generic
- Lyophilized powder for injection: 200 mcg and 500 mcg in 10 mL vials; generic

### SIDE EFFECTS

**Dogs**

- Rare: associated with excessive amounts of levothyroxine sodium supplementation or concurrent hepatic or renal disease due to impaired drug metabolism. Side effects include panting, polyuria, polydipsia, polyphagia, weight loss, nervousness, excitability, and tachycardia. Adjust the dose accordingly and discontinue therapy for a few days if side effects are severe. Resolution of clinical signs should occur after 1–3 days of dose adjustment. Measure post-pill serum concentrations after 2–4 weeks of dose readjustment

**Cats**

- Rare: anorexia and listlessness

### DRUG INTERACTIONS

**Amiodarone:** may reduce T3 and T4 metabolism

**Antacids (oral), cholestyramine, ferrous sulfate, high fiber diet, sucralfate:** may decrease levothyroxine absorption; administer 4 hours apart

**Catecholamines and sympathomimetics:** enhanced action of these drugs

**Digoxin or digitoxin:** therapeutic effect of digoxin or digitoxin may be reduced

**Insulin:** may increase insulin requirements

**Ketamine:** tachycardia and hypertension may develop

**Tricyclic/tetracyclic antidepressants:** increase in cardiac arrhythmias and risk for CNS stimulation

**Warfarin:** may increase the catabolism of vitamin-dependent coagulation factors; the anticoagulation effects of warfarin may therefore be potentiated

**Drugs that may reduce serum T4 concentrations:** corticosteroids; nonsteroidal anti-inflammatory drugs (NSAIDs); potentiated sulfas; phenylbutazone; phenytoin; phenobarbital; clomipramine

### MONITORING

- Response to therapy
- Serum T4 concentration at 4–8 weeks after initiating therapy. Collect samples 4–6 hours post-pill (peak level) if administering drug twice daily and 24 hours post-pill (through level) if administering drug once daily

## Lincomycin Hydrochloride

**Trade/brand name:** *Lincocin*® (US, CA, UK) (Rx)
**Classification:** Antibacterial (lincosamide)

### INDICATIONS

**Dogs and cats:** Pyoderma or other soft tissue infections caused by susceptible aerobic Gram-positive cocci, including *Staphylococcus* and *Streptococcus*, and

anaerobic organisms including *Bacteroides fragilis*, *Fusobacterium*, *Clostridium perfringens*, *Peptostreptococcus*, *Actinomyces*, and *Peptococcus*. Other organisms generally susceptible to lincomycin include *Erysipelothrix*, *Mycoplasma*, *Nocardia asteroides*, and *Corynebacterium diphtheriae*.

**Note:** The empirical use of lincomycin to treat bacterial skin infections should be avoided because of the common development of resistance.

### CONTRAINDICATIONS

Individuals with hypersensitivity to the drug. As lincomycin is bacteriostatic, it should be avoided in immune-compromised dogs and cats.

### MECHANISM OF ACTION

Similarly to other lincosamide antibiotics (e.g., clindamycin), lincomycin inhibits bacterial protein synthesis by reversibly binding to the 50S ribosomal subunit of sensitive organisms. Complete cross-resistance occurs between lincomycin and clindamycin, and at least partial cross-resistance occurs between these two antibiotics and the macrolide erythromycin. Lincosamides are typically bacteriostatic at the recommended dose, but can be bactericidal, depending on the susceptibility of the organism and drug concentration at the infection site.

### DOSAGES

Lincomycin should ideally be administered on an empty stomach.

**Dogs:** 15 mg/kg PO q8h or 22 mg/kg PO q12h for 7–14 days past resolution of clinical signs. Success rates of 100% and 69% were reported for the treatment of superficial and deep pyoderma, respectively.

**Cats:** 15–22 mg/kg PO q12h.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats
- Oral tablets: 100 mg, 200 mg, 500 mg; *Lincocin®*
- Oral solution: 50 mg/kg in 20 mL vials; *Lincocin® Aquadrops*

**Human-labeled products**
- Oral capsules: 500 mg; *Lincocin®*
- Injection: 300 mg/mL in 2 mL and 10 mL vials; *Lincocin®*

### SIDE EFFECTS

**Dogs**
- Common: vomiting and diarrhea
- Rare: hemorrhagic diarrhea

**Cats**
- Common: vomiting and diarrhea

### DRUG INTERACTIONS

**Erythromycin, chloramphenicol:** these drugs may antagonize the effect of lincomycin

**Kaolin, bismuth subsalicylate, pectin:** these drugs reduce absorption of lincomycin

**Neuromuscular blocking agents:** should be used carefully with lincomycin, because of its intrinsic neuromuscular blocking effect

### MONITORING

- Efficacy and adverse effects
- Plasmid-mediated resistance is common and bacterial culture and susceptibility should be performed if recurrence of infection occurs in patients previously treated with lincomycin

## Lomustine

**Trade/brand name:** *CCNU®* (US, UK), *CeeNU®* (US, CA), *Lomustine®* (UK), generic (Rx)
**Classification:** Antineoplastic, Chemotherapeutic

### INDICATIONS

**Dogs and cats:** Epitheliotropic and non-epitheliotropic lymphomas, mast cell tumor, histiocytic sarcoma.

### CONTRAINDICATIONS

Avoid use in patients hypersensitive to lomustine. Caution if using with other myelosuppressive agents (e.g., chloramphenicol, flucytosine, colchicine) or immunosuppressive drugs (e.g., azathioprine, cyclosphosphamide, corticosteroids) and live virus vaccines. Use with caution or avoid in patients with anemia, bone marrow suppression, pulmonary function impairment, current infections, renal or hepatic impairment, or previous chemotherapy or radiotherapy.

### MECHANISM OF ACTION

Lomustine, also known as CCNU [1-(2-chloroethyl)–3-cyclohexyl-1-nitrosourea], is an alkylating agent and a member of the nitrosourea family. The alkylating metabolite binds preferentially at the O-6 of guanine, causing inter-strand crosslinking and cytotoxicity. It is lipophilic, resulting in high oral absorption and membrane penetration.

### DOSAGES

**Dogs:** 50–90 mg/m$^2$ (typical dose: 60–75 mg/m$^2$) PO every 21–28 days until a measurable response is achieved. Most dogs will have a response in 3–6 weeks. Although typically 4–6 treatments with lomustine are planned at initiation of therapy, the total number of treatments given depends on tumor response and tolerability of the patient to the chemotherapy. If progressive disease is observed during this period of time, consider an alternative treatment. In a retrospective study where 36 dogs with epitheliotropic lymphoma were treated with lomustine, the median starting dose was 70 mg/m$^2$ and the median number of treatments administered was three (Williams *et al*. 2006). A measurable response was seen in 78% of the cases, with 16% achieving complete response. The overall median response duration was 106 days. Another retrospective study evaluating 46 dogs with epitheliotropic lymphoma reported a median lomustine dose of 60 mg/m$^2$ and a median of four treatments administered (Risbon *et al*. 2006). Complete remission was recorded in 33% of the cases, but 83% of the dogs experienced a measurable response. The overall median

response duration was 86 days. When lomustine was used to treat 23 dogs with mast cell tumor at the dose of 90 mg/m$^2$, a measurable response rate was noted in 42% of the cases and the response duration ranged from 21 to 440 days (Rassnick *et al*. 1999). Greater response rates have been achieved combining lomustine with vinblastine for the treatment of canine mast cell tumors (Cooper *et al*. 2009).

Treatment of 59 dogs with histiocytic sarcoma with lomustine at the dose range of 60–90 mg/m$^2$ resulted in an overall response rate of 46% and a median survival time of 106 days (Skorupski *et al*. 2007).

**Cats:** 50–60 mg/m$^2$ PO every 21–42 days or 10 mg per cat. In a retrospective study in which 38 cats with mast cell tumor were treated with lomustine, the median dose was 56 mg/m$^2$ (range: 48–65 mg/m$^2$) and the overall response rate was 50% (7 cats had a complete response and 12 cats had a partial response) (Rassnick *et al*. 2008). The median number of treatments was two (range: 1–12). Although typically 4–6 treatments with lomustine are planned at initiation of therapy, the total number of treatments given depends on tumor response and individual tolerability of the chemotherapy. If progressive disease is observed during this period, consider an alternative treatment.

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 10 mg, 40 mg, 100 mg with mannitol; *CCNU®*, *CeeNu®*, generic

## SIDE EFFECTS

**Dogs**

- Common: myelosuppression in the form of neutropenia and thrombocytopenia. Nadir neutropenia typically occurs 7–10 days post-treatment and thrombocytopenia at 7–21 days; higher doses and prolonged treatment duration are more likely to cause myelosuppression; increase in liver enzymes (typically ALT)
- Uncommon: hepatotoxicity has been reported to occur in 11/179 (6.1%) cases, with 7/11 dying of progressive liver disease (Kristal *et al*. 2004). A recent randomized clinical trial showed that Denamarin has a protective effect against lomustine-induced hepatotoxicity (Skorupski 2010). Other uncommon side effects include vomiting, diarrhea, weight loss, lethargy, unexplained fever, renal toxicosis, bicavitary effusion

**Cats**

- Common: neutropenia (median and mean day of neutrophil nadir was 14 and 15 days, respectively, in one study), thrombocytopenia (nadir platelet count occurred after 14–21 days of therapy in one study)
- Rare: anorexia, vomiting, diarrhea, increase in liver enzymes (typically ALT), pleural effusion

**Note:** Lomustine is potentially embryotoxic and teratogenic.

## DRUG INTERACTIONS

**Cimetidine**: enhances lomustine toxicity in humans

**Immunosuppressive drugs (e.g., azathioprine, cyclosphosphamide, corticosteroids):** may increase risk of infections

**Myelosuppressive drugs (e.g., chloramphenicol, flucytosine, amphotericin B, colchicine):** potential additive bone marrow suppression

**Phenobarbital:** hydroxylation by hepatic microsomal enzymes is required for the production of antitumor metabolites; therefore, lomustine should be used carefully with drugs that induce liver enzyme activity

### MONITORING

- Efficacy and adverse effects
- Liver profiles prior to starting lomustine therapy and prior to each subsequent administration, and for a period of time after treatment discontinuation. Hepatic damage in dogs has been shown to be cumulative and may occur as late as 49 weeks after the last dose of lomustine
- CBCs before each lomustine administration and 7–10 days post-treatment

## Loratadine

**Trade/brand name:** *Claritin®* (US, CA), *Claritin® RediTabs®* (US), *Tavist ND®* (US), *Alavert®* (US), *Clarityn®* (UK), generic
**Classification:** Antihistamine (second-generation)

### INDICATIONS

**Dogs and cats:** Histamine-mediated pruritic and allergic skin conditions. A double-blind, placebo-controlled randomized clinical trial evaluating the efficacy of loratadine to treat dogs with atopic dermatitis was unable to show sustained relief of pruritus in any of the treated patients (Paradis 1996). Moreover, currently there is insufficient evidence in favor of or against recommending second-generation antihistamines to treat dogs with atopic dermatitis.

**Note:** If antihistamines are tried for the management of allergic skin diseases, they should be given as preventative therapy and on a daily basis to keep the histamine receptors blocked before histamine is released.

### CONTRAINDICATIONS

Hypersensitivity to loratadine. Use carefully in patients with urinary tract retention, angle-closure glaucoma, or pyeloduodenal obstruction. Loratadine may reduce seizure threshold. Safety in pregnant dogs and cats is unknown. Antihistamines will interfere with intradermal testing results. Drug withdrawal is usually recommended for at least 2 weeks prior to allergy testing.

### MECHANISM OF ACTION

Loratadine is a second-generation antihistamine of the piperidine class. It binds to $H_1$ receptors, blocking histamine binding.

### DOSAGES

Doses are empirical and not based on pharmacokinetic studies.

**Dogs:** 5–15 mg PO q24h used in one report. Other recommendations: 0.25–0.5 mg/kg PO q24h; 10 mg PO q12h if >18 kg (40 lb); 10 mg PO q24h or 5 mg PO q12h if 6.8–17.7 kg (15–39 lb); 5 mg PO q24h if <6.8 kg (15 lb)

**Cats:** 5 mg PO q24h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 5 mg and 10 mg; *Claritin®*, *Claritin® RediTabs®* (disintegrating), *Alavert®* (disintegrating), *Clarityn®*, *Loradamed®*, *Tavist ND®*, generic
- Oral syrup (preserved in propylene glycol and should not be used in cats): 1 mg/mL; *Claritin®*, *Clarityn®*, generic

**Note:** Some brands such as *Claritin-D®* (US) and *Chlor-Tripolon ND®* (CA) contain pseudoephedrine. Do not use these formulations to treat allergic dermatitis in dogs and cats.

### SIDE EFFECTS

**Dogs and cats:** none reported

**Note:** xerostomia, headache, somnolence and fatigue have been reported in humans.

### DRUG INTERACTIONS

**Amiodarone:** may result in increased risk of QT interval prolongation and torsade de pointes

**Cimetidine, erythromycin, fluconazole, fluoxetine, ketoconazole, quinidine:** these drugs may increase loratadine blood levels through inhibition of cytochrome P450 isoenzymes CYP3A4 and CYP2D6 and cause mild drowsiness

### MONITORING
- Efficacy and adverse effects

## Lorazepam

**Trade/brand name:** *Ativan®* (US, CA, UK), *Alzapam®* (US), *Lorazepam Intensol®* (US), *Loraz®* (US), *Apo-Lorazepam®* (CA), generic (Rx)
**Classification:** Tranquilizer, CNS depressant, Benzodiazepine

### INDICATIONS

Management of psychogenic dermatoses mostly associated with anxiety. Benzodiazepines, such as lorazepam, are short-term anxiolytics and therefore may be more effective for acute or time-limited stress. It is important to note that concurrent environmental and behavior management may increase the efficacy of pharmacologic intervention.

**Dogs:** Self-mutilations, acral lick dermatitis, excessive tail or nail biting/chewing, excessive anal or foot licking, flank sucking, tail dock neuroma.

**Cats:** Excessive grooming or psychogenic self-induced alopecia, tail sucking, excessive nail or foot biting/chewing, hyperesthesia syndrome.

### CONTRAINDICATIONS

Patients with hypersensitivity to lorazepam and other benzodiazepines, or with severe respiratory insufficiency. Avoid use in nursing animals. When using regularly, make sure to withdraw the drug gradually to avoid a rebound effect.

### MECHANISM OF ACTION

The exact mechanism of action of lorazepam is unknown. Postulated mechanisms include potentiation of the effects of GABA by binding to specific benzodiazepine receptors, antagonism of serotonin, and attenuation of the release or turnover of acetylcholine in the CNS.

### DOSAGES

**Dogs:** 0.025–0.25 mg/kg PO q12–24h

**Cats:** 0.025–0.2 mg/kg PO q12–24h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 0.5 mg, 1 mg, 2 mg; *Ativan®*, *Alzapam®*, *Apo-Lorazepam®*, *Loraz®*, generic
- Oral solution: 2 mg/mL in 10 mL and 30 mL bottles with dropper; *Lorazepam Intensol®*, generic
- Solution for injection: 2 mg/mL and 4 mg/mL in 1 mL prefilled syringes, 1 mL single use vials and 10 mL multidose vials; *Ativan®*, generic

### SIDE EFFECTS

**Dogs and cats**: increased appetite, paradoxical excitement, vocalization, aggression, anxiety, sleep disturbances, physiologic dependence

**Note:** In contrast to diazepam, hepatocellular toxicity is unlikely to occur in cats taking lorazepam, because no active intermediate metabolite is formed. Benzodiazepines may interfere with learning and short-term memory.

### DRUG INTERACTIONS

**CNS depressant drugs (e.g., opiates, barbiturates, sedatives, anticonvulsants):** concurrent use with lorazepam will result in additive CNS effects

**Ketoconazole:** inhibits lorazepam metabolism

**Probenecid:** decreases lorazepam renal clearance

**Scopolamine:** increased CNS depression and irrational behavior can occur if used concurrently with lorazepam

**Theophylline:** decreased sedation from lorazepam

**Valproate:** increases lorazepam serum concentration

### MONITORING

- Efficacy and adverse effects

- If cat develops inappetence, lethargy, ataxia or vomiting, medication needs to be discontinued
- Liver function tests (especially serum ALT and AST) should be performed in cats at baseline and within 5 days of treatment initiation

## Lufenuron ± Milbemycin Oxime

**Trade/brand name:** *Program®* (US, CA, UK), *Sentinel®* (US, CA, UK) (Rx)
**Classification:** Antiparasitic (insect growth regulator)

### INDICATIONS

**Dogs and cats:** Lufenuron is marketed for flea control in dogs and cats 4–6 weeks of age or older. It inhibits flea eggs from developing into adults and it is often used in combination with an adulticide product. Despite the optimistic results of a study showing rapid clinical and mycological resolution of dermatophytosis in cats and dogs treated with lufenuron (Ben-Ziony and Arzi 2000), additional reports and the experience of various dermatologists do not corroborate the findings of this study. Lufenuron is not currently recommended as sole therapeutic or preventive agent for feline or canine dermatophytosis, but it can be used as adjunctive therapy.

### CONTRAINDICATIONS

The cat injectable formulation may cause severe local reaction in dogs.

### MECHANISM OF ACTION

Lufenuron is a benzoylurea compound and inhibits chitin synthesis, polymerization, and deposition. Chitin is an important component of the exoskeleton of insects. It is also present in fungal cell wall – thus the rationale for using lufenuron to treat dermatophytosis.

### DOSAGES

**Dogs**

- Flea control: 10 mg/kg PO q30 days

**Cats**

- Flea control: 30 mg/kg PO q30 days or injection of 10 mg/kg SC every 6 months
- Dermatophytosis (see comments above under indication): 80 mg/kg PO for house cats; 100 mg/kg PO for cats housed in catteries. Retreat after 14 days and monthly thereafter

### FORMULATIONS

**Veterinary-labeled products**: Approved for dogs and cats

- Oral suspension (*for cats ≥6 weeks of age*): 135 mg (cats ≤4.5 kg or 10 lb); 270 mg (cats 5–9 kg or 11–20 lb); packs should be combined appropriately for cats >9 kg or 20 lb: 6-tube color-coded packs; *Program® Oral Suspension*
- 6-month injectable (*for cats ≥6 weeks of age*): 100 mg/mL in 10-syringe packages: 40 mg (cats ≤4 kg or 8.8 lb); 80 mg (cats 4.1–8 kg or 8.9–17.6 lb); *Program® 6 Month Injectable*
- Oral flavor tablets (*for dogs and cats ≥4 weeks of age*)

  - Dogs: 45 mg (dogs ≤4.5 kg or 10 lb); 90 mg (dogs 5–9 kg or 11–20 lb); 204.9 mg (dogs 9.5–20 kg or 21–45 lb); 409.8 mg (dogs 21–41 kg or 46–90 lb); packs should be combined appropriately for dogs >41 kg or 90 lb; *Program® Oral Flavor Tabs*
  - Cats: 90 mg (cats ≤2.7 kg or 6 lb); 204.9 mg (cats 3.2–6.8 kg or 7–15 lb); packs should be combined appropriately for cats >6.8 kg or 15 lb; *Program® Oral Flavor Tabs*
- Oral flavor tablets: milbemycin oxime/lufenuron (*for dogs ≥4 weeks of age*): 2.3 mg/46 mg (dogs 0.9–4.5 kg or 2–10 lb), 5.75 mg/115 mg (dogs 5–11.4 kg or 11–25 lb), 11.5 mg/230 mg (dogs 11.8–22.7 kg or 26–50 lb), 23 mg/460 mg (dogs 23.2–45.5 kg or 51–100 lb); dogs 46–56.8 kg or 101–125 lb should receive the appropriate combination tablet of milbemycin and lufenuron. Labeled for monthly use; *Sentinel® Flavor Tabs* [may be combined with nitenpyram (*Capstar®*)]

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs and cats**
- Rare (<5 animals in 1 million doses): vomiting, diarrhea, lethargy/depression, pruritus, urticaria, erythema. The cat injectable formulation may cause a small nodule at the injection site

### DRUG INTERACTIONS
None reported

### MONITORING
- Efficacy and adverse effects

## Lysine (L-Lysine)

**Trade/brand name:** *Enisyl®* (US, CA, UK), *Viralys®* (US), *Duralactin®* (US), *Vetri-lysine®* (US), generic
**Classification:** Antiviral, Amino acid

### INDICATIONS

**Cats:** Treatment of herpes virus type 1 (FHV-1) dermatitis; however, no studies have been conducted on client-owned cats to document clinical effect, and the few reports that are available are anecdotal.

### CONTRAINDICATIONS
None has been reported.

### MECHANISM OF ACTION
Arginine is an essential amino acid for FHV-1 replication, and lysine is thought to antagonize the growth-promoting effect of arginine.

### DOSAGES
No studies have been conducted to determine the ideal dose regimen for feline herpetic dermatitis.

**Cats:** 250–500 mg per cat PO q12–24h

**Note:** Lysine should be used long-term only if helping reduce clinical signs.

### FORMULATIONS

**Veterinary-labeled products:** Approved for cats
- Oral gel: 5 oz, each 1.25 mL contains about 250 mg of lysine; *Viralys® Gel*
- Oral powder: 100 g, each 322 mg contains about 250 mg of lysine; *Viralys® Powder*
- Oral paste (cats may not like the taste): 100 mL or 300 mL, each mark in the syringe corresponds to 1 mL or 250 mg of lysine; *Enisyl-F® Paste*
- Oral solution/pump: 100 mL, each mL contains 250 mg of lysine; *Enisyl-F®* 100 mL Dose Pump
- Oral suspension: 32.5 mL, 2.5 mL (half-teaspoon) contains 250 mL of lysine; *Duralactin® Feline L-lysine*
- Oral chewable tablets (soft chews – chicken liver flavor): 250 mg of lysine per 2 chews; *Vetri-lysine Plus Soft Chews®*

**Human-labeled products**
- Oral tablets, capsules, powder or other formulations: 250–1000 mg. Tablets can be crushed or capsules can be emptied and then mixed with food to facilitate administration; generic

### SIDE EFFECTS

**Cats**: rare side effects include diarrhea and vomiting

**Note:** Avoid preparations containing propylene glycol as they can be toxic for cats. Do not reduce the dietary intake of arginine because cats are very sensitive to arginine deficiency.

### DRUG INTERACTIONS

**Calcium:** concomitant oral administration may increase the gastrointestinal absorption of calcium and reduce its excretion in the urine

### MONITORING
- Efficacy and adverse effects

## Marbofloxacin Hydrochloride

**Trade/brand name:** *Zeniquin®* (US, CA), *Marbocyl®* (UK) (Rx)
**Classification:** Antibacterial (second-generation fluoroquinolone)

### INDICATIONS

**Dogs and cats:** Marbofloxacin is registered to treat feline and canine skin and soft tissue infections associated with susceptible bacteria such as *Staphylococcus*, *Pseudomonas*, *Proteus*, *Escherichia coli*, and *Pasteurella*. It can also be efficacious against *Mycobacterium* but has poor activity against anaerobes. Marbofloxacin, concurrently with topical therapy, may be beneficial for the treatment of chronic ear infections, particularly otitis media, caused by susceptible

organisms such as *Pseudomonas*. However, tissue concentration is not known for the external or middle ear canals, and this indication is controversial with unpredictable efficacy.

**Note:** The authors do not recommend the use of fluoroquinolones as first-line therapy for pyoderma. Fluoroquinolones should be considered primarily for chronic deep pyodermas associated with extensive scar tissue, because of their excellent tissue penetration. Antibiotic selection should be based on culture and susceptibility results.

### CONTRAINDICATIONS

Fluoroquinolones can be potentially toxic to condrocytes and should not be given to immature dogs during their rapid growth phase (small and medium-sized breeds between 2 and 8 months, large breeds younger than 12 months, giant breeds younger than 18 months). Marbofloxacin may cause CNS stimulation and should be used cautiously in patients with a history of seizure activity. The pathomechanism associated with CNS effect is believed to be inhibition of the inhibitory neurotransmitter GABA. It should not be used in dogs or cats with hypersensitivity to marbofloxacin or other fluoroquinolones.

### MECHANISM OF ACTION

Marbofloxacin is a bactericidal antibiotic and inhibits DNA supercoiling and synthesis by inhibition of bacterial DNA gyrase (i.e., topoisomerase II) and topoisomerase IV. Fluoroquinolones have been reported to have anti-inflammatory properties including inhibition of TNF-alpha synthesis and suppression of induced leukotriene production by neutrophils, lymphocytes, monocytes, and basophils. Similarly to other fluoroquinolones, marbofloxacin accumulates inside inflammatory cells, in particular macrophages.

### DOSAGES

**Dogs and cats:** 2.75–5.5 mg/kg PO q24h for 7–14 days past resolution of clinical signs

**Note:** For *Pseudomonas* infections where minimum inhibitory concentration (MIC) values are typically high, doses at the high end of the accepted range should be used.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats
- Oral tablets: 25 mg, 50 mg, 100 mg, 200 mg; *Zeniquin*®
- Oral tablets: 8 mg, 20 mg, 80 mg; *Marbocyl*® (available in UK only)

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs and cats:** Marbofloxacin is generally well tolerated but it may cause nausea, vomiting, diarrhea, soft stools, and lethargy. It can induce seizure when administered at high doses. It has not caused blindness in cats (as reported for enrofloxacin and nalidixic acid) with doses 3–5 times the high recommended dosage; nevertheless, use higher doses cautiously.

### DRUG INTERACTIONS

**Antacids containing divalent or trivalent cations (e.g., $Mg^{++}$, $Al^{++}$, $Ca^{++}$), iron, zinc:** decreased marbofloxacin absorption; separate administration of these products and marbofloxacin by at least 2 hours

**Aminoglycosides, third-generation cephalosporins, extended spectrum penicillins:** drug synergism may occur, especially against *Pseudomonas*

**Cimetidine:** use carefully, because cimetidine has been shown to interfere with the metabolism of fluoroquinolones

**Cyclosporine:** may reduce the metabolism of cyclosporine

**Methotrexate:** may increase methotrexate levels

**Nitrofurantoin:** may reduce the antimicrobial effect of fluoroquinolones

**Theophylline:** may increase theophylline blood levels

**Warfarin:** may increase the effects of warfarin

### MONITORING

- Efficacy and adverse effects

## Masitinib Mesylate

**Trade/brand name:** *Kinavet*® (US), *Masivet*® (EU) (Rx)
**Classification:** Antineoplastic

### INDICATIONS

**Dogs:** Masitinib mesylate is approved by the European Medicines Agency for the treatment of grade II or III cutaneous non-metastatic, non-resectable, or recurrent (post-surgery) mast cell tumors that have not previously received radiotherapy or chemotherapy except corticosteroids. A double-blind, randomized, placebo-controlled clinical trial showed that masitinib is effective in delaying mast cell tumor progression and appears to have better efficacy in patients that did not receive prior therapy (Hahn *et al*. 2008). Masitinib has been recommended for the treatment of canine atopic dermatitis. A recent randomized, double-blind, placebo-controlled trial showed significant decrease in pruritus scores and extent and severity of skin lesions in dogs with atopic dermatitis treated with masitinib compared to dogs receiving placebo (Cadot *et al*. 2011).

### CONTRAINDICATIONS

Do not use in patients with known hypersensitivity to the drug, in dogs used for breeding, and in pregnant or lactating bitches. Moreover, do not initiate masitinib treatment in dogs with any of the following clinical pathological abnormalities: albumin < 1 × lower limit of normal; urine protein-to-creatinine ratio > 1; blood urea nitrogen or creatinine > 1 upper limit of normal; hematocrit < 30% or hemoglobin < 10 g/dL; neutrophil count < 2000/mcL; AST or ALT > 3 × upper limit

of normal; or bilirubin >1.5 × upper limit of normal. Safety has not been evaluated in dogs under 2 years of age. Masitinib cannot be safely dosed in dogs <7 kg (15.4 lb) body weight. Refer to package insert for special precautions to be taken by the person administering masitinib.

## MECHANISM OF ACTION

Masitinib mesilate is a selective tyrosine kinase inhibitor of the c-Kit receptor. It has also shown to inhibit platelet-derived growth factor receptor (PDGFR)-alpha, PDGFR-beta and to a lesser extent fibroblast growth factor receptor (FGFR)-3 and the focal adhesion kinase (FAK) activation pathway. Another target of masitinib of interest to dermatologists is Lyn, an intracellular kinase that interacts with the high-affinity IgE receptor (FcεRI), inhibiting FcεRI-mediated degranulation of mast cells in vitro. This function of masitinib has spurred interest in investigating its effect in canine atopic dermatitis.

## DOSAGES

**Dogs:** 12.5 mg/kg PO q24h

**Note:** Treatment will require adjustments or permanent discontinuation in the following circumstances:

- Urinary protein-to-creatinine ratio >2 or albumin <0.75 × lower limit of normal: discontinue treatment until values return to normal, then resume at the same dose. If these events occur a second time, treatment should be permanently discontinued
- Hemoglobin <8 g/dL and free bilirubin >1.5 × upper limit of normal, or hemoglobin <8 g/dL and reticulocytes <80,000/mm$^3$: treatment should be discontinued
- In cases of ALT/AST increase >3 × upper limit of normal, neutrophil count <1500/mm$^3$, or any severe adverse event, adjust treatment as follows: at the first occurrence, treatment is interrupted until resolution and then resumed at the same dose level; if the event occurs a second time, treatment is interrupted until resolution and then dose is reduced to 9 mg/kg/day; if the event occurs a third time, treatment is interrupted until resolution and then dose is reduced to 6 mg/kg/day; if severe adverse reactions still occur at the 6 mg/kg/day dose, treatment should be discontinued

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs in EU

- Oral tablets (non-divisible): 50 mg, 150 mg; *Kinavet®*, *Masivet®*

**Human-labeled products:** None

## SIDE EFFECTS

**Dogs**

- Common: anorexia, vomiting, diarrhea
- Uncommon/rare: lethargy, weakness, behavioral changes, elevated liver enzymes, elevated bilirubin, ascites, neutropenia, lymphopenia, thrombocytopenia, peripheral edema, renal insufficiency, protein-losing nephropathy, nephrotic syndrome, glomerulonephritis, hemolytic anemia, non-regenerative anemia, alopecia

**Note:** A recent, randomized, double-blind, placebo-controlled trial evaluating the efficacy of masitinib to treat atopic dermatitis showed that proteinuria, hypoalbuminaemia, anorexia and increase in liver transaminases were more frequent in dogs treated with masitinib compared to dogs receiving placebo (Cadot *et al*. 2011).

### DRUG INTERACTIONS

**Drugs metabolized by the liver CYP enzymes 3A4 (e.g., alprazolam, astemizole, calcium channel blockers, carbamazepine, cisapride, cyclosporine, doxorubicin, erythromycin, fentanyl, midazolam, quinidine, tacrolimus, terfenadine, traizolam), 3A5, 2C9 (e.g., amitriptyline, diclofenac, ibuprofen, naproxen, phenytoin, piroxicam, sulfamethoxazole, tolbutamide, warfarin), and 2D6 (e.g., amitriptyline, clomipramine, codeine, desipramine, imipramine, paroxetine, timolol, tramadol):** the manufacturer states that concomitant treatment with these drugs may result in higher or lower plasma levels of either masitinib or those drugs, and they should be used with caution

### MONITORING

- Hypoalbuminemia and proteinuria every 2 weeks
- Azotemia, anemia, neutropenia, elevation of liver enzymes (AST, ALT), and hyperbilirubinemia every 4 weeks

## Megestrol Acetate

**Trade/brand name:** *Ovaban*® (US, CA), *Ovarid*® (UK) (Rx)
**Classification:** Hormone

### INDICATIONS

**Dogs:** Acral lick dermatitis.

**Cats:** Self-inflicted symmetrical alopecia, indolent ulcer, eosinophilic plaque, or eosinophilic granuloma.

**Note:** Megestrol acetate was originally marketed to suppress estrus in dogs. Because of the potential severe side effects associated with megestrol acetate, it is currently used by most veterinarians only when other treatment options have failed.

### CONTRAINDICATIONS

Pregnancy, diabetes mellitus, or mammary neoplasia.

### MECHANISM OF ACTION

Similarly to other progestational compounds, megestrol acetate suppresses the release of gonadotropin and ACTH. According to the dose and the target organ, it has variable effects on androgens and estrogens in different animal species. It also induces the release of growth hormone and acts on the hypothalamus and limbic systems. Megestrol acetate has a potent anti-inflammatory effect and, in the usual dose, it has been shown to cause stronger and longer-lasting adrenal

suppression than anti-inflammatory doses of prednisolone. It may interfere with intradermal and allergy serum test results. Drug withdrawal should be at least 4 weeks prior to allergy testing.

### DOSAGES

**Dogs:** 2–4 mg/kg PO q24h

**Cats:** Start with 2.5–5 mg per cat q48h. After remission is achieved reduce dose to 2.5–5 mg every 7–14 days as maintenance

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs only
- Oral tablets: 5 mg, 20 mg; *Ovaban®*, *Ovarid®*

**Human-labeled products**
- Oral tablets: 20 mg, 40 mg; *Megace®*, generic
- Oral suspension: 40 mg/mL, 125 mg/mL; *Megace®*, *Megace ES®*

### SIDE EFFECTS

**Dogs and cats:** decreased spermatogenesis, pyometra, estrus postponement, acromegaly, mammary gland fibroadenomatous hyperplasia in intact or neutered male or female cats, diabetes mellitus (mainly in cats and typically reversible), lethargy, polyuria/polydipsia, polyphagia, weight gain, hepatotoxicity (rare), adrenocortical suppression (may occur with low dosages and persist for many weeks), alopecia, cutaneous atrophy, xanthomas, poor wound healing

### DRUG INTERACTIONS

**Glucocorticoids:** may worsen adrenocortical suppression and increase the risks for diabetes mellitus

**Rifampin:** increase the metabolism of progestagens by inducing hepatic microsomal enzymes resulting in decreased progestagens activity

### MONITORING
- Efficacy and adverse effects
- Blood glucose should be monitored before and during therapy
- Adrenocortical function, liver enzymes, and body weight should be monitored during long-term therapy

## Meglumine Antimoniate

**Trade/brand name:** *Glucantime®* (EU) (Rx)
**Classification:** Antiparasitic (antiprotozoal)

### INDICATIONS

**Dogs:** Treatment of leishmaniasis as sole therapy or in combination with allopurinol. Parasitological cure is not typically obtained, and relapses are not uncommon after therapy is discontinued.

### CONTRAINDICATIONS

Previous hypersensitivity to antimony compounds, renal or hepatic failure, cardiac arrhythmias, leukopenia.

### MECHANISM OF ACTION

Pentavalent antimony compounds such as meglumine antimoniate interfere with metabolism of *Leishmania* parasites by selectively inhibiting the enzymes required for glycolytic and fatty acid oxidation.

### DOSAGES

**Dogs**

- 100 mg/kg SC q24h for 3–4 weeks or until resolution of clinical signs. Combination with allopurinol at 15–30 mg/kg q12h may reduce the frequency of relapses. Allopurinol should be continued daily or intermittently (1 week treatment per month) for 8–9 months
- 50–75 mg/kg SC q12h for 30–40 days combined with allopurinol at 20 mg/kg PO q12h for about 4–8 months

### FORMULATIONS

None available in the US.

**Veterinary-labeled products**

- Injectable solution: 300 mg/mL as antimony in 5 mL ampoules; *Glucantime*®

**Human-labeled products**

- Injectable solution: 1.5 g of meglumine antimoniate (equivalent to 425 mg of pentavalent antimony) per 5 mL; *Glucantim*® (Italy), *Glucantime*® (Brazil, France, Spain, Venezuela)

### SIDE EFFECTS

**Dogs:** anorexia, vomiting, nausea, lethargy, transient increase in liver enzymes, myalgia when administered intramuscularly; at higher doses, nephrotoxicity and electrocardiogram abnormalities may develop

### DRUG INTERACTIONS

**Tricyclic antidepressants, disopyramide, quinidine, procainamide:** these drugs can prolong QT interval, and meglumine antimoniate may prolong it further, increasing the risks for arrhythmias

### MONITORING

- Efficacy and adverse effects

## Melatonin

**Trade/brand name:** *Dermatonin*® (US, CA), *Regulin*® (UK), generic
**Classification:** Hormone, Nutraceutical

### INDICATIONS

**Dogs:** Melatonin is used to stimulate hair regrowth in canine seasonal flank alopecia, canine pattern baldness/alopecia, various follicular dysplasia syndromes

and alopecia X. No controlled studies have confirmed the efficacy of melatonin to manage these disorders.

### CONTRAINDICATIONS

Pregnancy or sexually immature animals. Animals that are nursing young may not benefit from implant therapy.

### MECHANISM OF ACTION

The mechanism involved in stimulating hair regrowth in these canine alopecic dermatoses is not well understood. It may be related to modulation of sex hormone levels, interference with cortisol production, blockage of estrogen receptors at the hair follicle level, or deficiency of melatonin.

### DOSAGES

Doses are anecdotal, and not based on controlled trials.

**Dogs**

- Oral formulation: 3 mg PO q8–12h for dogs ≤10–15 kg and 6 mg PO q8–12h for dogs ≥10–15 kg. Continue treatment until maximal response (typically 2 months for canine seasonal flank alopecia and canine pattern alopecia, and 4 months for alopecia X); thereafter, discontinue until relapse. Other recommendations suggest reducing the dose after maximal response to once daily for a month and then taper slowly until reaching a weekly maintenance dose regimen. To prevent episodes of seasonal flank alopecia, it is recommended to start treatment 1–2 months before the onset of alopecia
- Implant formulation: one melatonin implant per dog SC based on body weight: 8 mg (dogs <9 kg), 12 mg (dogs 9–18 kg), and 18 mg (dogs >18 kg). Re-treatment may be necessary 1–2 times a year. Improvement is usually seen in the first month or two, with maximal improvement in 3–4 months. Implant treatment may have better results than oral therapy

**Note:** For implant application technique, refer to manufacturer's package instructions.

### FORMULATIONS

**Veterinary-labeled products:** No oral formulations available

- Implant (marketed for dogs and cats): 8 mg, 12 mg, 18 mg; *Dermatonin*®
- Sustained-release implant (marketed for sheep and goats): 18 mg; *Regulin*® (available only in EU, including UK)
- Sustained-release implant (marketed for minks and foxes): 2.5 mg, 12 mg; different brands in several countries
- Implanter (marketed for ferrets): 5.4 mg; *Ferretonin*®

**Human-labeled products**

- Oral tablets and capsules: 0.5 mg, 5 mg; generic
- Sustained-release oral capsules: 2 mg, 3 mg; generic
- Oral solution: 0.5 mg/5 mL, 1 mg/1 mL; generic

**Note:** Because melatonin is a nutraceutical, no product standardization exists, and this may result in variation in melatonin content, absorption, and bioavailability amongst products. Use a reliable source (e.g., Nature's Bounty is suggested by many dermatologists).

### SIDE EFFECTS

**Dogs:** Melatonin appears to be quite safe in dogs.
- Rare: sedation (at the recommended treatment regimen), sex hormone secretion and fertility may be affected, sterile abscesses or granulomas may occur with implant therapy

**Note:** Altered sleep patterns, sedation, confusion, headache, hypothermia, tachycardia, and pruritus have been reported in humans.

### DRUG INTERACTIONS

**Benzodiazepines or succinylcholine:** effects of these drugs may be potentiated

### MONITORING
- Efficacy and adverse effects

## Methylprednisolone/Methylprednisolone Acetate

**Trade/brand name:** *Medrol*® (US, CA), *Depo-Medrol*® (US, CA), *Medrone*® (UK), *Depo-Medrone*® (UK) (Rx)
**Classification:** Anti-inflammatory (glucocorticoid), Immunomodulatory (immunosuppressive), Hormone

### INDICATIONS

**Dogs and cats:** Allergic skin disorders such as atopic dermatitis, autoimmune skin disorders such as pemphigus complex, and various sterile inflammatory or immune-mediated dermatoses.

### CONTRAINDICATIONS

Infectious diseases, hyperadrenocorticism (can be carefully used to balance treatment-induced hypoadrenocorticism), gastric ulcer, corneal ulcer, diabetes mellitus, renal failure, pregnancy, modified live vaccines (should be avoided when using immunosuppressive doses of glucocorticoids). Use methylprednisolone acetate cautiously in cats with any cardiovascular disorders that alter the compensatory mechanisms for increased plasma volume, to avoid congestive heart failure (Ployngam *et al*. 2006). Methylprednisolone will interfere with the intradermal test reactivity. Long-term use may also interfere with the allergy serum test results. Drug withdrawal is usually recommended for at least 4 weeks prior to allergy testing for oral administration and 8 weeks for injectable administration. Injectable methylprednisolone is considered unsuitable for management of chronic dermatologic diseases due to potential severe effect on the HPA-axis.

### MECHANISM OF ACTION

Methylprednisolone is an intermediate glucocorticoid 1.25 times more potent than prednisolone and 5 times more potent than hydrocortisone. Its mineralocorticoid effect is insignificant. The mechanisms of action of glucocorticoids are complex. Through genomic and non-genomic mechanisms they exert anti-inflammatory and immunosuppressive effects by decreasing the synthesis of inflammatory cytokines, chemokines, adhesion molecules, prostaglandins, and leukotrienes (both mediated by increasing the expression of lipocortin-1);

enhancing the clearance of foreign antigens; decreasing the ability of dendritic cells to present antigen and activate T cells; suppressing the cellular immune response through inhibition of IL-12 synthesis and suppression of a Th-1 response, but promotion of a Th-2 response.

## DOSAGES

### Dogs

- Allergic and inflammatory disorders: 0.8–1.0 mg/kg PO q24h. After remission of clinical signs, reduce the dose to the lowest amount needed to maintain the disease under control. Long-term treatment should be administered every other day, or less frequently if possible
- Autoimmune disorders: 0.8–1.5 mg/kg PO q12h. If remission is not noted after 7–14 days of the induction dose, combination immunosuppressive therapy or a more potent oral glucocorticoid should be considered. Long-term treatment should be administered every other day, or less frequently if possible

**Note:** When used long-term, the drug should be discontinued gradually. There is no plausible justification for the use of long-acting injectable glucocorticoids to manage canine skin disorders, because of their potent effect on the hypothalamic–pituitary–adrenal axis and potential for severe side effects. Therefore, the authors do not recommend their use.

### Cats

- Oral methylprednisolone (*Medrol*®)
  - *Allergic and inflammatory disorders*: 2.2 mg/kg PO q24 h. After remission of clinical signs reduce the dose to the lowest amount needed to maintain the disease under control. Long-term treatment should be administered every other day, or less frequently if possible.
  - *Autoimmune disorders*: 4.0–6.0 mg/kg PO q24 h. Apply the same recommendation for long-term treatment as above.

**Note:** When used long-term, the drug should be discontinued gradually.

- Injectable methylprednisolone acetate (*Depo-Medrol*®)
  - *Inflammatory or autoimmune disorders*: 4–5 mg/kg SC or IM. Duration of effects for skin conditions may vary, but usually 3–5 weeks. Repeat dose once or twice every 2–3 weeks if needed to achieve remission. After remission, do not administer this drug more frequently than every 3–4 months (if long-term use is needed to control the disease, the authors recommend oral methylprednisolone instead)

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats

- Oral tablets (methylprednisolone): 4 mg; *Medrol*®
- Oral tablets (methylprednisolone): 2 mg, 4 mg; *Medrone*® (available in UK only)
- Injection (methylprednisolone acetate): 20 mg/mL in 10 and 20 mL vials, 40 mg/mL in 5 mL vials; *Depo-Medrol*®, generic
- Depot suspension for injection (methylprednisolone acetate): 40 mg/mL in 5 mL vials; Depo-*Medrone*® (UK)

**Human-labeled products**
- Oral tablets (methylprednisolone): 2 mg, 4 mg, 8 mg, 16 mg, 24 mg, 32 mg; *Medrol®*, generic
- Suspension for injection (methylprednisolone acetate): 20 mg/mL, 40 mg/mL, 80 mg/mL in 1, 5 and 10 mL vials; *Depo-Medrol®*, generic

## SIDE EFFECTS

**Dogs**
- Common (associated with long-term therapy): iatrogenic Cushing's disease (i.e., poor dull hair coat, polyuria, polydipsia, polyphagia, panting, muscle atrophy, thin skin, hypotrichosis or alopecia, pot-belly appearance, weight gain, calcinosis cutis, comedones, milia); secondary bacterial skin and bladder infections
- Uncommon: diarrhea, gastrointestinal ulceration, pancreatitis, diabetes mellitus, behavior changes (i.e. aggression), demodicosis, dermatophytosis, hypoadrenocorticism

**Cats**
- Common: diabetes mellitus (occurs more often in cats than dogs)
- Uncommon: cats are less prone to develop iatrogenic Cushing's disease when treated with long-term glucocorticoids; however, this syndrome will also develop if glucocorticoids are not used carefully. Signs of iatrogenic Cushing's in cats include polyuria, polydipsia, polyphagia, fragile skin, distended abdomen, alopecia, or hypotrichosis. Skin fragility syndrome may develop as the sole sign of inappropriate glucocorticoid use
- Rare: congestive heart failure has been reported in cats treated with corticosteroids (Smith *et al*. 2004), diarrhea, depression

## DRUG INTERACTIONS

**Amphotericin B or potassium-depleting diuretics (furosemide, thiazides):** hypokalemia may develop

**Aspirin:** glucocorticoids may reduce salicylate levels

**Cyclosporine:** may increase blood levels of both drugs increasing the risk of cyclosporine and glucocorticoid side effects

**Ketoconazole or other azole antifungals and macrolide antibiotics (e.g., erythromycin, clarithromycin):** may increase methylprednisolone levels by decreasing its metabolism

**Non-steroidal anti-inflammatory drugs (NSAIDs):** increased risks of gastrointestinal ulcer

**Phenobarbital, rifampin, barbiturates:** may increase the metabolism of glucocorticoids and decrease methylprednisolone levels

**Pyridostigmine or neostigmine:** profound muscle weakness may occur

## MONITORING
- Response to therapy and adverse effects
- The authors recommend having serum chemistry profile, urinalysis, and urine culture performed every 6–12 months for animals on long-term glucocorticoid therapy

## Methyltestosterone

**Trade/brand name:** *Android*® (US), *Methitest*® (US), *Testred*® (US), *Virilon*® (US), *Orandrone*® (UK), generic (Rx)
**Classification:** Hormone (androgenic/anabolic)

### INDICATIONS

**Dogs:** Anecdotally recommended for neutered dogs with alopecia X. However, because of the potential for serious side effects and lack of scientific evidence supporting its use, the authors only recommend methyltestosterone for alopecia X if all other treatment options have failed and owners insist on treating the pet's alopecia despite its merely cosmetic nature.

### CONTRAINDICATIONS

Methyltestosterone should not be used in patients with liver disease or during pregnancy. Treat animals with heart failure only if the benefits outweigh the risks.

### MECHANISM OF ACTION

Methyltestosterone is an androgen with anabolic effects including stimulation of erythropoiesis, enhancement of nitrogen balance and protein anabolism, and retention of sodium, potassium, and phosphorus. Its anabolic effects are mediated by binding to nuclear DNA and altering the transcription of proteins responsible for cellular metabolism.

### DOSAGES

**Dogs:** 1 mg/kg (maximum 30 mg) PO q24h until hair regrowth is noted (approximately 1–3 months). Thereafter, 1 mg/kg (maximum 30 mg) q48h for 2 months, followed by 1 mg/kg (maximum 30 mg) twice per week for 2 months, and finally once weekly for maintenance.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 10 mg, 25 mg; *Methitest*®, generic
- Buccal tablets: 10 mg; *Android*®, generic
- Oral capsules: 10 mg; *Testred*®, *Virilon*®

### SIDE EFFECTS

**Dogs:** increased aggression in male dogs, hepatotoxicity, virilization of female dogs (clitoral hypertrophy), vaginal discharge, prostatic hyperplasia, seborrhea oleosa

### DRUG INTERACTIONS

**Cyclosporine:** may increase cyclosporine serum concentrations

**Insulin, oral antidiabetic agents:** may decrease serum glucose levels

**Warfarin:** may increase anticoagulant effects

### MONITORING
- Efficacy and side effects
- Liver enzymes and signs of liver disease

## Milbemycin Oxime

**Trade/brand name:** *Interceptor®* (US, CA), *Sentinel®* (US, CA, UK), *Milbemax®* (CA, UK) (Rx)
**Classification:** Antiparasitic (macrocyclic lactone)

### INDICATIONS

**Dogs:** Juvenile-onset generalized or adult-onset demodicosis, sarcoptic mange, cheyletiellosis, and nasal mites (*Pneumonyssoides caninum*) infection. Flea control if using *Sentinel®*, which also contains lufenuron, an insect development inhibitor.

**Note:** Milbemycin oxime is licensed in the US, CA, and UK as a heartworm and intestinal parasite (e.g., nematodes) preventative. Any other heartworm and intestinal parasite preventatives should be discontinued during treatment with milbemycin.

### CONTRAINDICATIONS

Do not use in dogs less than 4 weeks old or less than 1 lb (0.5 kg). Milbemycin oxime, similarly to ivermectin, is a member of the macrolide family; however, it has a higher index of safety when used in ivermectin-sensitive breeds. The authors, nevertheless, recommend checking the ABCB1-1 (formerly MDR1) genotype before using this drug in canine breeds susceptible to ivermectin toxicity such as collies, Shetland sheepdogs, Australian shepherds, old English sheepdogs, white Swiss shepherds, longhaired whippets, silken windhounds, McNab and Border collies. Do not use without up-to-date negative heartworm test, or in patients with heartworm disease.

### MECHANISM OF ACTION

Milbemycin oxime is a macrocyclic lactone that, similarly to other milbemycins (i.e., moxidectin), acts by potentiating glutamate- and GABA-gated chloride ion channels in parasites, resulting in hyperpolarization of nerve cells, flaccid paralysis, and parasite death.

### DOSAGES

**Dogs**
- Generalized demodicosis: 0.5–2 mg/kg PO q24h for 30 days past two consecutive negative skin scrapings obtained at intervals of 4–6 weeks. An evidence-based review found good evidence for recommending 2 mg/kg PO q24h for canine generalized demodicosis (Mueller 2004).
- Sarcoptic mange: various treatment protocols have been reported to be successful: 2 mg/kg PO weekly for 3–8 weeks; 2 mg/kg PO with two treatments administered at 14-day intervals; 1 mg/kg PO every other day for 14 days. Duration of therapy, however, should be dictated by clinical response at the recheck evaluations. Some of these studies included ivermectin-sensitive breeds, and no side effects were reported.

- Cheyletiellosis: 2 mg/kg PO q24h weekly for 3–9 treatments. Most cases respond to three treatments; however, duration of therapy should be dictated by clinical response at recheck evaluations.
- Nasal mites infection: 0.5–1 mg/kg PO once weekly for two consecutive weeks.
- Flea control: *Sentinel® Flavor Tabs* (milbemycin oxime and lufenuron): 2.3 mg/46 mg (dogs 2–10 lb), 5.75 mg/115 mg (dogs 11–25 lb), 11.5 mg/230 mg (dogs 26–50 lb), 23 mg/460 mg (dogs 51–100 lb); dogs 100–125 lb should receive the appropriate combination tablet of milbemycin and lufenuron. Labeled for monthly use. May be combined with *Capstar®*.

**Cats:** Not reported as a treatment modality for feline ectoparasitic skin disorders. *Sentinel®* may be used extra-label for flea control in cats.

### FORMULATIONS

**Veterinary-labeled products**
- Oral tablets (artificial beef flavored, derived from pork and soy): 2.3 mg, 5.75 mg, 11.5 mg, 23 mg; *Interceptor® Flavor Tabs*
- Oral tablets (beef flavored): milbemycin oxime/lufenuron = 2.3 mg/46 mg, 5.75 mg/115 mg, 11.5 mg/230 mg, 23 mg/460 mg; *Sentinel® Flavor Tabs* (may be combined with *Capstar®*)
- Oral non-chewable and chewable tablets (chicken flavored): milbemycin oxime/praziquantel = 2.5 mg/25 mg (for puppies and small dogs), 12.5 mg/125 mg (for large dogs); *Milbemax® Chewable Tabs* (available in CA and UK)

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs**
- Rare: lethargy, vomiting, ataxia, trembling, and stupor. If used at doses of 2.0 mg/kg or lower, the side effects are transient and very sporadic

### DRUG INTERACTIONS

**Drugs that inhibit P-glycoprotein such as amiodarone, azole antifungals (e.g., ketoconazole), cyclosporine, carvedilol, diltiazem, erythromycin, clarithromycin, quinidine, spironolactone, tamoxifen, verapamil:** concurrent use with any one of these drugs may increase milbemycin penetration across the blood–brain barrier and potentiate side effects

**Benzodiazepines:** may potentiate benzodiazepines effects; concurrent use of these drugs is not recommended in humans

### MONITORING
- Efficacy and adverse effects
- Heartworm status before initiating treatment

## Minocycline Hydrochloride

**Trade/brand name:** *Minocin®* (US, CA, UK), *Arestin®* (US, CA), *Aknemin®* (UK), generic (Rx)
**Classification:** Antibacterial (tetracycline), Anti-inflammatory

## INDICATIONS

**Dogs and cats:** Treatment of infections susceptible to minocycline. It has been used in the treatment of nocardiosis and actinomycosis. In one study, minocycline was shown to be effective against 81.3% of rapidly growing members of the genus *Mycobacterium* (Jang and Hirsh 2002). Because of its anti-inflammatory effect, it could replace tetracycline in the combination therapy with niacinamide for the treatment of various sterile inflammatory skin disorders such as discoid lupus erythematosus, German shepherd dog metatarsal fistulae, cutaneous reactive histiocytosis, sterile granuloma/pyogranuloma syndrome, sterile nodular panniculitis, and lupoid onychodystrophy/onychitis.

## CONTRAINDICATIONS

Hypersensitivity to tetracyclines, pregnancy, nursing, animals less than 6 months of age.

## MECHANISM OF ACTION

Minocycline is a second-generation, long-acting, lipid-soluble tetracycline. Similarly to other tetracyclines, minocycline binds to the 30S ribosomal subunit and inhibits bacterial protein synthesis. It is mainly bacteriostatic. Minocycline has a broad spectrum of action against Gram-positive (e.g., some strains of *Staphylococcus* and *Streptococcus*, *Actinomyces*, *Bacillus anthracis*, *Nocardia*) and Gram-negative bacteria (e.g., *Bordetella*, *Brucella*, *Bartonella*, *Haemophilus*, *Pasteurella multocida*, *Shigella*, *Yersinia pestis*), spirochetes, *Chlamydia*, *Mycoplasma*, and *Rickettsia*. Additionally, minocycline has an anti-inflammatory effect completely independent of its antimicrobial action. It reduces the expression and activity of cyclooxygenase (COX)-2, caspases, IL-1-beta and prostaglandin $E_2$. Moreover, it inhibits polymorphonuclear cell and eosinophil chemotaxis and matrix metalloproteinase (it has been shown to reduce hypertrophic scarring in a rabbit model).

## DOSAGES

### Dogs and cats

- Nocardiosis and actinomycosis: 5–25 mg/kg PO or IV q12h for at least 4 weeks past clinical resolution
- Atypical mycobacteriosis: 5–12.5 mg/kg PO or IV q12h for at least 4 weeks past clinical resolution
- Sterile inflammatory skin disorders (this dose regimen is empirical): 12.5–25 mg/kg PO q12h for at least 6 weeks; if significant improvement is noted, it should be continued to maintain the disease under control

**Note:** Selection of minocycline to treat infectious diseases should be based on culture and susceptibility results. Surgical removal of lesions and drainage are commonly recommended as part of the treatment protocol for some diseases.

## FORMULATIONS

**Veterinary-labeled products:** None

### Human-labeled products

- Oral tablets: 50 mg, 75 mg, 100 mg; *Dynacin®*, *Myrac®*, *Solodyn®*, generic
- Extended-release oral tablets: 45 mg, 90 mg, 135 mg; *Dynacin®*, *Myrac®*, *Solodyn®*, generic

- Oral capsules: 50 mg, 75 mg, 100 mg; *Minocin®*, *Dynacin®*, generic
- Oral suspension: 50 mg/5 mL in 60 mL; *Minocin®*
- Powder for injection (cryodessicated): 100 mg/vial; *Minocin®*
- Sustained-release powder for injection: 1 mg/vial; *Arestin®*

### SIDE EFFECTS

**Dogs and cats**

- Common: vomiting and nausea. Administration with food can reduce these side effects without significant reduction in drug absorption
- Rare: increase in liver enzymes, ototoxicity, dental and bone discoloration (yellow) if exposure to minocycline occurs in-utero or early in life; intravenous administration in dogs has caused hypotension, shivering, dyspnea, cardiac arrhythmias, urticaria and shock

**Note:** Photosensitivity reactions, rare blood dyscrasias, hepatotoxicity, and vestibular signs (as a result of a peculiar biotransformation of minocycline) have been reported in humans.

### DRUG INTERACTIONS

**Antacids (oral), saline cathartics, or other gastrointestinal products containing aluminum, calcium, magnesium, zinc, or bismuth cations:** can decrease the absorption of these antacids or tetracyclines; administer minocycline 1–2 hours before or after these products

**Iron:** oral iron products should be administered 3 hours before or 2 hours after tetracyclines because they may reduce their absorption

**Isotretinoin:** may increase the risk for nervous system effects when used with minocycline

**Kaolin, pectin, bismuth subsalicylate:** may reduce minocycline absorption

**Penicillins, cephalosporins, aminoglycosides:** the bactericidal activity of the penicillins, cephalosporins, and aminoglycosides may be reduced by bacteriostatic drugs such as tetracyclines; however, the clinical significance of this effect is debatable

**Warfarin:** patients on anticoagulants may need dose adjustment because tetracyclines may decrease plasma prothrombin levels

### MONITORING

- Efficacy and adverse effects
- Thyroid function. Minocycline was shown in vitro to inhibit thyroid peroxidase-catalyzed iodination of tyrosine residues of thyroglobulin and coupling of monoiodotyrosine and diiodotyrosine; therefore, it seems advisable to monitor thyroid function in patients receiving long-term minocycline therapy

## Misoprostol

**Trade/brand name:** *Cytotec®* (US, CA, UK) (Rx)
**Classification:** Hormone, Antiulcer agent

## INDICATIONS

**Dogs:** Treatment of atopic dermatitis. The interest in misoprostol in veterinary dermatology stems from one randomized placebo-controlled clinical trial showing a modest (median 30%) improvement of skin lesions and pruritus scores during treatment of 12 dogs with atopic dermatitis (Olivry *et al*. 2003). However, its common gastrointestinal side effects, modest efficacy, and cost do not make this drug a very attractive option as monotherapy for canine atopic dermatitis.

## CONTRAINDICATIONS

It should not be used in pregnant animals, since it may cause congenital malformation or embryotoxicity.

## MECHANISM OF ACTION

Misoprostol is a synthetic prostaglandin $E_1$ ($PGE_1$) analog, and it is primarily used as an anti-ulcer medication because of its cytoprotective effect on the gastrointestinal mucosa. Misoprostol has also shown anti-inflammatory/anti-allergic effects in various in-vivo and in-vitro studies in humans and rats. It inhibits the late-phase reaction to intradermal allergen injections by reducing eosinophil chemotaxis and survival but has no effect on the immediate cutaneous allergic inflammation. It also inhibits histamine release from basophils and mast cells after allergen-specific and non-allergenic stimulation. Moreover, it reduces the secretion of IL-1-beta and TNF-alpha by endotoxin-stimulated monocytes. A study in dogs showed that the modest effect of misoprostol in reducing the clinical signs of dogs with atopic dermatitis does not appear to be mediated by inhibition of inflammatory cells chemotaxis or reduction of TNF-alpha synthesis (Olivry *et al*. 2003).

## DOSAGES

**Dogs:** 5 mcg/kg PO q8h. Perform a 4–6-weeks trial. If no significant reduction in pruritus and skin lesions consider another treatment option.

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 100 mcg, 200 mcg; *Cytotec®*, generic

## SIDE EFFECTS

**Dogs**

- Common: vomiting, diarrhea, gastrointestinal discomfort

## DRUG INTERACTIONS

**Magnesium-containing antacids:** may aggravate the diarrhea associated with misoprostol therapy. Food and antacids reduce the rate of misoprostol absorption and may reduce the systemic drug availability but not efficacy

## MONITORING

- Efficacy and adverse effects

## Mitotane (o,p'-DDD)

**Trade/brand name:** *Lysodren®* (US, CA, UK) (Rx)
**Classification:** Hormone, (adrenolytic agent)

### INDICATIONS

**Dogs:** Pituitary-dependent (primarily) or adrenal-dependent hyperadrenocorticism.

### CONTRAINDICATIONS

Do not use in pregnant or lactating animals. Use cautiously in animals with hepatic or renal diseases.

### MECHANISM OF ACTION

Mitotane binds to cells of the adrenal cortex and forms a reactive metabolite, resulting in complete or partial necrosis of the adrenal cortex according to the dosage used. This effect is relatively specific, and cells of the zona reticularis and fasciculata are typically affected. However, in a small percentage of dogs, cells of the zona glomerulosa will also be destroyed, resulting in aldosterone deficiency.

### DOSAGES

**Dogs**

- Pituitary-dependent hyperadrenocorticism: **during the induction phase** give 50 mg/kg PO divided twice a day until one of the following occurs first: 7–10 days of therapy; or signs of corticosteroid deficiency develop such as lethargy, depression, vomiting, and/or diarrhea; or dog refuses to eat or appetite is significantly reduced. When one of these end points is reached, the treatment is discontinued and an ACTH stimulation test is performed to evaluate the degree of adrenal necrosis induced by the drug. If the post-ACTH cortisol serum level is between 2 and 4 mcg/dL (55.18–110.36 nmol/L) the **maintenance dose** is instituted at 50 mg/kg PO per week divided in 2–3 administrations. An ACTH stimulation test should be performed after 30–90 days and the maintenance dose adjusted as needed.
- Adrenal-dependent hyperadrenocorticism: 50–100 mg/kg PO divided twice a day. Follow the same end points discussed above to decide when to start maintenance therapy; however, the induction phase may be longer for cases of adrenal tumor, and the maintenance dose may need to be readjusted more frequently.

**Note:** At any point during therapy, the dog may develop signs of corticosteroid deficiency, and a low dose of prednisolone or prednisone (0.25 mg/kg PO q24h) should be administered. Make sure to discontinue the oral prednisone or prednisolone at least 24 hours before the ACTH stimulation test, since these drugs cross-react with the measured serum cortisol. To improved oral absorption and systemic bioavailability, administer the drug with food rich in oil/fat content.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets (scored): 500 mg; *Lysodren®*

### SIDE EFFECTS

**Dogs**

- Common: usually associated with glucocorticoid and/or mineralocorticoid deficiency, and include lethargy, depression, ataxia, anorexia, vomiting and/or diarrhea. If any of these adverse effects occurs, discontinue the mitotane and administer a low dose of oral glucocorticoid (e.g., prednisolone at 0.25 mg/kg PO q24h). If no improvement is noted within 3 hours, the dog should be examined immediately for an ACTH stimulation test and evaluation of at least $Na^+$ and $K^+$ serum levels
- Rare: liver congestion, centrolobular atrophy and moderate to severe fatty degeneration. These hepatic changes are typically asymptomatic and may be more marked in dogs with pre-existing liver disease, or with long-term therapy

### DRUG INTERACTIONS

**Drugs that cause CNS depression:** potential additive depressant effects

**Phenobarbital:** can induce hepatic microsomal enzymes and may reduce the efficacy of mitotane

**Spironolactone:** has been shown to block the action of mitotane in dogs

**Warfarin:** mitotane may induce hepatic microsomal enzymes and increase the metabolism of warfarin

### MONITORING

- Response to therapy: periodic ACTH stimulation tests
- Adverse effects: owners should be educated to monitor the dog's water consumption and food intake and signs of corticosteroid deficiency. If water consumption and food intake are reduced significantly, mitotane therapy should be discontinued and the veterinarian should be contacted. If signs of corticosteroid deficiency are noted, mitotane therapy should be discontinued, a small dose of glucocorticoid administered, and the veterinarian contacted
- Chemistry profile should be performed at baseline and regularly at recheck visits

## Moxidectin

**Trade/brand name:** *Cydectin*® (US), *Proheart 6*® (US, CA), *Guardian*® (CA) (Rx)
**Classification:** Antiparasitic (macrocyclic lactone)

### INDICATIONS

**Dogs:** Generalized demodicosis, sarcoptic mange, and otoacariosis.

**Cats:** Otoacariosis.

**Note:** Moxidectin is not labeled in the US for the treatment of these disorders in dogs and cats.

### CONTRAINDICATIONS

Animals with known hypersensitivity to the drug. It should be used cautiously or avoided in animals with ABCB1-1 (formerly MDR1) mutation, at the extra-label

dosages recommended for the treatment of acarioses. Do not use without up-to-date negative heartworm test, or in patients with heartworm disease.

## MECHANISM OF ACTION

Moxidectin is a macrocyclic lactone in the milbemycin class produced by the fermentation of actinomycetes. It interacts with GABA and glutamate-gated channels, which increases the influx of chloride ions into the cell and results in flaccid paralysis and death of the parasite.

## DOSAGES

### Dogs

- Generalized demodicosis: 0.2–0.5 mg/kg PO q24h. A recent evidenced-based review of treatment protocols for canine demodicosis reported good evidence for recommending a dose of 0.4 mg/kg PO q24h of moxidectin for the treatment of generalized demodicosis (Mueller 2004). To monitor for potential side effects (particularly in puppies), it is recommended to increase the dose gradually by 0.1 mg/kg per day until the desired dose is achieved (e.g., 0.1 mg/kg on day 1, followed by 0.2 mg/kg on day 2, etc.). Treatment for generalized demodicosis should be continued for 30 days past two consecutive negative skin scrapings at 2–4-week intervals. The patient should thereafter be monitored for 1 year before declared cured.
- Sarcoptic mange: 0.2–0.25 mg/kg PO or SC weekly for 3–6 weeks. This dose is based on one anecdotal study (Wagner and Wendlberger 2000). In this study, the duration of treatment (3–6 weeks) was based on resolution of clinical signs; therefore, if a treatment trial is performed when no mites are found on skin scrapings ideally at least 6 treatments should be administered.
- Otoacariosis: 0.2 mg/kg PO or SC administered twice at 10 days apart. However, re-infestation may occur with this protocol and additional treatment may be required.

### Cats

- Otoacariosis: 0.2 mg/kg SC. Re-evaluate in 30 days to determine if additional treatment is required.

## FORMULATIONS

### Veterinary-labeled products

- Oral tablets (approved for dogs): 30 mcg, 68 mcg, 136 mcg; *Guardian*® (CA only)
- Sustained-release suspension for injection (approved for dogs): 5–10% moxidectin microspheres, 528 mg/vial in 17 mL vial; *Proheart*®
- Solution for injection (approved for cattle): 1% (10 mg/mL) in 200 mL and 500 mL vials. It also contains benzoyl alcohol (40 mg) and EDTA (0.27 mg); *Cydectin*®
- Solution for injection (approved for sheep): 1% (10 mg/mL) in 50 mL, 200 mL and 500 mL vials. It also contains benzyl alcohol (40 mg) and butylhydroxytoluene (2.50 mg); *Cydectin*®
- Solution for injection (approved for sheep): 2% (20 mg/mL) in 50 mL, 200 mL and 500 mL vials. It also contains benzyl alcohol (70 mg); *Cydectin*®
- Solution for injection (approved for cattle): 10% (100 mg/mL) in 50 mL and 200 mL vials. It also contains benzyl alcohol (70 mg); *Cydectin*®

- Pour-on (approved for cattle): 0.5% (5 mg/mL) in 500 mL, 1 L, 2.5 L, and 5 L containers. It also contains butylated hydroxyanisole (0.1 mg) and tertiary butyl hydroquinone (0.03 mg); *Cydectin®*
- Oral drench (approved for sheep): 0.1% (1 mg/mL) in 1 L, 2.5 L and 5 L. It also contains benzyl alcohol (40 mg), betylhydroxytoluene (2.50 mg), disodium edentate (0.27 mg); *Cydectin®*

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs:** generalized urticaria, angioedema, generalized erythema, restless, ataxia, lethargy, anorexia, vomiting. The risk for side effects increases with subcutaneous administration

### DRUG INTERACTIONS

None reported; nevertheless, moxidectin should be used cautiously in conjunction with other drugs that inhibit P-glycoprotein. It is wise to test dogs at risk for the ABCB1-1 mutation before using moxidectin if they are receiving the following drugs: amiodarone, carvedilol, clarithromycin, cyclosporine, diltiazem, erythromycin, itraconazole, ketoconazole, quinidine, spironolactone, tamoxifen, verapamil.

### MONITORING

- Efficacy and adverse effects
- Check heartworm status prior to administration

## Moxifloxacin

**Trade/brand name:** *Avelox®* (US, UK), generic (Rx)
**Classification:** Antibacterial (fourth-generation fluoroquinolone)

### INDICATIONS

**Dogs and cats:** Skin and soft tissue infections caused by susceptible Gram-negative bacilli and Gram-positive cocci. The chemical structure of moxifloxacin is slightly different from the second-generation veterinary fluoroquinolones (enrofloxacin, orbifloxacin, danofloxacin, and marbofloxacin), giving this compound a greater activity against anaerobes and Gram-positive cocci. A recent in-vitro study showed that moxifloxacin may be efficacious for the treatment of rapidly growing mycobaterial infections associated with *Mycobacterium fortuitum* and *M. smegmatis* in dogs and cats (Govendir *et al*. 2011).

**Note:** Moxifloxacin is not commonly used, because veterinary fluoroquinolones are preferred for initial treatment. The authors do not recommend the use of fluoroquinolones as first-line therapy for pyoderma. Antibiotic selection should be based on culture and susceptibility results.

### CONTRAINDICATIONS

Fluoroquinolones can be potentially toxic to chondrocytes and should not be given to immature dogs during their rapid growth phase (small and medium-sized breeds between 2 and 8 months, large breeds younger than 12 months,

giant breeds younger than 18 months). Cautious use is advised for animals susceptible to seizures (e.g., epileptics).

### MECHANISM OF ACTION

Moxifloxacin is a fourth-generation fluoroquinolone that inhibits DNA supercoiling and synthesis by inhibition of bacterial DNA gyrase (type II topoisomerase). Similarly to other fluoroquinolones, moxifloxacin is bactericidal in a concentration-dependent manner and accumulates inside inflammatory cells, in particular macrophages.

### DOSAGES

**Dogs and cats:** 10 mg/kg PO q24h until 1–2 weeks past resolution of clinical signs

**Note:** For rapidly growing mycobacterial infections, the animals should be treated for at least 4 weeks past resolution of clinical signs.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 400 mg; *Avelox®*, generic

### SIDE EFFECTS

**Dogs and cats**: vomiting may occur occasionally. Arthropathy may occur in young animals. Dogs between 4 and 28 weeks of age, and large rapidly growing dogs, are the most susceptible. CNS toxicity may develop with high drug concentrations, especially in animals with renal failure. High doses of moxifloxacin have been associated with prolonged QT interval, but the clinical significance of this finding is currently unknown.

**Note:** In humans, common reported side effects include nausea, diarrhea, and dry eyes. Less common side effects include Stevens–Johnson syndrome, toxic epidermal necrolysis, agranulocytosis, aplastic anemia, hemolytic anemia, pancytopenia, thrombocytopenia, hepatic necrosis, hepatitis, liver failure, seizures, acute renal failure, prolonged QT interval, anaphylactoid reaction, extrinsic allergic alveolitis.

### DRUG INTERACTIONS

**Antacids containing divalent or trivalent cations (e.g., $Mg^{++}$, $Al^{++}$, $Ca^{++}$), iron, zinc:** decrease moxifloxacin absorption; separate administration by at least 2 hours

**Theophylline**: may increase theophylline blood levels

### MONITORING

- Efficacy and adverse effects

## Mycophenolate Mofetil

**Trade/brand name:** *CellCept®* (US, CA, UK), *Myfortic®* (US, CA, UK) (Rx)
**Classification:** Immunomodulatory (immunosuppressive)

## INDICATIONS

**Dogs:** Pemphigus foliaceus. There is very limited experience in veterinary dermatology using this drug for canine pemphigus foliaceus. The only study in dogs to treat pemphigus foliaceus with mycophenolate mofetil reported a success rate of 50% (3/6 dogs), with most dogs requiring concurrent glucocorticoid therapy to control the disease (Byrn and Morris 2001). Some of the treated dogs had the prednisone discontinued completely, but in others the disease relapsed when glucocorticoid was decreased to a very low dose. It has been used in humans to treat a variety of skin diseases (e.g., different types of pemphigus and pemphigoid, severe forms of atopic dermatitis, cutaneous lupus, psoriasis, and refractory pyoderma gangrenosum). It is frequently administered with glucocorticoids. Treatment may be very expensive.

**Cats:** There are currently no anecdotal reports or clinical trials using this drug to treat skin diseases in cats.

## CONTRAINDICATIONS

Patients known to have hypersensitivity to mycophenolate mofetil. Patients with renal dysfunction may require dose adjustment. Avoid use of live attenuated vaccines during treatment. Because of concerns that this drug can cause birth defects in humans, the manufacturer recommends that tablets or capsules not be crushed, split, or opened.

## MECHANISM OF ACTION

Mycophenolate mofetil is metabolized to the active antiproliferative agent mycophenolic acid (MPA). It specifically and reversibly inhibits the enzyme inosine monophosphate dehydrogenase which is important for the de-novo synthesis of guanine in T and B lymphocytes. Therefore, it suppresses lymphocytes proliferation and reduces antibody production by B cells.

## DOSAGES

**Dogs:** 20–40 mg/kg/day PO divided into three daily doses (administer on an empty stomach – either 1 hour before feeding or at least 2 hours after)

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 250 mg; *CellCept®*
- Oral tablets: 500 mg; *CellCept®*
- Powder for oral suspension: 200 mg/mL in 225 mL btl; *CellCept®*
- Oral tablets (delayed-release; sodium salt): 180 mg, 360 mg; *Myfortic®*

## SIDE EFFECTS

**Dogs**: vomiting, diarrhea, anorexia, lethargy (gastrointestinal signs may be severe), pyoderma and *Malassezia* dermatitis. There is minimal risk for bone marrow suppression. Increased systemic infection and malignancy rates are possible.

**Note:** Drug may be administered with food if severe gastrointestinal side effects occur. In humans, the following side effects have been reported: constipation, diarrhea, nausea, vomiting, headache, hypertension, peripheral edema,

leukopenia, gastrointestinal bleeding, severe neutropenia, cough, confusion, tremor, infection, malignant lymphoma.

### DRUG INTERACTIONS

**Acyclovir:** increase in plasma levels of both drugs

**Antacids and iron:** may reduce absorption of mycophenolate mofetil; separate dosing by at least 2 hours

**Aspirin or other salicylates:** these drugs may increase the concentration of free mycophenolic acid

**Azathioprine**: increased risk for myelosuppression

**Other drugs that undergo active renal tubular secretion:** mycophenolate mofetil will compete with these drugs resulting in increased concentration of either drug

### MONITORING

- Efficacy and adverse effects

## Naltrexone Hydrochloride

**Trade/brand name:** *Revia*® (US, CA), generic (Rx)
**Classification:** Behavior modifying drug (opioid antagonist)

### INDICATIONS

**Dogs:** Acral lick dermatitis. It may also be beneficial for other compulsive or stereotypical disorders.

**Note:** The indication for acral lick dermatitis has been supported by one study in which 7/11 treated dogs successfully responded to naltrexone (i.e., licking stopped or reduced markedly and re-epithelialization occurred) (White 1990). Unfortunately, all dogs relapsed after discontinuation of therapy, with 6/7 dogs relapsing between 1 week and 6 months, showing the short-lived effect of naltrexone.

**Cats:** No anecdotal reports or clinical trials using this drug to treat skin diseases in cats are currently available.

### CONTRAINDICATIONS

Avoid or use cautiously in patients with hepatic failure or acute hepatitis, since dose-dependent hepatotoxicity has been reported occasionally in humans. Avoid in animals that have had major surgery or trauma, because its use may result in severe acute discomfort.

### MECHANISM OF ACTION

Naltrexone competitively antagonizes opioid receptors, reversing the effects of endogenous (e.g., endorphins) or exogenously administered opioid agonists. Opioids have an endogenous analgesic effect, which theoretically could reinforce compulsive stereotypic behaviors. By reducing the analgesic effect of opioids,

naltrexone may increase the pain or discomfort perception, discouraging the animal from licking or chewing itself.

### DOSAGES

**Dogs**: 2 mg/kg PO q24h for 10–14 days. If no improvement is noted increase the dose to 2 mg/kg PO q12h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablet: 50 mg; *Revia*®, generic

### SIDE EFFECTS

**Dogs**
- Uncommon/rare: drowsiness and withdrawal from owner was reported in 1/11 dogs (White 1990), and severe generalized pruritus in one dog within hours of receiving naltrexone at the dose of 2 mg/kg PO q6h (Schwartz 1993); the pruritus rapidly resolved after reducing the dose

**Note:** In humans, naltrexone is relatively safe at recommended doses. Uncommon to rare side effects include abdominal cramping, nausea, vomiting, nervousness, insomnia, joint or muscle pain, skin reaction and pruritus, dose-dependent hepatotoxicity.

### DRUG INTERACTIONS

**Clonidine:** may reduce the hypotensive and bradycardic effects of clonidine

**Opioid partial-agonists (e.g., butorphanol, pentazocine, nalbuphine):** may also antagonize the effects of these agents (respiratory depression, analgesia)

**Yohimbine:** may increase the CNS effects of yohimbine (e.g., anxiety, nausea, tremors, palpitation) and increase plasma cortisol levels

### MONITORING
- Efficacy and adverse effects
- Liver enzymes should be monitored if using high doses for a long period of time (recommendation based in reported side effects in humans)

## Niacinamide

**Trade/brand name:** Nicotinamide and Vitamin $B_3$ (US, CA, UK), generic
**Classification:** Anti-inflammatory, Vitamin

### INDICATIONS

**Dogs:** Used in combination with a tetracycline to treat various canine sterile inflammatory skin disorders such as discoid lupus erythematosus, sterile granulomatous/pyogranulomatous syndrome, sterile nodular panniculitis, cutaneous

reactive histiocytosis, cutaneous vesicular lupus erythematosus, pemphigus erythematosus, pemphigus foliaceus, lupoid onychodystrophy/onychitis, German shepherd dog metatarsal fistulae, vasculitis, arteritis of the nasal philtrum, sebaceous adenitis, and dermatomyositis.

**Note:** In most of these disorders, niacinamide and a tetracycline will be used with other immunomodulatory drugs.

### CONTRAINDICATIONS

Niacinamide may interfere with intradermal and allergy serum testing. Drug withdrawal of at least 2 weeks prior to allergy testing may be indicated. In humans niacinamide is contraindicated in patients with liver disease, hypersensitivity to niacinamide products, and peptic ulcer.

### MECHANISM OF ACTION

Niacinamide (nicotinamide) blocks antigen IgE-induced histamine release in vivo and in vitro, and inhibits mast cell degranulation. It also blocks protease and phosphodiesterase release.

### DOSAGES

**Dogs:** 250 mg PO q8h for dogs weighing ≤10 kg, and 500 mg PO q8h for dogs weighing >10 kg

**Note:** Used in combination with tetracycline (same dose protocol for niacinamide) or doxycycline (5 mg/kg PO q12h or 10 mg PO q24h). Clinical response may not be seen before 6–8 weeks of treatment. Frequency of administration may be reduced to twice daily if clinical response is noted.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 50 mg, 100 mg, 125 mg, 250 mg and 500 mg; Niacinamide (Nicotinamide), generic
- Oral capsules: 50 mg; Niacinamide (Nicotinamide), generic

### SIDE EFFECTS

**Dogs**

- Rare: vomiting, diarrhea, anorexia, increased liver enzymes, increased seizure activity (anecdotal report)

**Note:** In humans, rare side effects typically reported to be associated with high doses of niacinamide include diarrhea, dizziness, headache, nausea, pruritus, temporary feeling of warmth or flushing of the skin, and hepatotoxicity.

### DRUG INTERACTIONS

**Carbamazepine:** may decrease the clearance of carbamazepine and increase the risk for toxicity; monitor carbamazepine plasma levels when administering niacinamide concomitantly

**Insulin, oral antidiabetic agents:** the dosage of insulin or antidiabetic agents may need to be adjusted

### MONITORING
- Efficacy and adverse effects

## Nitenpyram

**Trade/brand name:** *Capstar*® (US, CA, UK), generic (Rx)
**Classification:** Antiparasitic (neonicotinoid)

### INDICATIONS

**Dogs and cats:** Flea control in dogs and cats 4 weeks of age or older.

### CONTRAINDICATIONS
Not labeled for animals younger than 4 weeks or <1 kg body weight.

### MECHANISM OF ACTION
Nitenpyram binds to postsynaptic nicotinic acetylcholine receptors and blocks acetylcholine-mediated neuronal transmission, resulting in paralysis and death of the flea. Manufacturer states that it starts working in 30 minutes. Studies have shown that it kills adult fleas within 6 hours of application.

### DOSAGES

**Dogs:** 11.4 mg tablet PO q24h (dogs 1–11.4 kg or 2–25 lb); 57 mg tablet PO q24h (dogs 11.5–56.8 kg or 25.1–125 lb)

**Cats:** 11.4 mg tablet PO q24h (cats 1–11.4 kg or 2–25 lb)

**Note:** A single dose is usually needed; however, it can be administered once daily several times as needed. It should be combined with an insect growth regulator or insect development inhibitor such as *Frontline Plus*®, *Sentinel*®, or *Program*®.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats
- Oral tablets: 11.4 mg, 57 mg; *Capstar*®, generic

**Human-labeled products:** None

### SIDE EFFECTS
None reported.

### DRUG INTERACTIONS
None reported.

**Note:** The manufacturer states that *Capstar*® may be used with other products, including heartworm preventatives, corticosteroids, antibiotics, vaccines, de-worming medications, shampoos, and other flea products.

### MONITORING
- Efficacy

# Norfloxacin

**Trade/brand name:** *Noroxin*® (US, CA, UK), *Apo-Norflox*® (CA), generic (Rx)
**Classification:** Antibacterial (second-generation fluoroquinolone)

## INDICATIONS

**Dogs and cats:** Treatment of skin and soft tissue infections associated with susceptible bacteria such as *Staphylococcus*, *Pseudomonas*, *Proteus*, *Escherichia coli*. Norfloxacin has less activity against *Pseudomonas aeruginosa* than other fluoroquinolones. Veterinary fluoroquinolones have more favorable pharmacokinetics and a superior spectrum of activity compared to norfloxacin. Norfloxacin, concurrently with topical therapy, may be of benefit for treatment of chronic ear infections, particularly otitis media, caused by susceptible organisms; however, tissue concentration is not known for the external or middle ear, and this indication is controversial with unpredictable efficacy.

**Note:** The authors do not recommend the use of fluoroquinolones as first-line therapy for pyoderma. Antibiotic selection should be based on culture and susceptibility results. Fluoroquinolones should be considered primarily for chronic deep pyodermas associated with extensive scar tissue, because of their excellent tissue penetration.

## CONTRAINDICATIONS

Fluoroquinolones can be potentially toxic to chondrocytes and should not be given to immature dogs during their rapid growth phase (small and medium-sized breeds between 2 and 8 months, large breeds younger than 12 months, giant breeds younger than 18 months). Norfloxacin may cause CNS stimulation and should be used cautiously in patients with a history of seizure activity. The pathomechanism associated with CNS effect is believed to be inhibition of the inhibitory neurotransmitter GABA.

## MECHANISM OF ACTION

Norfloxacin is a bactericidal antibiotic and inhibits DNA supercoiling and synthesis by inhibition of bacterial DNA gyrase (a type II topoisomerase). Similarly to other fluoroquinolones, norfloxacin accumulates inside inflammatory cells, in particular macrophages. Fluoroquinolones have been reported to have anti-inflammatory properties including inhibition of TNF-alpha synthesis and suppression of induced leukotriene production by neutrophils, lymphocytes, monocytes, and basophils.

## DOSAGES

**Dogs and cats:** 22 mg/kg PO q12h for 7–14 days past resolution of clinical signs

**Note:** The twice daily administration is a disadvantage compared to the veterinary fluoroquinolones.

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablet: 400 mg; *Noroxin®*, *Apo-Norflox®*
- Oral tablet: 100 mg, 200 mg, 400 mg; generic

### SIDE EFFECTS

**Dogs and cats:** Norfloxacin is generally well tolerated, but it may cause vomiting, diarrhea, and soft stools at high doses. CNS toxicity may develop at high concentrations, especially in animals with renal failure. Arthropathy may develop in young animals, and rapidly growing dogs at 4–28 weeks of age are more susceptible.

### DRUG INTERACTIONS

**Cimetidine:** use carefully, because cimetidine has been shown to interfere with the metabolism of fluoroquinolones

**Nitrofurantoin:** may reduce the antimicrobial effect of fluoroquinolones

**Products containing divalent or trivalent cations, such as aluminum (e.g., sucralfate), iron, calcium, zinc:** may decrease absorption of norfloxacin; separate administration by at least 2 hours

**Theophylline:** may increase theophylline blood levels

### MONITORING
- Efficacy and adverse effects

## Orbifloxacin

**Trade/brand name:** *Orbax®* (US, CA, UK) (Rx)
**Classification:** Antibacterial (third-generation fluoroquinolone)

### INDICATIONS

**Dogs and cats:** Orbifloxacin is registered to treat skin and soft tissue infections associated with susceptible bacteria such as *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, coagulase-positive staphylococci, *Pseudomonas*, *Proteus mirabilis*, *Escherichia coli*, beta-hemolytic streptococci (group G) and *Pasteurella multocida*. Orbifloxacin has poor activity against anaerobes. It may also be of benefit, if used in combination with topical therapy, for the treatment of chronic ear infections, particularly otitis media, caused by susceptible organisms such as *Pseudomonas*. However, tissue concentration is not known for the external or middle ear, and this indication is controversial with unpredictable efficacy.

**Note:** The authors do not recommend the use of fluoroquinolones as first-line therapy for pyoderma. Fluoroquinolones should be considered primarily for chronic deep pyodermas associated with extensive scar tissue, because of their excellent tissue penetration. Antibiotic selection should be based on culture and susceptibility results.

### CONTRAINDICATIONS

Fluoroquinolones can be potentially toxic to chondrocytes and should not be given to immature dogs during their rapid growth phase (small and

medium-sized breeds between 2 and 8 months, large breeds younger than 12 months, giant breeds younger than 18 months). Orbifloxacin may rarely cause CNS stimulation and should be used cautiously in patients with a history of seizure activity. The pathomechanism associated with increased CNS activity appears to be inhibition of the inhibitory neurotransmitter GABA. It should not be used in dogs or cats with hypersensitivity to orbifloxacin or other fluoroquinolones.

### MECHANISM OF ACTION

Orbifloxacin is a bactericidal antibiotic and inhibits DNA supercoiling and synthesis by inhibition of bacterial DNA gyrase (a type II topoisomerase). Similarly to other fluoroquinolones, orbifloxacin accumulates inside inflammatory cells, in particular macrophages. Fluoroquinolones have been reported to have anti-inflammatory properties including inhibition of TNF-alpha synthesis and suppression of induced leukotriene production by neutrophils, lymphocytes, monocytes, and basophils.

### DOSAGES

**Dogs and cats:** 2.5–7.5 mg/kg PO q24h (oral tablet formulation) for 7–14 days past resolution of clinical signs. *Pseudomonas* infections and chronic deep pyodermas associated with extensive scar tissue may initially need doses at the high end of the dosing range.

**Note:** The manufacturer's recommended dose of the oral suspension for cats is 7.5 mg/kg PO q24h because it provides lower and more variable plasma concentrations of orbifloxacin than the oral tablet formulation. The manufacturer warns to not administer doses higher than 7.5 mg/kg once daily.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats
- Oral tablets: 5.7 mg (250/btl), 22.7 mg (250/btl), 68 mg (100/btl); *Orbax®*
- Oral suspension (malt-flavored): 30 mg/mL (20 mL/btl); *Orbax®*

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs and cats:** Orbifloxacin is generally well tolerated but it may cause nausea, vomiting, diarrhea, soft stools, and lethargy at high doses. It has not caused blindness in cats (as reported for enrofloxacin and nalidixic acid) with doses up to 15 mg/kg; nevertheless, use higher doses cautiously. CNS toxicity may develop at high concentrations, especially in animals with renal failure. Arthropathy may develop in young animals, and rapidly growing dogs at the age of 4–28 weeks are more susceptible.

### DRUG INTERACTIONS

**Antacids containing divalent or trivalent cations (e.g., $Mg^{++}$, $Al^{++}$, $Ca^{++}$), iron, zinc:** decrease orbifloxacin absorption; separate administration by at least 2 hours

**Aminoglycosides, third-generation cephalosporins, extended-spectrum penicillins:** drug synergism may occur, especially against *Pseudomonas*

**Cimetidine:** use carefully, because cimetidine has been shown to interfere with the metabolism of fluoroquinolones

**Cyclosporine:** may reduce the metabolism of cyclosporine

**Methotrexate:** may increase methotrexate blood levels

**Nitrofurantoin:** may reduce the antimicrobial effect of fluoroquinolones

**Phenytoin:** may alter phenytoin levels

**Sucralfate:** may inhibit absorption of orbifloxacin; separate administration by at least 2 hours

**Theophylline:** may increase theophylline blood levels

**Warfarin:** may increase the effects of warfarin

### MONITORING

- Efficacy and adverse effects

## Ormetoprim+Sulfadimethoxine

**Trade/brand name:** *Primor®* (US) (Rx)
**Classification:** Antibacterial (potentiated sulfonamide)

### INDICATIONS

**Dogs:** Ormetoprim+sulfadimethoxine is approved to treat canine bacterial skin infections and soft tissue infections caused by susceptible staphylococcal strains.

**Note:** Antibiotic selection should be based on culture and susceptibility results.

### CONTRAINDICATIONS

Dogs sensitive to sulfonamides, and those with severe liver parenchymal damage and blood dyscrasias. Animals with low Schirmer's tear test values should not be treated with sulfonamides. Use cautiously in Doberman pinschers, samoyeds, and miniature schnauzers, as these breeds have been reported to have a high risk for developing reactions to sulfonamides.

### MECHANISM OF ACTION

Potentiated sulfas are bactericidal and sequentially inhibit the enzymes involved in the folic acid pathway, resulting in the inhibition of bacterial thymidine synthesis. The sulfonamide inhibits the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid, and ormetoprim inhibits the conversion of dihydrofolic acid to tetrahydrofolic acid by inhibiting the bacterial enzyme dihydrofolate reductase.

### DOSAGES

**Dogs:** 55 mg/kg PO q24h on the first treatment day, then 27.5 mg/kg PO q24h for 7–14 days past resolution of clinical signs

**Note:** The manufacturer does not recommend treatment longer than 21 days as a result of increased risks for side effects, mainly hypothyroidism.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs
- Oral tablets (sulfadimethoxine + ormetoprim): 120 mg (100 mg/20 mg), 240 mg (200 mg/40 mg), 600 mg (500 mg/100 mg), 1200 mg (1000 mg/200 mg); *Primor®*

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs:** fever, thrombocytopenia, hepatopathy, keratoconjunctivitis sicca, neutropenia, hemolytic anemia, crystalluria, arthropathy, uveitis, skin and mucocutaneous lesions, urticaria, angioedema, proteinuria, facial palsy, hypothyroidism, diarrhea, vomiting, anorexia, seizures.

### DRUG INTERACTIONS

These drug interactions have been reported for trimethoprim + sulfadiazine (TMP/sulfa) and are likely to also occur with ormetoprim + sulfadimethoxine.

**Antacids:** may decrease the absorption of sulfonamides

**Cyclosporine:** may increase cyclosporine nephrotoxicity risks

**Digoxin:** may increase digoxin levels

**Hypoglycemic agents, oral:** may potentiate effects of these drugs

**Methotrexate:** may compete with methotrexate for binding to plasma proteins, resulting in higher serum unbound fraction and increased risk for toxic effects

**Phenytoin, phenylbutazone, salicylates, thiazide diuretics, probenecid:** may increase the effects and toxicity of these drugs

**Tricyclic antidepressants:** may decrease efficacy of these drugs

**Warfarin:** clotting times may be prolonged

### MONITORING

- Efficacy and adverse effects
- Schirmer's tear tests: baseline and weekly during treatment
- Thyroid function should be monitored if the drug is administered for longer than 21 days, since sulfonamides inhibit the activity of thyroid peroxidase, resulting in iatrogenic hypothyroidism
- CBC: biweekly if long-term therapy (longer than 2 weeks) is required

## Oxacillin Sodium

**Trade/brand name:** *Bactocill®* (US), *Prostaphlin®* (US), generic (Rx)
**Classification:** Antibacterial (beta-lactam)

### INDICATIONS

**Dogs and cats:** Treatment of susceptible bacterial skin infections such as penicillinase-producing strains of Gram-positive cocci, particularly staphylococcal

species. The penicillinase-resistant penicillins are ineffective against *Mycobacterium*, *Rickettsia*, *Mycoplasma*, and viruses.

**Note:** Oxacillin use has diminished because of its required frequent dosing (every 6–8 hours), and because of the availability of other drugs such as cephalosporins and amoxicillin/clavulanate. Antibiotic selection should ideally be based on culture and susceptibility results. Oxacillin is typically used as the surrogate antibiotic for methicillin in susceptibility tests. *Staphylococci* strains resistant to oxacillin should be considered resistant to all cephalosporins.

### CONTRAINDICATIONS

Patients with hypersensitivity to penicillins or other beta-lactam antibiotics.

### MECHANISM OF ACTION

Similarly to other beta-lactam antibiotic, oxacillin binds to penicillin-binding proteins (carboxypeptidases, transpeptidases, endopeptidases) involved in the bacterial cell wall mucopeptide synthesis, resulting in osmotic instability.

### DOSAGES

**Dogs and cats:** 22–40 mg/kg PO q6–8h for 7–14 days past resolution of clinical signs

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 250 mg, 500 mg: *Bactocill®*, *Prostaphlin®*, generic
- Powder for oral solution: 250 mg/5 mL in 100 mL; *Prostaphlin®*, generic

### SIDE EFFECTS

**Dogs and cats:** anorexia, vomiting, diarrhea, dose-unrelated hypersensitivity reactions (e.g., rashes, fever, eosinophilia, neutropenia, agranulocytosis, thrombocytopenia, leukopenia, anemia, lymphadenopathy, anaphylaxis). Ataxia has occurred with prolonged use and very high doses in dogs. Elevated liver enzymes have been reported. Other side effects reported in dogs include dyspnea, tachypnea, tachycardia and edema.

### DRUG INTERACTIONS

**Aminoglycosides:** synergism with oxacillin against *Staphylococcus aureus* has been demonstrated in vitro

**Cyclosporine:** may reduce serum levels of cyclosporine

**Probenecid:** increases serum levels and serum half-lives of oxacillin by competitively blocking its tubular secretion

**Tetracyclines:** may antagonize the activity of oxacillin

**Warfarin:** efficacy may be reduced by oxacillin

### MONITORING

- Efficacy and adverse effects

## Oxazepam

**Trade/brand name:** *Serax*® (US), generic (Rx)
**Classification:** Tranquilizer, CNS depressant, Benzodiazepine

### INDICATIONS

Management of psychogenic dermatoses mostly associated with anxiety. Benzodiazepines, such as oxazepam, are short-term anxiolytics and therefore may be more effective for acute or time-limited stress. It is important to note that environmental and behavior management used concurrently may increase the efficacy of any pharmacologic intervention.

**Dogs:** Self-mutilations, acral lick dermatitis, excessive tail or nail biting/chewing, excessive anal or foot licking, flank sucking, tail dock neuroma.

**Cats:** Excessive grooming or psychogenic self-induced alopecia, tail sucking, excessive nail or foot biting/chewing, hyperesthesia syndrome.

### CONTRAINDICATIONS

Patients with known hypersensitivity to oxazepam or other benzodiazepines and with acute narrow-angle glaucoma. Use cautiously in patients with hepatic dysfunction and in those susceptible to seizures (it may precipitate tonic–clonic seizures). Benzodiazepines such as oxazepam may intensify the clinical signs associated with myasthenia gravis. Avoid use in nursing animals. When using regularly, make sure to withdraw the drug gradually to avoid a rebound effect.

### MECHANISM OF ACTION

The exact mechanism of action of oxazepam is unknown. Postulated mechanisms include potentiation of the effects of GABA by binding to specific benzodiazepine receptors, antagonism of serotonin, and attenuation of the release or turnover of acetylcholine in the CNS.

### DOSAGES

**Dogs:** 0.2–1 mg/kg PO q12–24h

**Cats:** 0.2–0.5 mg/kg PO q12–24h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 15 mg; *Serax*®
- Oral capsules: 10 mg, 15 mg, 30 mg; *Serax*®, generic

### SIDE EFFECTS

**Dogs and cats**
- Common: sedation, ataxia
- Uncommon: paradoxical excitability, aggression and vocalization
- Rare: tonic-clonic seizures

**Note:** In contrast to diazepam, hepatocellular toxicity is unlikely to occur in cats taking oxazepam, because no active intermediate metabolite is formed. Benzodiazepines may interfere with learning and short-term memory.

### DRUG INTERACTIONS

**Cimetidine, erythromycin, ketoconazole, propranolol:** may decrease the metabolism of oxazepam, resulting in excessive sedation

**CNS depressant drugs (e.g., barbiturates, narcotics, anesthetics):** additive CNS effects may occur

**Phenytoin:** may decrease serum concentrations of oxazepam

**Probenecid:** in dogs, it may impair glucuronide conjugation and prolong effects

**Rifampin:** may induce hepatic microsomal enzymes and decrease the pharmacologic effects of benzodiazepines

**St. John's wort, theophylline:** may decrease oxazepam effectiveness

### MONITORING

- Efficacy and adverse effects
- If cat develops inappetence, lethargy, ataxia, or vomiting, medication needs to be discontinued
- Hepatic profile (especially ALT and AST) in cats (particularly with long-term treatment): baseline and within 5 days of initiation of treatment

## Paroxetine Hydrochloride

**Trade/brand name:** *Paxil*® (US), *Seroxat*® (UK), generic (Rx)
**Classification:** Behavior modifying drug (selective serotonin reuptake inhibitor)

### INDICATIONS

Management of behavior disorders such as psychogenic or compulsive dermatoses.

**Dogs:** Self-mutilations, acral lick dermatitis, excessive tail or nail biting/chewing, excessive anal or foot licking, flank sucking, tail dock neuroma.

**Cats:** Psychogenic alopecia and dermatitis, tail sucking, excessive grooming, hair pulling, hyperesthesia syndrome.

**Note:** Paroxetine is most effective when combined with a behavior modification program.

### CONTRAINDICATIONS

Avoid in patients with hypersensitivity to this drug, in patients receiving monoamine oxidase (MAO) inhibitors, and in pregnant bitches, since fetal malformations may occur in early pregnancy. Use cautiously in patients with seizure disorders or in combination with drugs that lower the seizure threshold (e.g., acepromazine, chlorpromazine) and in patients with cardiac disease. In contrast to fluoxetine, no active metabolites are formed during the metabolism of

paroxetine; therefore, this drug may be preferred in elderly animals or patients with liver or kidney disorders.

### MECHANISM OF ACTION

Paroxetine selectively inhibits serotonin reuptake in the CNS and downregulates 5-$HT_1$ receptors, resulting in potentiation of serotonin pharmacologic activity (antidepressive activity). Paroxetine has minor dopamine or norepinephrine reuptake inhibition properties. It has some anticholinergic effects, which may increase the risk for development of constipation in cats.

### DOSAGES

**Dogs**: 1 mg/kg PO q24h

**Cats:** 0.5–1 mg/kg PO q12–24h

**Note:** The dose may be gradually increased to the highest required dose. Lag phase of 4–6 weeks.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 10 mg, 20 mg, 30 mg, 40 mg; *Paxil®*, generic
- Controlled-release oral tablets: 12.5 mg, 25 mg, 37.5 mg; *Paxil® CR*
- Oral suspension: 2 mg/mL (250 mL/btl); *Paxil®*

### SIDE EFFECTS

**Dogs:** lethargy, anorexia (common but usually transient), vomiting, diarrhea, tremors, anxiety, irritability, aggressive behavior, insomnia/hyperactivity, panting, vocalization, mydriasis, nystagmus, ataxia, and alterations in cardiac conduction

**Cats:** anorexia, constipation, vomiting, diarrhea, tremors, anxiety, vocalization, irritability, sleep disturbances, mydriasis, changes in elimination patterns and alterations in cardiac conduction

### DRUG INTERACTIONS

**Buspirone, isoniazid, pentazocine:** increased risk for serotonin syndrome

**Cimetidine:** may increase paroxetine blood levels

**Cyproheptadine:** may decrease or reverse the effects of SSRIs

**Insulin:** may alter insulin requirements

**Monoamine oxidase (MAO) inhibitors (e.g., amitraz, selegiline):** high risk for serotonin syndrome – use is contraindicated. May need a 5-week washout period after discontinuing paroxetine and a 2-week washout period if first discontinuing the MAO inhibitor

**Phenobarbital:** may reduce paroxetine levels

**Phenytoin:** paroxetine may increase phenytoin plasma levels and phenytoin may decrease paroxetine levels

**Propranolol, metoprolol:** may increase plasma levels of these drugs and cause hypotension; atenolol may be safer to use concurrently with paroxetine

**Theophylline:** increased plasma levels of theophylline

**Tricyclic antidepressants (e.g., clomipramine, amitriptyline):** may increase plasma levels of these drugs increasing the risk for serotonin syndrome; concurrent use is contraindicated.

**Warfarin:** paroxetine may increase the risk for bleeding

### MONITORING

- Efficacy and adverse effects

## Pentoxifylline

**Trade/brand name:** *Trental*® (US, CA, UK), generic (Rx)
**Classification:** Anti-inflammatory, Hemorheologic

### INDICATIONS

**Dogs and cats:** Pentoxifylline has been used as a single or adjunctive agent for the management of various dermatologic conditions, including canine familial dermatomyositis, allergic contact dermatitis, vasculitis, pinnal thrombovascular disease, vaccine-induced ischemic dermatopathies, erythema multiforme, discoid lupus erythematosus, idiopathic mucinosis of the Chinese shar-pei dog, lupoid onychodystrophy/onychitis, German shepherd dog deep pyoderma, vesicular cutaneous lupus erythematosus, exfoliative cutaneous lupus erythematosus, acral lick dermatitis, greyhound vasculopathy, metatarsal fistulae of the German shepherd dog, sterile nodular pyogranulomatous/granulomatous syndrome, sterile nodular panniculitis, interdigital furunculosis, and atopic dermatitis.

### CONTRAINDICATIONS

Use cautiously in patients with known sensitivity to the drug or other methylxanthine derivatives, in patients with cerebral or retinal hemorrhage, in those at risk for hemorrhage, and in those with severe hepatic or kidney impairment.

### MECHANISM OF ACTION

Pentoxifylline is a methylxanthine derivative with rheologic and immunomodulatory properties. Its rheologic effect (blood flow modulation) is mediated by increase in erythrocyte and leukocyte deformability, decrease in fibrinogen levels and increase in fibrinolytic activity (both effects as a result of prostacyclin stimulation), decrease in platelet aggregation, decreased leukocyte adhesion and aggregation, and increase in neutrophil chemotaxis and motility. The blood flow modulation will ultimately result in increased peripheral tissue perfusion and oxygenation. Its immunomodulatory effect is mediated by decrease in cytokine production (IL-1, IL-4, IL-12, TNF-alpha), decrease in leukocyte responsiveness to IL-1 and TNF-alpha, inhibition of B- and T-lymphocyte activation, decrease in natural killer cell activation, inhibition of T-cell adherence to keratinocytes, and phosphodiesterase-4 inhibition. Pentoxifylline also has an effect in wound healing by increasing collagenase production and decreasing the synthesis of collagen, fibronectin, and glycosaminoglycans.

### DOSAGES

Dosages are empirical and vary widely.

**Dogs:** 10–30 mg/kg PO q8–12h. Perform a trial of 2–3 months before evaluating response to therapy

**Cats:** 100 mg (one-quarter of a 400 mg tablet) PO q12h

**Note:** For dogs, the authors typically use 15–20 mg/kg q8–12h. The bioavailability benefits of the extended-release tablets may be lost when the tablets are crushed for dosing.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Extended-release oral tablets: 400 mg; *Trental*®, generic

### SIDE EFFECTS

Pentoxifylline is considered quite safe and it is generally well tolerated. Administering with food may reduce the gastrointestinal side effects.

**Dogs and cats:** vomiting, diarrhea, anorexia, thrombocytopenia (anecdotally reported)

**Note:** In humans, common side effects reported include vomiting, diarrhea, and anorexia; rare side effects include dizziness, headache, and CNS and cardiovascular abnormalities.

### DRUG INTERACTIONS

**Antihypertensive drugs:** may increase hypotensive effect

**Platelet-aggregation inhibitors (e.g., aspirin), warfarin, and other anticoagulants:** increased risk of bleeding

**Theophylline:** increased theophylline serum levels

### MONITORING

- Efficacy and adverse effects

## Piperacillin Sodium

**Trade/brand name:** *Pipracil*® (US) (Rx)
**Classification:** Antibacterial (beta-lactam)

### INDICATIONS

**Dogs:** In veterinary dermatology, piperacillin sodium has been rarely used for susceptible *Pseudomonas* otitis cases. It is typically used as adjunctive therapy in refractory cases, in conjunction with topical treatment.

**Note:** As for any case of *Pseudomonas* otitis, this antibiotic choice should be based on bacterial culture and susceptibility results.

### CONTRAINDICATIONS

Patients with known allergy to beta-lactam antibiotics or other penicillin drugs. High doses contribute to the patient's sodium load and may adversely affect patients with hypernatremic disorders and heart failure.

### MECHANISM OF ACTION

Piperacillin is a beta-lactam bacteriostatic antibiotic of the acylureidopenicillin class. Similarly to other beta-lactam antibiotics, piperacillin binds to penicillin-binding proteins (carboxypeptidases, transpeptidases, endopeptidases) involved in the bacterial cell wall mucopeptide synthesis, resulting in cell wall weakness or lysis and osmotic instability. Similar to other penicillins, it is a time-dependent drug (i.e., drug concentration should ideally be maintained above the minimum inhibitory concentration (MIC) during the dose interval for better efficacy) and it is very active against *Pseudomonas aeruginosa*.

### DOSAGES

**Dogs:** 20 mg/kg SC q8h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Powder for injection: 2 g, 3 g and 4 g (as base) vials and 40 g (bulk) vials; *Pipracil®*

### SIDE EFFECTS

**Dogs:** hypersensitivity reactions may occur

**Note:** In humans, piperacillin has caused coagulation disorders (inhibits platelet function) and seizures, especially if high doses are used in patients with reduced renal function.

### DRUG INTERACTIONS

**Anticoagulants:** piperacillin may rarely affect platelet function; therefore, monitor coagulation parameters more frequently in patients on warfarin or heparin

**Methotrexate:** may increase methotrexate levels

**Probenecid:** can reduce the renal tubular secretion of piperacillin, resulting in high systemic levels for longer periods

**Vecuronium:** neuromuscular blockage may be prolonged by piperacillin

### MONITORING

- Efficacy and adverse effects

## Piroxicam

**Trade/brand name:** *Feldene®* (US, CA, UK), generic (Rx)
**Classification:** Anti-inflammatory, Antineoplastic

## INDICATIONS

**Dogs and cats:** The interest in piroxicam in veterinary dermatology is related to its use in the treatment of oral and cutaneous squamous cell carcinomas, nasal carcinoma, mammary adenocarcinoma, and transmissible venereal tumor.

**Note:** It is typically used as adjunctive therapy, and the clinical results are variable.

## CONTRAINDICATIONS

Avoid in patients allergic to non-steroidal anti-inflammatory drugs (NSAIDs), and in those with active gastrointestinal ulcer or bleeding or that are prone to develop gastrointestinal ulcer. Do not use in dehydrated patients. Use cautiously in animals with renal or cardiac dysfunction, hypertension, or coagulation disorders.

## MECHANISM OF ACTION

Piroxicam has anti-inflammatory, analgesic and antipyretic effects. Its antineoplastic effect is not clear. NSAIDs inhibit cyclooxygenases (COX-1 and COX-2), which are involved in prostaglandin synthesis. Several tumors in dogs (e.g., squamous cell carcinoma, transitional cell carcinoma, nasal and gastrointestinal carcinomas) and the adjacent stromal tissues show expression of the inducible COX-2 enzyme. At the cancer cell level, COX-2 expression is linked to apoptosis resistance, stimulation of cancer cell proliferation, and enhanced cell migration. The stromal expression promotes neovascularization and altered macrophage function. In addition, COX-2 expression is associated with direct oxidative damage to DNA and increased production of the P-glycoprotein MDR1 (ABCB1-1), which confers multi-drug resistance. Its antineoplastic effects are therefore thought to be associated with the induction of apoptosis and the inhibition of tumor proliferation, invasion, and angiogenesis.

## DOSAGES

Administer with food to reduce gastrointestinal side effects.

**Dogs and cats:** 0.3 mg/kg PO q24–48h

**Note:** Use cautiously in cats, as this species is much more sensitive to the potential side effects of NSAIDs.

## FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral capsules: 10 mg and 20 mg; *Feldene*®, generic

## SIDE EFFECTS

**Dogs and cats:** the main side effect is gastrointestinal ulceration and bleeding. Renal papillary necrosis may also occur, especially in animals at risk for dehydration and with renal dysfunction.

**Note:** Alteration in liver function tests, pruritus, rash and peripheral edema have been reported in humans.

## DRUG INTERACTIONS

**Aminoglycosides:** increased risk for nephrotoxicity

**Anticoagulants:** increased risk for bleeding

**Aspirin:** may decrease piroxicam plasma levels and potentially increase risk for gastrointestinal blood loss

**Bisphosphonates:** may increase risk for gastrointestinal ulceration

**Cisplatin:** may potentiate the renal toxicity of cisplatin

**Corticosteroids:** the risks for gastrointestinal adverse effects may increase significantly

**Furosemide:** may reduce the saluretic and diuretic effects of furosemide

**Highly protein bound drugs (e.g., phenytoin, valproic acid, oral anticoagulants, salicylates, sulfonamides, sulfonylurea antidiabetic agent, other anti-inflammatory drugs):** increased serum levels and duration of action may occur when using highly protein-bound drugs concurrently with piroxicam, which is 99% protein-bound

**Methotrexate:** concurrent use with NSAIDs may increase methotrexate levels by decreasing its clearance and result in serious toxicity; in general, do not administer NSAIDs within 10 days of high-dose methotrexate (i.e., used for cancer therapy)

### MONITORING

- Efficacy and adverse effects
- Animals receiving long-term treatment should be monitored for gastrointestinal bleeding and have kidney and liver function monitored regularly

## PO7P (Chinese Herbal Supplement)

**Trade/brand name:** *Phytopica*® (UK)
**Classification:** Anti-inflammatory, Herbal supplement

### INDICATIONS

**Dogs:** PO7P is labeled for sensitive skin and atopic dermatitis. One double-blind randomized placebo-controlled trial (Schmidt *et al*. 2010) indicated that *Phytopica*® can be an effective glucocorticoid-sparing agent (similarly to antihistamines and pentoxifylline) in the management of canine atopic dermatitis.

### CONTRAINDICATIONS

No information available.

### MECHANISM OF ACTION

Standardized mixture of extracts obtained from three plants (*Glycyrrhisa uralensis*, *Paeonia lactiflora*, *Rehmania glutinosa*). These extracts have been shown to have immunomodulatory properties, which might explain the potential benefit for atopic dermatitis. *G. uralensis* potentiates the expression of the immunosuppressive cytokine IL-10 by human peripheral blood mononuclear cells, inhibits cytochrome P450, induces apoptosis in leukemic cells, and has antioxidant and antibacterial activities. *R. glutinosa* inhibits production of pro-inflammatory cytokines (e.g., TNF-alpha and IL-1), suppresses histamine release and cyclooxigenase

activity in rodent cell models, and has an antioxidant effect in vitro. *P. lactiflora* inhibits cyclooxygenase activity in leukocytes and nitric oxide synthase in activated macrophages, induces apoptosis in leukemic cell lines, and has antioxidant activity.

### DOSAGES

**Dogs:** 200 mg/kg PO q24h; administer in food

**Note:** Beneficial effects should be seen in the first month of therapy.

### FORMULATIONS

**Veterinary-labeled products:** Labeled for dogs
- Oral powder: 2 g sachets (for small and medium dogs) and 7.5 g sachets (for large dogs); *Phytopica*® (not available in the US; may be imported via Phytopharm in EU)

**Human-labeled products:** There is one brand called *Zemaphyte*®; however, it contains other types of herbs and its use has not been reported in dogs.

### SIDE EFFECTS

**Dogs:** PO7P appears to be well tolerated in dogs. Self-limiting diarrhea, vomiting and flatulence may occur.

### DRUG INTERACTIONS

No information available.

### MONITORING

- Efficacy and adverse effects

## Posoconazole

**Trade/brand name:** *Noxafil*® (US, UK), *Posanol*® (CA) (Rx)
**Classification:** Antifungal (triazole, second-generation)

### INDICATIONS

Posoconazole is approved for the treatment of human oropharyngeal candidiasis, and for the prevention of invasive *Candida* and *Aspergillus* infections in patients at high risk for acquiring infections with these agents. Moreover, it has been reported to be efficacious against various other yeasts and filamentous fungi such as *Cryptococcus*, *Histoplasma*, *Blastomyces*, *Coccidioides*, *Fusarium*, *Rhizopus*, *Mucor*, and zygomycetes.

**Cats:** It was used successfully in a cat with invasive orbital aspergillosis after itraconazole and amphotericin B had failed (McLellan *et al*. 2006).

**Dogs:** No reports on the use of posoconazole to treat canine fungal infections are available.

### CONTRAINDICATIONS

Patients with hypersensitivity to posoconazole or any of its ingredients. It should be used cautiously in patients with hypersensitivity to other azoles. It should be

used during pregnancy only if the benefit outweighs the risks. The concomitant use of posoconazole and terfenadine, astemizole, cisapride, pimozide, halofantrine, or quinidine (all CYP3A4 substrates) is contraindicated because of potential for QT interval prolongation.

### MECHANISM OF ACTION

Posoconazole is a lipophilic broad-spectrum, second-generation triazole with a molecular structure similar to that of itraconazole. Like other triazoles it inhibits lanosterol 14-alpha demethylase (CYP51), the enzyme responsible for ergosterol synthesis, which is an important component of the fungal cell wall.

### DOSAGES

Posoconazole should be taken with food (ideally a high-fat meal) to enhance absorption.

**Cats:** 5 mg/kg PO q24h

**Dogs:** Despite lack of reports on the use of posoconazole to treat canine fungal infections, a pharmacokinetic study showed that 10 mg/kg PO q24h provided drug concentrations above the minimum inhibitory concentration (MIC) and minimum fungicidal concentrations

**Note:** Dividing the dose to twice-a-day administration has been shown to increase drug exposure in people.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral suspension: 40 mg/mL in a 123 mL (4 oz)/btl; *Noxafil®*, *Posanol®* (CA)

### SIDE EFFECTS

There is currently very limited experience with use of this drug in dogs and cats.

**Cats:** the only side effect reported in a cat with orbital aspergillosis treated with posoconazole for 16 weeks was facial and ear pruritus and erythema.

**Note:** The most commonly reported side effects in humans are vomiting, nausea, abdominal pain, and diarrhea. Increase in liver enzymes is reported, but severe hepatic dysfunction is rare. Other side effects include skin rash, headache, tremors, hypertension, anorexia, and weakness.

### DRUG INTERACTIONS

It is important to keep in mind that posoconazole is a strong inhibitor of CYP3A4, and increase in plasma concentrations of drugs primarily metabolized by this enzyme may occur. It is also a P-glycoprotein substrate, and the concomitant use of drugs that inhibit or induce this clearance pathway may alter posoconazole plasma levels. Listed are some of the drugs that can interact with posoconazole through one of these mechanisms.

**Cimetidine:** reduces posoconazole exposure

**Cyclosporine, midazolam, phenytoin, rifabutin, sirolimus:** increase blood concentration of these drugs through posoconazole inhibition of CYP3A4

**Vincristine:** increases vincristine blood levels

### MONITORING

- Efficacy and adverse effects
- Liver enzymes should be monitored before and during therapy

## Pradofloxacin

**Trade/brand name:** *Veraflox*® (EU) (Rx)
**Classification:** Antibacterial (third-generation fluoroquinolone)

### INDICATIONS

**Dogs:** Pradofloxacin is a novel third-generation fluoroquinolone currently approved in Europe to treat canine wound infections and superficial and deep pyoderma associated with susceptible strains of *Staphylococcus pseudintermedius*. However, it has shown lower minimal inhibitory concentration (MIC) when compared to various fluoroquinolones for the following organisms: *Bordetella*, *Escherichia coli*, *Enterococcus*, *Klebsiella pneumonia*, *Staphylococcus*, *Staphylococcus pseudintermedius*, *Streptococcus*, *Pseudomonas*, *Proteus*, *Mycoplasma*, *Salmonella*, and *Pasteurella*. Moreover, in contrast to other fluoroquinolones, pradofloxacin has shown excellent in-vitro activity against anaerobic bacteria isolated from dogs and cats. Pradofloxacin, concurrently with topical therapy, may also be of benefit for treatment of chronic ear infections, particularly otitis media, caused by susceptible organisms such as *Pseudomonas*. However, tissue concentration is not known for the external or middle ear, and this indication is controversial with unpredictable efficacy.

**Note:** The authors do not recommend the use of fluoroquinolones as first-line therapy for pyoderma. Fluoroquinolones should be considered primarily for chronic deep pyodermas associated with extensive scar tissue, because of their excellent tissue penetration. Antibiotic selection, however, should be based on culture and susceptibility results.

### CONTRAINDICATIONS

Fluoroquinolones can be potentially toxic to condrocytes and should not be given to immature dogs during their rapid growth phase (small and medium-sized breeds between 2 and 8 months, large breeds younger than 12 months, giant breeds younger than 18 months). Moreover, do not use pradofloxacin in dogs with chronic articular cartilage lesions, to avoid worsening of lesions during treatment. Pradofloxacin may cause CNS stimulation and should be used cautiously in dogs with a history of seizure activity (mainly patients receiving NSAIDs because of potential pharmacodynamic interactions in the CNS). The pathomechanism associated with CNS effect is believed to be inhibition of the inhibitory neurotransmitter GABA. Do not use pradofloxacin in pregnant or lactating dogs, as safety data are not available. Use cautiously in dogs with abnormal kidney function, as the drug is primarily excreted by the kidneys in this species.

### MECHANISM OF ACTION

Pradofloxacin is a third-generation fluoroquinolone that inhibits DNA supercoiling and synthesis by inhibition of bacterial DNA gyrase and topoisomerase IV.

Because of these two fluoroquinolone targets, development of resistance is less likely than with other fluoroquinolones. Similarly to other fluoroquinolones, pradofloxacin accumulates inside inflammatory cells, in particular in macrophages.

### DOSAGES

**Dogs:** The manufacturer's recommended dose is 3 mg/kg PO q24h; however, because of the available tablet sizes the prescribed dose may range from 3 to 4.5 mg/kg PO q24h. It should be administered for 7–14 days past resolution of clinical signs.

### FORMULATIONS

**Veterinary-labeled products:** Currently only available in Europe
- Oral tablets: 15 mg, 60 mg, 120 mg; *Veraflox*®

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs:** pradofloxacin is generally well tolerated, but it may cause nausea, vomiting, diarrhea, soft stools, lethargy. These signs are typically mild and transient. It can induce seizure when administered at high doses.

### DRUG INTERACTIONS

**Antacids containing divalent or trivalent cations (e.g., $Mg^{++}$, $Al^{++}$, $Ca^{++}$), iron, zinc:** decrease pradofloxacin absorption; separate administration of these products and pradofloxacin by at least 2 hours

**Aminoglycosides, third-generation cephalosporins, extended spectrum penicillins:** drug synergism may occur, especially against *Pseudomonas*

**Digoxin:** may increase oral bioavailability of digoxin

**Cyclosporine:** may reduce the metabolism of cyclosporine

**Methotrexate, theophylline**: may increase the blood levels of these drugs

**Nitrofurantoin:** may reduce the antimicrobial effect of fluoroquinolones

### MONITORING
- Efficacy and adverse effects

## Prednisone/Prednisolone

**Trade/brand name:** *Prednis-Tab*® (US), *Pred Fort*® (UK), *Deltasone*® (CA), *Temaril P*® (US, CA), generics (Rx)
**Classification:** Anti-inflammatory (glucocorticoid), Immunomodulatory (immunosuppressive), Hormone

### INDICATIONS

**Dogs and cats:** Allergic skin disorders (e.g., atopic dermatitis), autoimmune skin disorders (e.g., pemphigus complex), and various sterile inflammatory or immune-mediated dermatoses.

## CONTRAINDICATIONS

Infectious diseases, hyperadrenocorticism (can be carefully used to balance treatment-induced hypoadrenocorticism), gastric ulcer, corneal ulcer, diabetes mellitus, renal failure, and pregnancy. Modified live vaccines should be avoided when using immunosuppressive doses of glucocorticoids. Use glucocorticoids cautiously in cats with any cardiovascular disorders that alter the compensatory mechanisms for increased plasma volume, to avoid congestive heart failure (Ployngam *et al*. 2006). Prednisone and prednisolone will interfere with the intradermal and allergy serum test results. Withdrawal of oral administration of these drugs is usually recommended for at least 4 weeks prior to allergy testing. Injectable prednisone and prednisolone are considered unsuitable for management of chronic dermatologic diseases due to potential severe effect on the HPA-axis.

## MECHANISM OF ACTION

The mechanisms of action of glucocorticoids are complex. Through genomic and non-genomic mechanisms they exert anti-inflammatory and immunosuppressive effects by decreasing the synthesis of inflammatory cytokines, chemokines, adhesion molecules, prostaglandins, and leukotrienes (both mediated by increasing the expression of lipocortin-1); enhancing the clearance of foreign antigens; decreasing the ability of dendritic cells to present antigen and activate T cells; suppressing the cellular immune response through inhibition of IL-12 synthesis and suppression of a Th-1 response, but promotion of a Th-2 response.

## DOSAGES

### Dogs

- Allergic and inflammatory skin disorders: 0.5–1 mg/kg PO q24h. Total dose can be divided twice daily. After remission of clinical signs, reduce the dose to the lowest amount needed to maintain the disease under control. Long-term treatment should be administered every other day or less frequently if possible
- Autoimmune disorders: 2.2–6 mg/kg PO q24h (doses over 2.2 mg/kg PO q24h are typically poorly tolerated). Total dose can be divided twice daily. Apply the same recommendation for long-term treatment as above

### Cats

- Allergic and inflammatory skin disorders: 2.2 mg/kg PO q24h. Total dose can be divided twice daily. After remission of clinical signs, reduce to the lowest dose needed to maintain the disease under control. Long-term treatment should be administered every other day or less frequently if possible
- Autoimmune skin disorders: 4–6 mg/kg PO q24h. Total dose can be divided twice daily. Apply the same recommendation for long-term treatment as above

**Note:** When used long-term, the drug should be discontinued gradually.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs

- Oral tablets (prednisolone): 5 mg, 20 mg; *Prednis-Tab®*, generic
- Oral tablets (trimeprazine + prednisolone): 5 mg/2 mg; *Temaril-P®*

### Human-labeled products

- Oral tablets: 1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, 50 mg; *Meticorten®*, *Orasone®*, *Panasol-S®*, *Deltasone®*, *Prednicen-M®*, *Sterapred®*, *Sterapred DS®*, generics

- Oral solution or syrup (prednisolone): 1 mg/mL and 3 mg/mL in 120, 237, 240 and 480 mL btl; *Prelone®*, *Pediapred®*, *Orapred®*, generics
- Oral solution or syrup (prednisone): 1 mg/mL in 120 mL, 240 mL, 500 mL btl and UD 5 mL; 5 mg/mL in 30 mL btl; *Prednisone and Prednisone Intensol® Concentrate, Liquid Pred®*

## SIDE EFFECTS

### Dogs

- Common (associated with long-term therapy): iatrogenic Cushing's disease (i.e., poor dull hair coat, polyuria, polydpsia, polyphagia, panting, muscle atrophy, thin skin, hypotrichosis or alopecia, pot-belly appearance, weight gain, calcinosis cutis, comedones, milia), secondary bacterial skin, bladder infections
- Less common: diarrhea, vomiting, gastrointestinal ulceration, pancreatitis, diabetes mellitus, behavior changes (i.e., aggression), demodicosis, dermatophytosis, hypoadrenocorticism

### Cats

- Common: diabetes mellitus (occur more often in cats than dogs)
- Rare: cats are less prone to develop iatrogenic Cushing's disease when treated with long-term glucocorticoids; however, this syndrome will develop if glucocorticoids are not used appropriately. Signs of iatrogenic Cushing's in cats include polyuria, polydipsia, polyphagia, fragile skin, distended abdomen, alopecia or hypotrichosis. Skin fragility syndrome may develop as the sole sign of inappropriate glucocorticoid use. Congestive heart failure has been reported in cats treated with corticosteroids (Smith *et al*. 2004). Diarrhea and depression may also occur

## DRUG INTERACTIONS

**Amphotericin B or potassium-depleting diuretics (e.g., furosemide, thiazides):** hypokalemia may develop

**Aspirin:** glucocorticoids may reduce salicylate levels

**Cyclophosphamide:** the hepatic metabolism of cyclophosphamide may be inhibited

**Cyclosporine**: may increase blood levels of both drugs

**Insulin:** insulin requirements may increase

**Ketoconazole or other azole antifungals and macrolide antibiotics (e.g., erythromycin, clarithromycin):** may increase prednisone/prednisolone blood levels by decreasing its metabolism

**Non-steroidal anti-inflammatory drugs (NSAIDs):** increased risk of gastrointestinal ulcer.

**Phenobarbital, rifampin, barbiturates:** may increase the metabolism of glucocorticoids and decrease prednisone/prednisolone blood levels

**Pyridostigmine or neostigmine:** profound muscle weakness may occur

## MONITORING

- Response to therapy and adverse effects
- The authors recommend performing serum chemistry profile, urinalysis and urine culture every 6–12 months

## *Propionibacterium acnes* Injection

**Trade/brand name:** *Immunoregulin*® (US) (Rx)
**Classification:** Immunomodulatory (immunostimulant)

### INDICATIONS

**Dogs:** *Propionibacterium acnes* is available as a killed bacterial vaccine labeled for use in conjunction with antibiotic therapy to manage chronic recurrent canine pyoderma. This treatment modality has the goal of decreasing the extent and severity of pyoderma lesions and increasing the interval between episodes of recurrences. In a randomized double-blind placebo-controlled study, dogs with chronic, recurrent pyoderma received antibiotic therapy and an injection of *Propionibacterium acnes* or placebo (Becker *et al*. 1989). At the end of the 12-week treatment duration, 12/15 (80%) dogs treated with antibiotic and *P. acnes* improved significantly, or pyoderma lesions completely resolved, compared to 5/13 (38%) dogs in the placebo group.

### CONTRAINDICATIONS

*P. acnes* injection should not be used in patients with hypersensitivity to it. It is recommended to withdraw glucocorticoid or other immunosuppressive agents at least 7 days prior to starting therapy with *P. acnes* injection, to avoid potential reduction of its immunostimulant effect. Use cautiously in animals with cardiac dysfunction. Safety in pregnant animals has not been evaluated.

### MECHANISM OF ACTION

The immunostimulant mechanism of *P. acnes* injection is non-specific. It may enhance cell-mediated immunity, increase the activity of natural killer cells, and induce lymphokine production and macrophage activation.

### DOSAGES

**Dogs:** Administer intravenously at the following dosages: 0.25 mL (dogs ≤6.8 kg or 15 lb); 0.5 mL (dogs 6.8–20.5 kg or 15–45 lb); 1 mL (dogs 20.5–34 kg or 45–75 lb); 2 mL (dogs >34 kg or 75 lb). Administer twice weekly for the first 2 weeks, then once weekly until the 12th week. Anecdotal reports indicate that if response occurs, it should be seen within 12 weeks of therapy. Monthly maintenance therapy may be recommended.

### FORMULATIONS

**Veterinary-labeled products:** Labeled for dogs
- Injection containing non-viable *P. acnes*: 0.4 mg/mL in 5 mL and 50 mL vials; *Immunoregulin*®

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs**: slight increase in body temperature, chills, temporary anorexia, listlessness may be noted a few hours after injection. Extravascular injection may cause tissue inflammation. Anaphylactic reactions may occur

### DRUG INTERACTIONS

**Glucocorticoids or other immunosuppressive agents:** these drugs should be discontinued at least 1 week before *P. acnes* administration, because of potential reduction of its immunostimulant effect

### MONITORING

- Efficacy and adverse effects

## Rifampin

**Trade/brand name:** *Rifadin*® (US, CA), *Rimactane*® (US, UK), *Rofact*® (CA) (Rx)
**Classification:** Antibacterial

### INDICATIONS

**Dogs and cats:** Rifampin has been used solely or in combination with a beta-lactamase-resistant antibiotic for cases of canine chronic pyoderma where other treatment options have failed, or for cases of methicillin-resistant *Staphylococcus pseudintermedius* infections susceptible to the drug. It has also been used to treat canine actinomycosis, aspergillosis, histoplamosis, and mycobacterial infections in dogs and cats.

**Note:** Major limiting factors associated with the use of this antibiotic include rapid development of resistance (thus the need for combined antibiotic therapy) and the potential for the development of severe hepatotoxicity.

### CONTRAINDICATIONS

Patients hypersensitive to rifampin or other rifamycins. Patients with pre-existing liver disease. Use cautiously in patients with risk for pancreatitis.

### MECHANISM OF ACTION

Rifampin is a lipid-soluble antibacterial agent that is active in acid pH and has good intracellular penetration. Its spectrum of action includes staphylococci, streptococci, and mycobacteria. It inhibits RNA synthesis in susceptible organisms by inhibiting the DNA-dependent RNA polymerase enzyme. It can be bactericidal or bacteriostatic according to the drug concentration and organism susceptibility.

### DOSAGES

Rifampin should be administered on an empty stomach, as food reduces its extent and rate of absorption.

#### Dogs

- Refractory pyoderma: 5–10 mg/kg PO q12h. Combine with a beta-lactamase-resistant antibiotic or a susceptible antibiotic not metabolized by the CYP enzymes
- Canine leproid granuloma syndrome: 10–15 mg/kg PO q24h until resolution of clinical signs (usually 4–8 weeks). It should be combined with clarithromycin or doxycycline
- Slow-growing mycobacterial infections: 10–20 mg/kg PO q24h. For *Mycobacterium tuberculosis*, combine with at least one of the following drugs: isoniazid, ethambutol, dihydrostreptomycin, pyrazinamide. For *M. microti*-like,

*M. terrae* group, and *M. simiae* infections combine with one or more of the following: enrofloxacin, marbofloxacin, clarithromycin, azithromycin. For *M. avium* complex infection, combine with one or more of the following: clarithromycin, clofazimine, doxycycline
- Actinomycosis: 10–20 mg/kg PO q12h
- Aspergillosis and histoplasmosis: 10–20 mg/kg PO q8h. Combine with amphotericin B or flucytosine

**Cats**
- Feline leprosy: 10–15 mg/kg PO q24h. Combine with clarithromycin or clofazimine
- Slow-growing mycobacterial infections: 10–20 mg/kg PO q24h. Refer to the above recommendations for dogs regarding drug combination
- Aspergillosis and histoplasmosis: 10–20 mg/kg PO q8h. Combine with amphotericin B or flucytosine

**Note:** Rifampin should always be administered with other drugs to prevent development of resistance.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral capsules: 150 mg and 300 mg; *Rifadin®*, *Rimactane®*, *Rofact®* (CA only), generic

### SIDE EFFECTS

**Dogs and cats:** hepatotoxicity (frequently seen with high doses and long-term therapy); pancreatitis; red-orange discoloration of urine, saliva, sweat, tears, sclera, feces, and mucous membranes; thrombocytopenia (rare reports in dogs); hemolytic anemia; anorexia; vomiting; diarrhea and death. Some cats have experienced pruritus and erythema, especially of the pinnae, and signs of anaphylaxis such as dyspnea and respiratory distress.

### DRUG INTERACTIONS

**Barbiturates, benzodiazepines, chloramphenicol, corticosteroids, cyclosporine, dapsone, digitoxin, ketoconazole, propanolol, quinidine, verapamil, theophylline, warfarin:** these drugs are metabolized by hepatic CYP enzymes and may have their serum levels decreased, as rifampin is a potent inducer of these enzymes.

### MONITORING
- Efficacy and adverse effects
- Liver enzymes at least every other week for the duration of therapy

## Selamectin

**Trade/brand name:** *Revolution®* (US, CA), *Stronghold®* (UK) (Rx)
**Classification:** Antiparasitic (macrocyclic lactone)

### INDICATIONS

**Dogs and cats:** Selamectin is indicated for the treatment of flea infestation, otoacariosis, cheyletiellosis, and biting lice infestation in dogs and cats, and for sarcoptic mange and tick infestations in dogs.

**Note:** It is labeled as a heartworm, hookworm, and roundworm preventative in dogs and cats.

### CONTRAINDICATIONS

The manufacturer recommends using selamectin with caution in sick, debilitated, or underweight dogs and cats. It should not be used in animals less than 6 weeks of age. At the dose recommended by the manufacturer, dog breeds at risk for ABCB1-1 gene (formerly MDR1) mutation should tolerate selamectin; nevertheless, use cautiously in these breeds. Do not apply to eroded or ulcerated skin (contains alcohol). Do not use without up-to-date negative heartworm test, or in patients with heartworm disease.

### MECHANISM OF ACTION

Selamectin is a semi-synthetic avermectin derived from doramectin. It interacts with GABA and glutamate-gated channels, which increases the influx of chloride ions into the cell and results in flaccid paralysis of the parasite. Selamectin forms reservoirs in skin sebaceous glands, and 5% of the drug becomes bioavailable, with peak plasma levels occurring about 3 days after application.

### DOSAGES

**Dogs and cats**

- Flea infestation treatment and prevention: 6 mg/kg once a month. The frequency of application may vary according to the flea burden in different geographic regions
- Biting lice: 6 mg/kg, one treatment
- Otoacariosis: 6–12 mg/kg, one or two treatments at 30 day-interval
- Cheyletiellosis
  - Dogs: 6–12 mg/kg every other week for four treatments
  - Cats: 6–12 mg/kg once monthly for three treatments

**Dogs**

- Sarcoptic mange: 6–12 mg/kg, two treatments at 30-day interval. The authors use a more aggressive protocol of 4–6 treatments at 2-week intervals
- Tick infestation and control: 6 mg/kg once a month

**Note:** The treatment protocols listed above have been used efficaciously in field trials; however, modifications may be required for individual cases. Refer to package insert for specific instruction on mode of administration.

### FORMULATIONS

**Veterinary-labeled products**

- *Revolution® Topical Solution for Cats* (color-coded sizes): 15 mg in 0.25 mL tube (cats ≤2.3 kg or 5 lb); 45 mg in 0.75 mL tube (cats 2.3–6.8 kg or 5.1–15 lb); 60 mg in 1 mL tube (cats 6.8–10 kg or 15.1–22 lb)
- *Revolution® Topical Solution for Dogs* (color-coded sizes): 15 mg in 0.25 mL tube (dogs ≤2.3 kg or 5 lb); 30 mg in 0.25 mL tube (dogs 2.4–4.5 kg or

5.1–10 lb); 60 mg in 0.5 mL tube (dogs 4.6–9 kg or 10.1–20 lb); 120 mg in 1 mL tube (dogs 9.1–18.1 kg or 20.1–40 lb); 240 mg in 2 mL tube (dogs 18.2–38.6 kg or 40.1–85 lb); one 120 mL tube and one 240 mg tube, total volume 3 mL (dogs 38.7–59 kg or 85.1–130 lb)

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs and cats**

- Uncommon: transient pruritus, erythema and alopecia at application site
- Rare (<0.5%)/reported in field trials: diarrhea, vomiting, anorexia, muscle tremors, lethargy, salivation and tachycardia. Seizure and ataxia reported in dogs

### DRUG INTERACTIONS

None reported. Nevertheless, it should be used cautiously in conjunction with other drugs that inhibit P-glycoprotein. It is wise to test dogs at risk for the ABCB1-1 (formerly MDR1) gene mutation before using selamectin if they are receiving the following drugs: amiodarone, carvedilol, clarithromycin, cyclosporine, diltiazem, erythromycin, itraconazole, ketoconazole, quinidine, spironolactone, tamoxifen, verapamil.

### MONITORING

- Efficacy and adverse effects
- Heartworm status prior to administration

## Selegiline Hydrocloride

**Trade/brand name:** *Anipryl*® (US, CA), *Eldepryl*® (US, CA), *Selgian*® (UK), generic (Rx)
**Classification:** Hormone (dopamine agonist)

### INDICATIONS

**Dogs:** Selegiline or L-deprenyl is the only FDA-approved drug for treating canine pituitary-dependent hyperadrenocorticism (PDH). However, various reports and individual experiences have indicated that this drug is not very effective to treat canine PDH compared to mitotane or trilostane.

**Note:** Selegiline is also approved to treat cognitive disorders in dogs.

### CONTRAINDICATIONS

Patients known to be hypersensitive to selegiline. It is not recommended for the treatment of canine adrenal-dependent hyperadrenocorticism. It should not be used with antidepressants (e.g., tricyclic antidepressants and serotonin reuptake inhibitors), with other monoamine oxidase (MAO) inhibitors (e.g., amitraz), or with ephedrine. Safety in breeding, pregnant, and lactating bitches has not been determined.

### MECHANISM OF ACTION

Selegiline irreversibly inhibits monoamine oxidase B, an enzyme responsible for metabolizing dopamine. This will result in increased central dopamine

concentrations. Several studies have shown that dopamine inhibits the release of ACTH by the pars intermedia of the pituitary gland. Because about 70% of the pituitary tumors arise from the pars distalis, which is not under dopaminergic control, selegiline has a potential to be effective only in a small percentage of PDH cases.

### DOSAGES

**Dogs:** Start with 1 mg/kg PO q24h. If no response is noted after 2 months increase the dose to 2 mg/kg PO q24h; if no response is noted after 1 month, alternative treatments should be explored

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs
- Oral tablets: 2 mg, 5 mg, 10 mg, 15 mg, 30 mg in blister-packs of 30 tablets; *Anipryl®*

**Human-labeled products**
- Oral tablets and capsules: 1.25 mg and 5 mg; *Eldepryl®*, *Carbex®*, *Zelapar®*, generic
- Oral tablets: 4 mg, 10 mg, 20 mg; *Selgian®* (UK only)

### SIDE EFFECTS

**Dogs:** Dogs tolerate selegiline very well.
- Common: vomiting, diarrhea, anorexia
- Uncommon/Rare: CNS signs (salivation, panting, repetitive movements, disorientation/ataxia, restlessness/agitation, diminished hearing), lethargy, pruritus, licking, tremors, stiffness, polydipsia, aggression. Increase in destructive behavior was reported in one dog with separation anxiety

**Note:** Decrease in hematocrit has been reported in clinical trials; however, the clinical significance of this finding is unknown.

### DRUG INTERACTIONS

**Amitraz:** concurrent use of another monoamine oxidase (MAO) inhibitor is not recommended by the manufacturer

**Bupropion and serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine):** potential for serotonin syndrome

**Ephedrine:** concurrent use is not recommended by the manufacturer

**Meperidine:** severe agitation, hallucinations, and death have been reported in humans treated with meperidine and selegiline concurrently

**Phenylpropanolamine, pseudoephedrine:** hypertension and hyperpyrexia may occur

**Tramadol:** serotonin syndrome, vomiting, nausea, cardiovascular collapse may occur. Use is contraindicated in humans

**Tricyclic and tetracyclic antidepressants (e.g., clomipramine, amitriptyline):** potential for serotonin syndrome to occur; separation of 2 weeks between the administration of selegiline and these compounds is recommended

**Note:** The manufacturer of *Anypril*® reported weakness, confusion, incoordination, and "seizure-like" activity in dogs being treated concurrently with metronidazole, prednisone, and trimethoprim-sulfa, suggesting a possible drug interactions with these drugs.

### MONITORING

- Efficacy and adverse effects
- Efficacy is monitored by observing changes in clinical signs and not based on test results (i.e., ACTH stimulation test or low-dose dexamethasone suppression test). A metabolite of selegiline (L-amphetamine) is a potent sympathomimetic and CNS stimulant; therefore, owners' perceived improvement in the behavior of their geriatric dogs may not be directly related to improvement of PDH

## Sertraline Hydrochloride

**Trade/brand name:** *Zoloft*® (US), *Lustral*® (UK) (Rx)
**Classification:** Behavior modifying drug (selective serotonin reuptake inhibitor)

### INDICATIONS

Management of psychogenic dermatoses associated with anxiety-related or other obsessive–compulsive behaviors.

**Dogs:** Tail biting, flank sucking, anal licking, acral lick dermatitis.

**Cats:** Psychogenic alopecia and dermatitis, tail sucking, excessive grooming, hair pulling, hyperesthesia syndrome.

**Note:** Sertraline is most effective when combined with a behavior modification program.

### CONTRAINDICATIONS

Avoid in patients with hypersensitivity to this drug, and in those receiving monoamine oxidase (MAO) inhibitors, (e.g., selegiline) or L-tryptophan. Use cautiously in patients with seizure disorders or taking drugs that lower the seizure threshold (e.g., acepromazine, chlorpromazine), and in patients with cardiac, liver, or renal disease.

### MECHANISM OF ACTION

Sertraline selectively inhibits serotonin reuptake in the CNS and downregulates $5\text{-HT}_1$ receptors, resulting in potentiation of serotonin pharmacologic activity (antidepressive activity). Sertraline has minor dopamine or norepinephrine reuptake inhibition properties.

### DOSAGES

**Dogs:** 1–3 mg/kg PO q24h

**Cats:** 0.5–1 mg/kg PO q24h

**Note:** The dose may be gradually increased to the highest dose. Lag phase of 4–6 weeks.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 25 mg, 50 mg, 100 mg; *Zoloft*®; generic
- Oral tablets: 50 mg and 100 mg; *Lustral*® (UK only)
- Oral concentrate: 20 mg/mL in 60 mL btl; *Zoloft*®

### SIDE EFFECTS

**Dogs:** lethargy, anorexia (common but usually transient), vomiting, diarrhea, tremors, anxiety, irritability, aggressive behavior, insomnia/hyperactivity, panting, vocalization, mydriasis, nystagmus, ataxia, and alterations in cardiac conduction

**Cats:** anorexia, constipation, vomiting, diarrhea, tremors, anxiety, vocalization, irritability, sleep disturbances, mydriasis, changes in elimination patterns and alterations in cardiac conduction

### DRUG INTERACTIONS

**Aspirin:** may increase the risk for bleeding

**Buspirone:** increased risk for serotonin syndrome

**Cimetidine:** may increase sertraline blood levels

**Cyproheptadine:** may decrease or reverse the effects of SSRIs

**Diazepam:** may decrease diazepam clearance

**Drugs that lower the seizure threshold (e.g., acepromazine, chlorpromazine):** use with caution

**Isoniazid:** increased risk for serotonin syndrome

**Monoamine oxidase (MAO) inhibitors (e.g., amitraz, selegiline):** high risk for serotonin syndrome; use is contraindicated. May need a 5-week washout period after discontinuing sertraline and a 2-week washout period if first discontinuing the MAO inhibitor

**Pentazocine:** possible serotonin syndrome-like side effects

**Tricyclic antidepressants (e.g., clomipramine, amitriptyline):** may increase plasma levels of these drugs increasing the risk for serotonin syndrome; concurrent use is contraindicated

**Warfarin:** sertraline may increase the risk for bleeding

### MONITORING
- Efficacy and adverse effects

## Sodium Stibogluconate/Sodium Antimony Gluconate

**Trade/brand name:** *Pentostam*® (UK) (Rx)
**Classification:** Antiparasitic (antileishmanial)

### INDICATIONS

**Dogs:** Treatment of cutaneous leishmaniasis as sole therapy or in combination with allopurinol, paromomycin, or pentamidine.

**Note:** Parasitological cure is not typically obtained, and relapses are not uncommon after therapy is discontinued.

### CONTRAINDICATIONS

Previous hypersensitivity to antimony compounds, renal failure, or cardiac arrhythmias.

### MECHANISM OF ACTION

The exact mechanism of action of sodium stibogluconate is unknown. It is believed that it interferes with energy metabolism of *Leishmania* amastigotes by reducing the synthesis of adenosine triphosphate (ATP) and guanosine triphosphate (GTP) in susceptible organisms.

### DOSAGES

**Dogs:** 30–50 mg/kg IV or SC q24h for 3–4 weeks

**Note:** If side effects occur, it can be administered every other day for longer periods. Intravenous administrations should be given over 5 minutes to prevent cardiac toxicity. The use of a fine needle or catheter is recommended to avoid thrombophlebitis.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products:** Only available in the US through CDC [Atlanta, GA, (404) 639-3670] and for human use; available in other countries

- Injection (antimony): 100 mg/mL in 6 mL or 100 mL vials; *Pentostam*®

### SIDE EFFECTS

**Dogs:** musculoskeletal pain or pain at injection site, increase in liver transaminases (usually reversible), pancreatitis, myocardial injury and arrhythmias, hemolytic anemia, leukopenia, vomiting, diarrhea, renal dysfunction, shock and sudden death; intravenous injections can cause thrombophlebitis

**Note:** Risks for side effects may increase with treatment duration longer than two months.

### DRUG INTERACTIONS

None reported

### MONITORING

- Efficacy and adverse effects
- CBCs, liver enzymes, renal function tests, and electrocardiograms should be monitored during treatment

## Somatotropin

**Trade/brand name:** *Posilac*® (US), *Genotropin*® (US, UK) (Rx)
**Classification:** Hormone

## INDICATIONS

**Dogs:** Treatment of canine pituitary dwarfism and growth-hormone-responsive dermatosis in the mature dog.

**Note:** The infrequent and inconsistent response of dogs with idiopathic non-inflammatory alopecia to growth hormone treatment resulted in disbelief in the existence of a growth-hormone-responsive disease by most dermatologists. More recent studies have shown that the majority of dogs previously diagnosed with adult-onset growth-hormone-responsive dermatosis fall in the category of alopecia X. Somatotropin should not be used as the first treatment choice for cases of alopecia X, because of the potential for serious side effects and the infrequent and inconsistent response to this treatment modality.

## CONTRAINDICATIONS

Patients hypersensitive to growth hormone derived from other species.

## MECHANISM OF ACTION

Somatotropin, also known as growth hormone, in combination with thyroid hormones, insulin, cortisol, and sex steroids, participates in the growth of the skeletal system, organs, and cells. It has an indirect anabolic effect (mediated by somatomedins or insulin-like growth factors) and a direct catabolic effect (enhanced lipolysis, insulin resistance). It is also important in thymus development and T-cell function.

## DOSAGES

### Dogs

- Pituitary dwarfism
  - Bovine growth hormone: 10 IU SC every other day for 30 days
  - Porcine growth hormone: 2 IU SC every other day or 0.1 IU/kg SC three times weekly for 4–6 weeks

**Note:** Improvement of skin and hair coat signs can be seen within 6–8 weeks. Because growth plates close rapidly, no significant change in stature is noted. Concurrent secondary adrenocortical insufficiency and hypothyroidism have to be treated appropriately.

- Alopecia X/growth-hormone-responsive dermatosis: bovine, porcine, and human growth hormone have shown to be effective but not ovine. 2.5 IU for dogs weighing <14 kg and 5 IU for dogs >14 kg given SC every other day for 10 treatments. Other reported treatment regimens include 0.1 IU/kg three times weekly for 6 weeks or 0.015 IU/kg twice weekly for 6 weeks

**Note:** Refer to comment under *Indications*, above.

## FORMULATIONS

### Veterinary-labeled products

- Porcine growth hormone apparently has minimal immunogenicity in dogs. It can be obtained at www.humc.edu/hormones
- *Posilac*®: it is a sustained release product and not easily diluted down to the small dosages required to treat the canine disorders

**Human-labeled products:** The various human recombinant DNA origin products are expensive and not sold for veterinary use.

### SIDE EFFECTS

**Dogs:** diabetes mellitus, hypersensitivity reaction (less likely with the porcine source), acromegaly

### DRUG INTERACTIONS

**Glucocorticoids:** may inhibit the growth-promoting effect of somatotropin

### MONITORING

- Efficacy and adverse effects
- Blood glucose weekly and urine glucose daily during treatment

## Spinosad ± Milbemycin Oxime

**Trade/brand name:** *Comfortis*® (US, CA, UK), *Trifexis*® (US, CA, UK) (Rx)
**Classification:** Antiparasitic (pediculicide)

### INDICATION

**Dogs:** Approved for the prevention and treatment of flea infestations on dogs 14 weeks of age and older. A formulation containing milbemycin oxime (*Trifexis*®) is also labeled for prevention of heartworm disease and treatment and control of intestinal parasite infections (hookworms, roundworms, and whipworms).

### CONTRAINDICATIONS

Spinosad should not be used concomitantly with high extra-label doses of ivermectin, typically used to treat canine demodex mange. Signs of ivermectin toxicity such as mydriasis, salivation, ataxia, lethargy, and seizures have been reported in this circumstance. Use cautiously in breeding females, and in dogs with pre-existing seizures. Avoid use in puppies less than 14 weeks of age or less than 2.3 kg (5 lb) body weight. Regarding *Trifexis*®, do not use without up-to-date negative heartworm test, or in patients with heartworm disease.

### MECHANISM OF ACTION

Spinosad stimulates the nicotinic acetylcholine receptor in insects, causing activation of motor neurons resulting in involuntary muscle contractions and tremors. Long-lasting hyperexcitation will ultimately cause prostration, paralysis, and death of the flea. It also binds secondarily to GABA sites and consequently may potentiate the nervous system dysfunction. Spinosad was demonstrated by the manufacturer (in a controlled laboratory study) to kill adult fleas within 30 minutes after administration, and to show 100% effectiveness within 4 hours.

### DOSAGES

**Dogs:** Administer orally (with food to maximize efficacy) once a month

- Dogs 2.0–4.5 kg (5–10 lb): one 140 mg tablet (*Comfortis*®), one 140 mg/2.3 mg tablet (*Trifexis*®)
- Dogs 4.6–9 kg (10.1–20 lb): one 270 mg tablet (*Comfortis*®), one 270 mg/4.5 mg tablet (*Trifexis*®)
- Dogs 9.1–18.1 kg (20.1–40 lb): one 560 mg tablet (*Comfortis*®), one 560 mg/9.3 mg tablet (*Trifexis*®)

- Dogs 18.2–27.3 kg (40.1–60 lb): one 810 mg tablet (*Comfortis*®), one 810 mg/13.5 mg tablet (*Trifexis*®)
- Dogs 27.4–54.5 kg (60.1–120 lb): one 1620 mg tablet (*Comfortis*®), one 1610 mg/27 mg tablet (*Trifexis*®)

**Note:** Dogs over 54.5 kg (120 lb) should be administered the appropriate combination of tablets. The maximum recommended dose is 60 mg/kg or 27.3 mg/lb. For treatment of flea infestation, it should be ideally combined with an insect growth regulator or insect development inhibitor.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs
- Chewable tablets (beef flavored): 140 mg, 270 mg, 560 mg, 810 mg, 1620 mg; *Comfortis*® (spinosad), *Trifexis*® (spinosad + milbemycin oxime)

**Note:** Tablets are flavored, and the sizes are color-coded and provided in packets of 6 or 12 tablets.

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs**: vomiting, decreased appetite, lethargy, diarrhea, cough, polydipsia, vocalization, erythema, hyperactivity, excessive salivation, seizure precipitation in epileptic dogs.

**Note:** Severe signs of ivermectin toxicity (e.g., mydriasis, blindness, tremors, salivation, ataxia, lethargy, seizures) can be triggered if spinosad is administered concurrently with high extra-label doses of ivermectin (typically used for the management of canine demodex mange).

### DRUG INTERACTIONS

**Ivermectin (high extra-label doses typically used for the management of canine demodicosis):** severe signs of ivermectin toxicity. The manufacturer states that concurrent use of spinosad and approved heartworm preventatives according to label directions should be safe

### MONITORING

- Efficacy and adverse effects
- Heartworm status prior to administration of *Trifexis*®

## Staphage Lysate

**Trade/brand name:** *Staphage Lysate (SPL)*® (US, CA) (Rx)
**Classification:** Immunomodulatory (immunostimulant)

### INDICATIONS

**Dogs:** Staphage Lysate (SPL) is licensed as adjunctive therapy in the management of canine idiopathic recurrent pyoderma caused by *Staphylococcus*, including *S. pseudintermedius*. Dermatologists have also used this product to reduce

recurrences of bacterial skin infections in allergic patients, but there is no scientific evidence to support or disfavor this indication.

**Note:** SPL should not be used to treat an infection, but to help reduce the frequency of recurrences and the severity of future infections.

### CONTRAINDICATIONS

SPL should not be used in patients with prior hypersensitivity reaction to the product. The manufacturer recommends starting with lower dosages in "highly allergic" patients. Use cautiously in patients with known hypersensitivity to beef (contains ultrafiltered beef heart infusion broth). Concurrent use of corticosteroids or other immunosuppressant drugs should be avoided, to prevent any potential reduction in the efficacy of Staphage Lysate.

### MECHANISM OF ACTION

SPL is a bacteriologically sterile staphylococcal vaccine containing the components of *Staphylococcus aureus*, a bacteriophage, and some culture medium ingredients (sodium chloride and ultrafiltered beef heart infusion broth). It has been shown to stimulate T and B lymphocytes in vitro and to enhance the capability of macrophages to kill staphylococci.

### DOSAGES

**Dogs:** Start with 0.5 mL SC twice weekly for a 10–14 week trial. If significant improvement is noted, 0.5–1 mL can be administered once weekly to once every 2–4 weeks depending on the individual patient. In most cases improvement is noted within 8–10 weeks.

If using in highly allergic dogs: the manufacturer recommends first performing a skin test (0.05–1 mL of Staphage Lysate intradermally) to check for any possible hypersensitivity to the product, and starting with 0.2 mL per week followed by weekly increments of 0.2 mL until reaching 1.0 mL.

**Note:** This treatment will not resolve an existing bacterial infection; therefore, antibiotic therapy has to be instituted if a bacterial infection is present. After the infection is cleared the antibiotic is discontinued and the Staphage Lysate therapy begins or continues. SPL does not contain any preservatives, and therefore it must be handled aseptically. SPL should be stored in the refrigerator, and the entire content should be used when the vial is opened.

### FORMULATIONS

**Veterinary-labeled products:** Approved (by the USDA) for dogs

- Staphylococcal phage lysate (serotypes I and III): 10 mL vials or 1 mL ampoules. Each mL contains 120–180 million colony-forming units of *Staphylococcus aureus* and 100 million staphylococcus bacteriophage plaque-forming units; *Staphage Lysate (SPL)®*

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs**

- Uncommon: transient injection-site reactions such as pain, erythema, swelling, and pruritus may develop within 2–3 hours post injection and may last up to 3 days

- Rare: systemic reactions such as vomiting, diarrhea, weakness, fast breathing, severe pruritus, fever, and malaise. If excessive, these reactions may be lessened by reducing the dose. Anaphylactic reactions should be treated immediately

### DRUG INTERACTIONS

**Cell-mediated immunosuppressive agents (e.g., glucocorticoids, cyclosporine):** these drugs may reduce the efficacy of SPL

### MONITORING

- Efficacy and adverse effects

## Sulfadiazine/Sulfamethoxazole+Trimethoprim

**Trade/brand name:** *Tribrissen*® (US, UK), *Bactrim*® (US), *Proloprim*® (US), *Septra*® (US), *Duphatrim*® (UK), generic
**Classification:** Antibacterial (potentiated sulfonamide)

### INDICATIONS

**Dogs and cats:** Approved to treat canine bacterial skin infections caused by susceptible staphylococcal strains, but it can also be used to treat feline bacterial skin infections. Potentiated sulfas have a broad antibacterial spectrum against common Gram-positive (e.g., *Staphylococcus*, most *Streptococci*, *Nocardia*) and Gram-negative bacteria (e.g., many organisms of the Enterobacteriaceae family). It is the drug of choice for the initial treatment of nocardiosis, and it can also be used to manage rapidly growing mycobacterial infections (reported susceptibility 57.1%), including atypical mycobacteriosis in dogs and cats caused by *Mycobacterium smegmatis*, *M. fortuitum*, and *M. chelonai*.

**Note:** Bacterial culture and sensitivity should ideally be performed prior to starting therapy.

### CONTRAINDICATIONS

Animals hypersensitive to sulfonamides, and those with severe liver parenchymal damage or blood dyscrasias. Animals with low Schirmer's tear test values should not be treated with sulfonamides. Doberman pinschers, samoyeds, and miniature schnauzers have been reported to have a higher risk to develop reactions to sulfonamides, and these drugs should only be used in these breeds if the benefits outweigh the risks. It was suggested that the predisposition of Doberman pinscher to sulphonamides' idiosyncratic toxicity may be due to a limited capacity to detoxify the hydroxylamine metabolites of sulfonamides.

### MECHANISM OF ACTION

Potentiated sulfas are bactericidal and sequentially inhibit the enzymes involved in the folic acid pathway, resulting in the inhibition of bacterial thymidine synthesis. The sulfonamide inhibits the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid, and trimethoprim inhibits the conversion of dihydrofolic acid to tetrahydrofolic acid by inhibiting the bacterial enzyme dihydrofolate reductase.

## DOSAGES

**Dogs and cats**

- Pyoderma or soft tissue infections: 30 mg/kg PO q24h or 15 mg/kg PO q12h. For chronic or deep infections use 30 mg/kg PO q12h
- Nocardiosis: 90–120 mg/kg PO q24h. Because of the potential serious side effects (e.g., non-regenerative anemia) at this high dose, only use it for the initial treatment phase
- Rapidly growing mycobacterial infections
  - Dogs: 15–30 mg/kg PO q12h
  - Cats: 10 mg/kg PO q12h

**Note:** The concentration of trimethoprim falls below the therapeutic levels with once-a-day administration at 30 mg/kg PO but the concentration of sulfadiazine is maintained within the therapeutic range throughout the dosing interval. Twice-a-day dosing at 15 mg/kg PO will maintain effective levels of both medications for longer periods of time, but peak concentrations of trimethoprim and sulfadiazine will be lower and more likely to be bacteriostatic rather than bactericidal. For practical purposes: for organisms that are highly susceptible to sulfadiazine or to the combination (sulfadiazine + trimethoprim), use 30 mg/kg q24h PO; for organisms that are susceptible to the combination (sulfadiazine + trimethoprim) but not to sulfadiazine alone, use 15 mg/kg q12h; for infections where the susceptibility is not known, or for serious infections, use 30 mg/kg q12h. The combination of sulfamethoxazole and trimethoprim is approved for human use. There are no studies showing differences in the efficacy between trimethoprim combined with sulfadiazine or sulfamethoxazole.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs in the US

- Oral tablets (sulfadiazine + trimethoprim): 5 mg/25 mg, 20 mg/100 mg, 80 mg/400 mg, 160 mg/800 mg; *Tribrissen®*, *Di-Trim®*, *Duphatrim®* (UK)
- Oral suspension (sulfadiazine + trimethoprim): 10 mg/50 mg; *Tribrissen®*

**Human-labeled products**

- Oral tablets (trimethoprim + sulfamethoxazole): 80 mg/400 mg, 160 mg/800 mg; *Bactrim®*, *Bactrim-DS®*, *Septra®*, *Septra-DS®*, generic
- Oral suspension (trimethoprim + sulfamethoxazole): 8 mg/mL + 40 mg/mL in 473 mL and 480 mL vials; *Septra®*, *Cotrim® Pediatric*, generic
- Injection (trimethoprim + sulfamethoxazole): 16 mg/5 mL + 80 mg/5 mL in 5 mL Carpuject; 80 mg/5 mL + 400 mg/5 mL in 5 mL, 10 mL, 20 mL, and 30 mL vials; *Bactrim® IV, Septra® IV*, generic

## SIDE EFFECTS

**Dogs:** fever, thrombocytopenia, hepatopathy, keratoconjunctivitis sicca (dogs weighing <12 kg may be at higher risk), neutropenia, hemolytic anemia, crystalluria, arthropathy, uveitis, skin and mucocutaneous lesions, urticaria, angioedema, proteinuria, facial palsy, clinical signs of hypothyroidism (associated with higher doses and prolonged therapy), diarrhea, vomiting, anorexia, seizures

**Cats:** anorexia, leukopenia, megaloblastic (folate acid deficiency) anemia, sulfonamide nephromicrolithiasis, polydipsia, polyuria, salivation, diarrhea, vomiting, ataxia with higher doses

### DRUG INTERACTIONS

**Antacids:** absorption of sulfonamides may be decreased

**Cyclosporine:** may increase the nephrotoxicity risks of cyclosporine

**Digoxin:** may increase digoxin blood levels

**Hypoglycemic agents, oral:** may potentiate hypoglycemic effects

**Methotrexate:** sulfonamides may compete with methotrexate for binding to plasma proteins resulting in higher methotrexate serum unbound fraction and increased risk for toxic effects

**Phenytoin, phenylbutazone, salicylates, thiazide diuretics, probenecid:** may increase the effects and toxicity of these drugs

**Tricyclic antidepressants:** may decrease the efficacy of tricyclic antidepressants

**Warfarin:** clotting times may be prolonged

### MONITORING

- Efficacy and adverse effects
- Schirmer's tear tests: baseline and weekly during treatment
- Thyroid function tests: monitor if the drug is administered longer than 21 days since sulfonamides inhibit the activity of thyroid peroxidase which may result in iatrogenic hypothyroidism
- CBCs: perform biweekly if long-term therapy (longer than 2 weeks) is required

## Sulfasalazine

**Trade/brand name:** *Azulfidine*® (US), *Salazopyrin*® (CA, UK) (Rx)
**Classification:** Antibacterial (potentiated sulfonamide), Anti-inflammatory

### INDICATIONS

**Dogs:** Treatment of neutrophilic vasculitis and cases of subcorneal pustular dermatosis that do not respond to dapsone. Sulfasalazine alone or in combination with oral glucocorticoid has been anecdotally reported for treatment of perianal fistulas.

### CONTRAINDICATIONS

Patients hypersensitive to sulfonamides or salicylates, patients with intestinal or urinary obstruction. Caution in animals with hematologic, liver, or renal diseases.

### MECHANISM OF ACTION

Sufasalazine is converted by colonic bacteria to sulfapyridine (sulfonamide) and 5-aminosalycilic acid (mesalamine). Mesalamine has an anti-inflammatory effect, believed to be mediated by anti-prostaglandin and/or anti-leukotriene activity.

### DOSAGES

**Dogs**

- Neutrophilic vasculitis: 20–40 mg/kg PO q8h or 15–22 mg/kg PO q8–12h
- Subcorneal pustular dermatosis: 10–20 mg/kg PO q8h

- Perianal fistula: 50 mg/kg/day PO divided q8–12h (dose extrapolated from treatment for inflammatory bowel disease) or 1 g per dog PO q8h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 500 mg; *Azulfidine®*, generic
- Delayed-release oral tablets (enteric coated): 500 mg; *Azulfidine® EN-tabs*
- Oral suspension: 250 mg/5 mL; *Azulfidine®*

### SIDE EFFECTS

**Dogs:** vomiting, anorexia, hypersensitivity reactions, keratoconjunctivitis sicca (long-term use), ataxia, depression, clinical signs of hypothyroidism (long-term use), hemolytic anemia, leukopenia, cholestatic jaundice, decreased sperm counts, orange-yellow discoloration of urine or skin

### DRUG INTERACTIONS

**Chlorpropamide:** may potentiate the hypoglycemic effect of chlorpropamide

**Cyclosporine:** decreases cyclosporine plasma levels by increasing its metabolism

**Digoxin:** digoxin absorption may be reduced

**Ferrous sulfate or other iron salts:** blood sulfasalazine concentration may be reduced

**Folic acid:** oral absorption of folic acid may be inhibited

**Methotrexate and pyrimethamine:** adverse effects caused by these drugs may be potentiated

**Warfarin:** may potentiate warfarin effect

### MONITORING
- Efficacy and side effects
- Schirmer's tear tests: baseline and weekly during treatment
- Thyroid function tests: monitor if the drug is administered longer than 21 days, because sulfonamides inhibit the activity of thyroid peroxidase, which may result in iatrogenic hypothyroidism
- CBC and liver function tests: monitor if long-term therapy (longer than 2 weeks) is required

## Tepoxalin

**Trade/brand name:** *Zubrin®* (US, UK) (Rx)
**Classification:** Anti-inflammatory

### INDICATIONS

**Dogs:** A recent randomized, double-blind, placebo-controlled, cross-over study showed moderate efficacy of tepoxalin in the management of canine atopic

dermatitis and recommended its use as adjunctive therapy (Horvath-Ungerboeck *et al*. 2009).

### CONTRAINDICATIONS

Avoid in patients hypersensitive to tepoxalin, and in patients with gastrointestinal ulcers. Use cautiously in patients with hepatic, cardiovascular, or renal function abnormality, and in dehydrated patients and those taking diuretic therapy, as these patients are at increased risk for developing nephrotoxicity associated with non-steroidal anti-inflammatory drugs (NSAIDs). The safety for dogs during breeding, pregnancy or lactation has not been studied.

### MECHANISM OF ACTION

Tepoxalin belongs to the pyrazol group of NSAIDs. It inhibits not only 5-lipoxygenase (5-LOX) but also cyclooxygenase (COX)-1 and COX-2 enzymes. It also inhibits lymphocyte proliferation, neutrophil migration, and the synthesis of pro-inflammatory cytokines such as IL-2, IL-6, IL-8, and TNF-alpha.

### DOSAGES

**Dogs:** 10 mg/kg PO q24h

**Note:** In a recent study investigating the efficacy of tepoxalin in treating dogs with atopic dermatitis, the mean dose used was 11.6 mg/kg (range: 10–19.1 mg/kg) q24h.

### FORMULATIONS

**Veterinary-labeled products:** Approved for use in dogs
- Oral tablets: 30 mg, 50 mg, 100 mg, 200 mg; *Zubrin®*

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs**
- Common: vomiting, diarrhea, anorexia/inappetance, lethargy, enteritis
- Rare: incoordination, increased appetite, incontinence, eating grass, hair loss, flatulence, trembling

### DRUG INTERACTIONS

**Aspirin:** risks of gastrointestinal side effects (e.g., ulceration, bleeding, vomiting, diarrhea) may increase

**Corticosteroids:** may increase gastric ulceration risks

**Digoxin:** digoxin serum levels may be increased by NSAIDs

**Fluconazole:** increased plasma levels of celecoxib in humans; it is not known if it will affect tepoxalin levels in dogs

**Furosemide:** diuretic and saluretic effects of furosemide may be reduced by NSAIDs

**Methotrexate:** serious toxicity may occur when used with NSAIDs

**Nephrotoxic drugs (e.g., aminoglycosides, amphotericin B, furosemide):** nephrotoxicity risk may increase when these drugs are used with NSAIDs

**Other NSAIDs:** increased risk for gastrointestinal toxicity

**Warfarin:** tepoxalin and warfarin may compete for plasma protein binding, because both drugs are highly bound to plasma proteins; monitor closely for side effects

### MONITORING

- Efficacy and adverse effects

## Terbinafine Hydrochloride

**Trade/brand name:** *Lamisil®* (US, CA, UK), generic (Rx)
**Classification:** Antifungal

### INDICATIONS

**Dogs and cats:** Terbinafine is indicated for the treatment of dermatophytosis, *Malassezia* dermatitis, aspergillosis, and sporotrichosis. Terbinafine has shown in-vitro susceptibility against *Candida*, *Coccidioides immitis*, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, and *Phythium insidiosum* organisms. A recent pharmacokinetics study in dogs provided evidence supporting the use of oral terbinafine for the treatment of deep dermatophytosis (*Microsporum canis* and *Trichophyton metagrophytes*), blastomycosis, histoplasmosis, sporotrichosis, and coccidiomycosis (Sakai *et al*. 2011). Terbinafine has been used in humans to treat select systemic mycoses in conjunction with other antifungal agents; however, reports of efficacy are limited.

### CONTRAINDICATIONS

Patients with known hypersensitive to the drug. Use very carefully (reduced dose) or do not use at all in patients with renal failure and chronic or active liver disease.

### MECHANISM OF ACTION

Terbinafine is an allylamine antifungal agent that inhibits the fungal squalene epoxidase enzyme responsible for converting squalene into squalene-2,3-epoxide, which is then converted to lanosterol and ergosterol. The resultant depletion of ergosterol within the fungal cell membrane and the intracellular accumulation of squalene are believed to be responsible for the fungicidal effect of terbinafine. It is highly keratinophilic and lipophilic, and high drug concentrations are found in the stratum corneum, hair, nails, sebum, and subcutaneous fat of humans. After 14 days of therapy, it has been shown to accumulate in cat hair at or above the minimum inhibitory concentration (MIC) for dermatophytes (0.03 mcg/mL) for 5.3 weeks (Foust *et al*. 2007).

### DOSAGES

**Dogs and cats**

- Dermatophytosis: 30–40 mg/kg PO q24h until 2–3 negative fungal cultures. For deep dermatophytosis in dogs, the most recently proposed dose interval is q12h (Sakai *et al*. 2011)
- *Malassezia* dermatitis: 30 mg/kg PO q24h for 3–4 weeks and then re-evaluate
- Systemic or deep mycosis: in dogs, the most recently proposed dose is 30–35 mg/kg PO (Sakai *et al*. 2011). The administration interval proposed vary

according to the type of fungal disease: blastomycosis and histoplasmosis: q12h; sporotrichosis and coccidiomycosis: q8h

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Oral tablets: 250 mg; *Lamisil®*, generic
- Oral granules: 125 mg, 187.5 mg; generic, *Lamisil®*

### SIDE EFFECTS

**Dogs and cats:** Terbinafine appears to be well tolerated by dogs and cats. Side effects include vomiting, lethargy, decreased appetite, mild lymphopenia, and mild elevation in alkaline phosphatase and alanine aminotransferase. In addition, ocular abnormalities including transient ocular swelling have been reported. Facial pruritus, urticaria, and a macular/papular skin eruption were reported to occur 7 days after discontinuing treatment in two cats.

### DRUG INTERACTIONS

**Itraconazole and fluconazole:** avoid concurrent use because of increased potential for cardiotoxicity

**Rifampin:** can significantly increase terbinafine clearance

### MONITORING
- Efficacy and adverse effects
- Liver enzymes: baseline and during therapy if administered long-term

## Tetracycline Hydrochloride

**Trade/brand name:** *Sumycin®* (US), generic (US, CA, UK) (Rx)
**Classification:** Antibacterial (tetracycline), Anti-inflammatory

### INDICATIONS

**Dogs:** In veterinary dermatology tetracycline has been used in conjunction with niacinamide to treat various sterile inflammatory dermatoses such as discoid lupus erythematosus, sterile granulomatous/pyogranulomatous syndrome, sterile nodular panniculitis, cutaneous reactive histiocytosis, cutaneous vesicular lupus erythematosus, pemphigus erythematosus, pemphigus foliaceus, lupoid onychodystrophy/onychitis, German shepherd dog metatarsal fistulae, vasculitis, arteritis of the nasal philtrum, sebaceous adenitis, and dermatomyositis. In most of these disorders, a tetracycline drug and niacinamide will be used with other immunomodulatory drugs.

**Note:** Tetracycline is not a good antibiotic choice for canine and feline staphylococcal pyoderma and should never be used empirically, because bacterial resistance develops very rapidly. Tetracycline is not commonly used in cats because of its side effects (doxycycline is usually used instead).

## CONTRAINDICATIONS

Patients hypersensitive to tetracyclines. Avoid during pregnancy and lactation and in young animals because it can affect skeletal and teeth formation and cause discoloration of deciduous teeth. Use cautiously (reduce dose or avoid) in patients with renal or hepatic insufficiency.

## MECHANISM OF ACTION

The anti-inflammatory and immunomodulatory effects of tetracyclines are not well understood, but it is believed to reduce chemotaxis of leukocytes in vivo and lymphocyte blastogenesis in vitro, to inhibit complement (C3) activation, prostaglandin synthesis, and collagenase and lipase activities. The antimicrobial effect is associated with the reversible binding of tetracycline to the 30S ribosomal subunit of susceptible bacteria and inhibition of protein synthesis by interfering with the binding of aminoacyl-transfer RNA.

## DOSAGES

### Dogs

- Sterile inflammatory dermatoses: 250 mg PO q8h for dogs ≤10 kg and 500 mg PO q8h for dogs >10 kg. Frequency of administration may be reduced to twice daily if clinical response is noted

**Note:** Clinical response may not be seen before 6–8 weeks of treatment. It is used in combination with niacinamide (at the same dosage protocol).

### Dogs and cats

- Staphylococcal pyoderma: 15–20 mg/kg PO q8h

**Note:** Consider using tetracycline to treat staphylococcal pyoderma only if the bacterial strain is proved to be susceptible to this antimicrobial. Recently, it has been used in some cases of methicillin-resistant staphylococcal skin infections. Response to therapy; however, is variable despite in-vitro susceptibility.

## FORMULATIONS

**Veterinary-labeled products:** None for dogs and cats

### Human-labeled products

- Oral capsules: 250 mg, 500 mg; *Sumycin®*, generic
- Oral syrup: 25 mg/mL in 473 mL; *Sumycin®*

## SIDE EFFECTS

**Dogs:** vomiting, nausea, anorexia, diarrhea, lethargy; renal tubular necrosis and hepatotoxicity at high doses; may aggravate azotemia in renal failure; urolith formation with long-term use; may cause gray, yellow, or brown tooth discoloration and affect bone and tooth formation in young animals; may cause phototoxic reactions such as cutaneous edema and erythema after sun exposure; may cause false-positive glucose urine test results when copper sulfate reagents are used and false-negative test results when glucose oxidase reagents are employed

**Cats:** they do not tolerate oral tetracycline and develop fever, depression, and colic

**Note:** Immune-mediate hemolytic anemia, leukocytosis, atypical lymphocytes, and neutropenia have been reported in humans.

### DRUG INTERACTIONS

**Divalent and tetravalent cations (e.g., aluminum, bismuth, calcium, iron, magnesium, zinc):** reduce absorption of tetracyclines, possibly leading to subtherapeutic levels; administer tetracyclines and such products at least 1–3 hours apart to minimize interaction

**Digoxin:** may increase the bioavailability of digoxin

**Methoxyflurane or other potentially nephrotoxic drugs:** potentiate the nephrotoxic effects of tetracyclines

**Penicillins, cephalosporins, and aminoglycoside antibiotics:** possible antagonist effect; avoid concurrent use

**Retinoids:** increased incidence of benign intracranial hypertension in humans

**Warfarin:** may decrease plasma prothrombin activity and increase the effect of oral anticoagulants

### MONITORING

- Efficacy and adverse effects

## Thyrotropin

**Trade/brand name:** *Thyrogen®* (US, UK) (Rx)
**Classification:** Hormone (thyroid)

### INDICATIONS

**Dogs:** Thyrotropin, or thyroid-stimulating hormone (TSH), is used to stimulate thyroid gland secretion and assess its hormone reserve. For many years it was used as the gold-standard test for diagnosing canine primary hypothyroidism because it has been shown to more accurately differentiate primary hypothyroidism from euthyroid sick syndrome. The bovine and recombinant human TSH (rhTSH) have been shown to adequately stimulate the canine and feline thyroid glands, but currently these hormones are either difficult to acquire (bovine TSH) or very expensive (rhTSH).

### CONTRAINDICATIONS

Repeated administration of the pharmaceutical-grade bovine TSH may cause anaphylactic reaction.

### MECHANISM OF ACTION

Thyrotropin increases iodine uptake by the thyroid gland, increasing the production of thyroid hormones. It also increases the hormones' release by inducing proteolysis of the thyroglobulin molecule in phagolysosomes.

### DOSAGES

**Dogs**

- Bovine-TSH: collect a pre-TSH blood sample then administer 0.1 IU/kg IV (maximum 5 IU) of bovine TSH, then collect a 6-hour post-TSH blood sample. Measure pre- and post-TSH serum T4 concentrations

- rhTSH: collect a pre-TSH blood sample then administer 50–150 mcg IV of rhTSH, then collect a 6-hour post-TSH blood sample. A recent study showed that 150 mcg IV was better than 75 mcg IV to differentiate hypothyroid dogs from dogs with euthyroid sick syndrome (Boretti *et al*. 2009); therefore, the authors recommend using the higher dose in sick dogs or in dogs receiving medications when the test cannot be delayed. Measure pre- and post-TSH serum T4 concentrations

**Note:** The manufacturer recommends disposing of any leftover dose after reconstitution. However, rhTSH stability has been shown to be preserved for 8 weeks if aliquots are frozen (–20 °C), or for 4 weeks if refrigerated (4 °C).

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**
- Solution for injection (thyrotropin-alpha): 1.1 mg per vial; *Thyrogen*®

### SIDE EFFECTS

**Dogs**: repeated administration of the pharmaceutical-grade bovine TSH may cause anaphylactic reaction

### DRUG INTERACTIONS

Drugs that decrease or increase basal T4 concentrations can make the TSH stimulation test results difficult to interpret (*see Levothyroxine Sodium for detailed information*).

### MONITORING

- Adverse effects

## Thyrotropin-Releasing Hormone

**Trade/brand name:** *Thypinone*® (US), *Protirelin*® (UK)
**Classification:** Hormone (thyroid)

### INDICATIONS

**Dogs:** Thyrotropin-releasing hormone (TRH) is used to assess pituitary and thyroid gland function. In theory, this test could be used to differentiate primary from secondary hypothyroidism. It is not, however, a reliable test to diagnose primary hypothyroidism because there is typically minimal increase in serum T4 concentration after TRH administration, which may result in normal dogs having post-TRH serum T4 values in the hypothyroid range.

### CONTRAINDICATIONS

No information available.

### MECHANISM OF ACTION

TRH directly stimulates TSH secretion by the pituitary gland and indirectly (via TSH) stimulates the synthesis and secretion of thyroid hormones by the thyroid gland.

### DOSAGES

**Dogs**

- Collect a pre-TRH blood sample; administer 0.1 mg/kg IV of TRH; collect a 6-hour post-TRH blood sample. Measure pre- and post-TRH serum T4 concentrations
- Collect a pre-TRH blood sample; administer 0.2 mg (200 mcg) per dog IV of TRH; collect a 4-hour post-TRH blood sample. Measure pre- and post-TRH serum T4 concentrations

**Note:** For measurement of TSH collect blood samples 30 minutes post-TRH administration.

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Solution for injection: 500 mcg/mL; *Thypinone*®, *Lopremone*®, *Relefact*®, *Thyroliberin*®
- Solution for injection: 200 mcg/mL; *Protirelin*® (UK only)

### SIDE EFFECTS

**Dogs:** increased salivation, vomiting, urination, defecation, miosis, tachycardia, tachypnea

**Note:** These side effects are most likely to occur when TRH doses higher than 0.1 mg/kg are administered.

### DRUG INTERACTIONS

Drugs that decrease or increase basal T4 concentrations can make the TRH stimulation test results difficult to interpret (*see Levothyroxine Sodium for detailed information*).

### MONITORING

- Adverse effects

## Ticarcillin Disodium+Clavulanate Potassium

**Trade/brand name:** *Timentin*® (US, CA, UK) (Rx)
**Classification:** Antibacterial (beta-lactam)

Ticarcillin disodium+clavulanate potassium is equivalent to ticarcillin disodium+clavulanic acid.

### INDICATIONS

**Dogs:** Otitis externa and/or media caused by susceptible Gram-negative bacteria, especially *Pseudomonas*.

**Cats:** Treatment of otitis externa/media with ticarcillin has not been reported.

### CONTRAINDICATIONS

Patients with known hypersensitivity to penicillins or other beta-lactam antibiotic. Use carefully in patients with renal failure.

### MECHANISM OF ACTION

Ticarcillin is a bactericidal beta-lactam antibiotic that binds penicillin-binding proteins involved in cell wall synthesis, resulting in cell wall weakness and inhibition of bacterial growth, division, and septum formation. It acts in a time-dependent manner, requiring drug concentrations above minimum inhibitory concentration (MIC) values during administration intervals. The addition of clavulanate potassium or clavulanic acid increases the drug spectrum of activity by inhibiting bacterial beta-lactamase. However, clavulanate does not enhance the ticarcillin activity against *Pseudomonas*.

### DOSAGES

**Dogs**

- *Pseudomonas* otitis media: 15–25 mg/kg IV q8h. This dose was based on a study of dogs with *Pseudomonas* otitis resistant to fluoroquinolones and aminoglycosides (Nuttall 1998). Only cases with ruptured tympanic membranes were treated with intravenous ticarcillin therapy

**Note:** For topical use of ticarcillin for treatment of *Pseudomonas* otitis externa/media, please refer to the topical monograph in Section 2.

**Cats:** Treatment of feline otitis externa/media with ticarcillin has not been reported; nevertheless, the same dose protocol described for dogs can be used in cats

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Solution for injection (ticarcillin + clavulanate potassium): 3 g/0.1 g in 3.1 g vials or 3 g/0.1 g in 100 mL premixed, frozen Galaxy plastic containers; *Timentin*®

### SIDE EFFECTS

**Dogs and cats:** diarrhea and hypersensitivity reactions

**Note:** High doses of ticarcillin have been reported to cause decreased platelet function and CNS signs (e.g., seizures) in humans.

### DRUG INTERACTIONS

**Aminoglycosides:** penicillins and aminoglycosides have synergistic or additive effect in vitro against certain bacteria. Beta-lactam antibiotics can inactivate aminoglycosides when used in very high doses or in patients with renal failure; therefore, do not mix these two antibiotic classes in the same syringe or vial

**Probenecid:** can reduce the renal elimination of ticarcillin

**Warfarin:** use carefully in patients receiving anticoagulants, as bleeding disorders have been rarely reported with ticarcillin

### MONITORING

- Efficacy and adverse effects

## Toceranib Phosphate

**Trade/brand name:** *Palladia*® (US, CA, UK) (Rx)
**Classification:** Antineoplastic

### INDICATIONS

**Dogs:** Toceranib phosphate is approved by the FDA for the treatment of recurrent grade II or III canine cutaneous mast cell tumor with or without lymph node involvement. In clinical trials, dogs without lymph node metastasis and with c-Kit activation mutation had better response.

### CONTRAINDICATIONS

Contraindicated in dogs used for breeding, and in pregnant or lactating bitches. Drug safety has not been evaluated in dogs weighing less than 5 kg or younger than 24 months. Use cautiously with steroidal and non-steroidal anti-inflammatory drugs to avoid an increased risk for gastrointestinal ulceration or perforation.

### MECHANISM OF ACTION

Toceranib phosphate is a tyrosine kinase inhibitor with both direct anti-tumor and anti-angiogenic effects.

### DOSAGES

**Dogs:** Manufacturer's recommended initial dose: 3.25 mg/kg PO every other day. Dose reductions of 0.5 mg/kg to a minimum dose of 2.2 mg/kg every other day may be recommended

**Note:** Treatment response has been seen at a lower initial dose and less frequent administrations (e.g., Monday, Wednesday, Friday). Treatment interruptions of up to 2 weeks may be necessary to manage adverse reactions.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs

- Oral tablets: 10 mg, 15 mg, 50 mg in 30 tabs/btl; *Palladia*®

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs**

- Common (reported by the manufacturer): anorexia, diarrhea, vomiting, blood in stool or hemorrhagic diarrhea, lethargy, lameness/skeletal pain
- Uncommon: weight loss, dermatitis, pruritus, dehydration, general pain, polydipsia, pyrexia, tachypnea, pigmentation disorder (nasal depigmentation and coat color changes from fawn to white and from deep red to blonde), alopecia, urinary tract infection, vascular dysfunction that can result in edema and thromboembolism
- Laboratory abnormalities: neutropenia, thrombocytopenia, increased alanine aminotransferase, hypoalbuminemia, decreased hematocrit, increased creatinine

**Note:** The manufacturer recommends temporary treatment interruption if anemia, azotemia, hypoalbuminemia, and hyperphosphatemia occur simultaneously. Temporary treatment discontinuation is recommended if any of the following abnormalities occur singly: hematocrit <26%, creatinine ≥2 mg/dL or albumin <1.5 g/dL. Moreover, treatment should be interrupted if neutrophil count is ≤1000/mcL. In all these circumstances treatment can be resumed at a lower dose (reduce by 0.5 mg/kg) when abnormalities resolve.

### DRUG INTERACTIONS

**CYP3A4 family, inhibitors (e.g., ketoconazole):** concurrent use of toceranib phosphate with strong inhibitors of the CYP3A4 family may increase toceranib blood concentration

**Non-steroidal anti-inflammatory drugs (NSAIDs):** use cautiously because of the increased risk of gastrointestinal ulceration or perforation

### MONITORING

- Efficacy and adverse effects
- During the first 6 weeks: perform CBC weekly, perform chemistry profile and urinalysis intermittently, and measure tumor at follow-up visits
- Therapy should be discontinued if the disease progresses

## Triamcinolone Acetonide

**Trade/brand name:** *Cortalone*® (US), generic (Rx)
**Classification:** Anti-inflammatory (glucocorticoid), Immunomodulatory (immunosuppressive), Hormone

### INDICATIONS

**Dogs and cats:** Allergic skin disorders, autoimmune skin disorders, and various sterile inflammatory or immune-mediated dermatoses.

### CONTRAINDICATIONS

Infectious diseases, hyperadrenocorticism (can be carefully used to balance treatment-induced hypoadrenocorticism), gastric ulcer, corneal ulcer, diabetes mellitus, renal failure, and pregnancy. Modified live vaccines should be avoided when using immunosuppressive doses of glucocorticoids. Use glucocorticoids cautiously in cats with any cardiovascular disorders that alter the compensatory mechanisms for increased plasma volume, to avoid congestive heart failure (Ployngam *et al*. 2006). Triamcinolone will interfere with intradermal and allergy serum test reactivity. Withdrawal of oral administration of this drug is usually recommended for at least 4 weeks prior to allergy testing. Injectable triamcinolone is considered unsuitable for management of chronic dermatologic diseases due to potential severe effect on the HPA-axis.

### MECHANISM OF ACTION

Triamcinolone is classified as an intermediate-acting glucocorticoid. There is discrepancy in the veterinary literature regarding the relative potency of triamcinolone. Many human references report the anti-inflammatory potency of triamcinolone as being similar to that of methylprednisolone (i.e., about 5 times the potency of cortisol or hydrocortisone and 1.25 times that of prednisolone). However, most dermatologists believe that it is about 5–10 times more potent than prednisolone, or as potent as dexamethasone. The mechanisms of action of glucocorticoids are complex: through genomic and non-genomic mechanisms they exert anti-inflammatory and immunosuppressive effects by decreasing the synthesis of inflammatory cytokines, chemokines, adhesion molecules, prostaglandins and leukotrienes (both mediated by increasing the expression of

lipocortin-1); enhancing the clearance of foreign antigens; decreasing the ability of dendritic cells to present antigen and activate T cells; and suppressing the cellular immune response through inhibition of IL-12 synthesis and suppression of a Th-1 response, although they promote a Th-2 response.

## DOSAGES

**Dogs and cats**

- Inflammatory skin disorders
  - Induction: 0.11–0.22 mg/kg PO q24h (manufacturer recommended dose)
  - Maintenance: 0.05–0.1 mg/kg (or lower if possible) PO q48–72h
- Autoimmune skin diseases
  - Induction: 0.4–0.6 mg/kg PO q 24h
  - Maintenance: 0.1–0.2 mg/kg PO q48–72h

**Note:** A retrospective study on feline pemphigus foliaceus reported an induction dose range for well-controlled cats of 0.6–2 mg/kg q24h and a maintenance dose range of 0.6–1 mg/kg every 2–7 days (Preziosi *et al*. 2003). The authors also reported that cats receiving triamcinolone had significantly fewer side effects than cats receiving prednisolone and chlorambucil. When used orally long-term, the drug should be discontinued gradually.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs and cats

- Oral tablets: 0.5 mg, 1.5 mg; *Cortalone*®, generic

**Human-labeled products:** No oral tablets currently available

## SIDE EFFECTS

**Dogs**

- Common (associated with long-term therapy): iatrogenic Cushing's disease (i.e., poor dull hair coat, polyuria, polydpsia, polyphagia, panting, muscle atrophy, thin skin, hypotrichosis or alopecia, pot-belly appearance, weight gain, calcinosis cutis, comedones, milia), secondary bacterial skin and urinary tract infections
- Uncommon: diarrhea, gastrointestinal ulceration, pancreatitis, diabetes mellitus, behavior changes (aggression), demodicosis, dermatophytosis, hypoadrenocorticism

**Cats**

- Common: diabetes mellitus (occur more often in cats than in dogs)
- Uncommon/rare: cats are less prone to develop iatrogenic Cushing's disease when treated with long-term glucocorticoids; however, this syndrome will also develop if glucocorticoids are not used appropriately. Signs of iatrogenic Cushing's in cats include polyuria, polydpsia, polyphagia, fragile skin, distended abdomen, alopecia, or hypotrichosis. Skin fragility syndrome may develop as the sole sign of inappropriate glucocorticoid use. Congestive heart failure has been reported in cats treated with corticosteroids (Smith *et al*. 2004). Diarrhea and depression may also occur

## DRUG INTERACTIONS

**Amphotericin B or potassium-depleting diuretics (furosemide, thiazides):** hypokalemia may develop

**Aspirin:** may reduce salicylate blood levels

**Cyclophosphamide:** may inhibit the hepatic metabolism of cyclophosphamide; therefore, dosage adjustment may be required

**Cyclosporine:** may increase blood levels of both drugs

**Estrogens:** may potentiate the effect of triamcinolone or other glucocorticoids

**Isoniazid:** may decrease isoniazid blood levels

**Ketoconazole or other azole antifungals:** may increase glucocorticoids levels by decreasing their metabolism

**Macrolide antibiotics (e.g., erythromycin, clarithromycin):** may increase triamcinolone levels by decreasing its metabolism

**Mitotane:** may increase the metabolism of glucocorticoids requiring higher than usual doses of glucocorticoids when treating mitotane-induced hypoadrenocorticism

**Non-steroidal anti-inflammatory drugs (NSAIDs):** increased risk of gastrointestinal ulcer

**Phenobarbital, rifampin, barbiturates:** may increase the metabolism of glucocorticoids and decrease their blood levels

**Pyridostigmine or neostigmine:** profound muscle weakness may occur

### MONITORING

- Efficacy and adverse effects
- The authors recommend having serum chemistry profile, urinalysis, and urine culture performed every 6–12 months for animals on long-term glucocorticoid therapy

## Trilostane

**Trade/brand name:** *Vetoryl®* (US, CA, UK) (Rx)
**Classification:** Hormone (adrenal suppressant)

### INDICATIONS

**Dogs:** Trilostane is approved for the treatment of hyperadrenocorticism. It may also be beneficial for treatment of alopecia X.

**Cats:** Hyperadrenocorticism.

### CONTRAINDICATIONS

Animals hypersensitive to trilostane. Avoid or use cautiously in animals with renal and hepatic disease and high potassium concentrations. It should not be used concurrently with spironolactone or other aldosterone antagonist. It should not be used in pregnant animals (abortigenic in monkeys and sheep).

### MECHANISM OF ACTION

Trilostane competitively and reversibly inhibits the adrenal cortex 3-beta-hydroxysteroid dehydrogenase enzyme that converts pregnenolone to

progesterone, resulting in a decrease in the synthesis of cortisol, aldosterone, and 4-androstenedione.

## DOSAGES

Trilostane should be administered with food for better absorption.

### Hyperadrenocorticism

**Dogs:** General recommendation: 2–5 mg/kg/day PO q12–24h for pituitary-dependent or adrenal tumor. If using the brand-name product (*Vetoryl*®) the manufacturer recommends the following: 30 mg for dogs ≥4.4 kg (10 lb) to <10 kg (22 lb); 60 mg for dogs ≥10 kg (22 lb) to <20 kg (44 lb); 120 mg for dogs ≥20 kg (44 lb) to <40 kg (88 lb); 180 mg for dogs ≥40 kg (88 lb) to <60 kg (132 lb). Dogs >60 kg (132 lb) should receive the appropriate combination of capsules. These doses correspond to 2.2–6.7 mg/kg PO q24h

**Note:** A recent prospective study showed that starting treatment at 0.21–1.1 mg/kg PO q12h (mean: 0.86 mg/kg q12h) is safer than starting at the manufacturer's recommended dose (Feldman 2011). Slow adjustment of the treatment protocol to achieve clinical improvement may be needed on a case-by-case basis. Three-quarters of the dogs in the study (35/47) never required >3 mg/kg/day to control their disease throughout the 1-year follow-up. The author commented that twice-daily administration appears to be more appropriate than once-a-day dosing, because the effect of trilostane has been shown to last less than 12 hours.

**Cats:** 30 mg per cat PO q12–24h. Start with once-a-day administration and increase to twice daily if clinical signs do not improve. Follow the same protocol for ACTH testing and dose adjustments as for dogs

**Note:** Very few cats with hyperadrenocorticism have been treated with trilostane, with variable results.

### Alopecia X

**Dogs:** In one study, trilostane was given at an average dose of 10.85 mg/kg/day PO q24h or divided q12h to manage 24 dogs with alopecia X, and hair regrowth was typically noted after 4–8 weeks of treatment (Cerundolo *et al*. 2004). In another study, three Alaskan malamutes with alopecia X were treated with 3–3.6 mg/kg PO q12h, and complete hair regrowth was observed after 4–6 months of therapy (Leone *et al*. 2005)

**Note:** The authors recommend starting trilostane at 2 mg/kg PO q12–24h.

## FORMULATIONS

**Veterinary-labeled products:** Approved for dogs
- Oral capsules: 10 mg, 30 mg, 60 mg; *Vetoryl*®

**Note:** In Europe it is also available in 120 mg capsules.

**Human-labeled products**
- *Modrastane*®: currently discontinued in the US

## SIDE EFFECTS

**Dogs and cats**
- Common: mild lethargy and decreased appetite a few days after initiating therapy (likely due to corticosteroid withdrawal). Vomiting and diarrhea may

also develop. Increase in serum potassium concentration as a result of aldosterone suppression
- Rare: adrenal gland necrosis resulting in iatrogenic hypoadrenocorticism and death

### DRUG INTERACTIONS

**Angiotensin-converting enzyme (ACE) inhibitors (e.g., enalapril, benazepril):** trilostane and ACE inhibitor drugs have an aldosterone-lowering effect and may cause hyperkalemia if used concurrently

**Potassium-sparing diuretics (e.g., spironolactone, amiloride):** trilostane and these drugs have the potential to inhibit aldosterone and cause hyperkalemia

**Potassium supplements or high potassium foods:** may increase the risk for kyperkalemia

### MONITORING

- Efficacy and adverse effects
- Perform an ACTH stimulation test 2–4 hours post-trilostane administration at 10–14 days after initiating therapy and, thereafter, at 60 and 90 days or at any time if the animal shows clinical signs of glucocorticoid or mineralocorticoid deficiency or recurrence of disease. Another recommendation is to perform ACTH stimulation tests monthly for the first 3 months, then every 3 months for the first year and then every 4–6 months thereafter. Adjust the dose accordingly (reduce or increase by 25–50%) with the goal of maintaining the post-ACTH cortisol levels between 2 and 4 mcg/dL (55.18 and 110.36 nmol/L)

**Note:** A recent study suggests that baseline cortisol concentration measured 4–6 hours post trilostane administration can be used to monitor response to therapy in cases where money or inconvenience is a concern for the client (Cook and Bond 2010). Based on their findings, a healthy patient with baseline cortisol concentration between 1.3 mcg/dL and 2.9 mcg/dL (or ≤50% of pre-treatment value) has adequate adrenal gland function; however, patients with values outside this range would need an ACTH stimulation test to better evaluate the adrenal status. Further studies; however, are needed before replacing the ACTH stimulation test with the baseline cortisol test to monitor response to trilostane therapy.
- Serum electrolytes (mostly sodium and potassium concentrations) should be performed if lethargy, decreased appetite, vomiting and/or diarrhea develop

## Trimeprazine Tartrate+Prednisolone

**Trade/brand name:** *Temaril P®* (US), *Vanectyl-P®* (CA) (Rx)
**Classification:** Anti-inflammatory (glucocorticoid), Antihistamine

### INDICATIONS

**Dogs:** Management of chronic pruritic skin disorders such as allergies.

### CONTRAINDICATIONS

Trimeprazine is a phenothiazine with antihistamine activity. Phenothiazines can lower seizure threshold in susceptible animals; however, this adverse event has not been reported for trimeprazine. It should not be administered to pregnant dogs.

**Note:** Prednisolone will interfere with the intradermal and allergy serum test results. Withdrawal of oral administration of these drugs is usually recommended for at least 4 weeks prior to allergy testing.

### MECHANISM OF ACTION

Trimeprazine has sedative, antihistaminic, antipruritic, and antitussive effects. The prednisolone component of the veterinary-approved formulation adds anti-inflammatory properties.

### DOSAGES

**Dogs:** one tablet/5 kg PO q12h for 4–7 days; then one tablet/5 kg q24h for 4–7 days and finally one tablet/5 kg q24h every other day. This schedule may change according to each patient's needs; however, the ultimate goal for long-term glucocorticoid therapy is to give the lowest dosage that keeps the animal's condition under control, and to administer this dosage every other day or less frequently if possible. On the other hand, antihistamines should be administered daily for optimal effect, which complicates the use of this combination product.

### FORMULATIONS

**Veterinary-labeled products:** Approved for dogs

- Oral tablets (trimeprazine tartrate + prednisolone): 5 mg/2 mg in 100 and 1000 tablets/btl; *Temaril P®*, *Vanectyl-P®*

**Human-labeled products:** None

### SIDE EFFECTS

**Dogs:** sedation, depression, hypotension, rigidity, tremors, weakness, restless, polyuria, polydpsia, polyphagia, panting, vomiting, diarrhea, muscle wasting, thin skin, hair loss, calcinosis cutis, increased susceptibility to skin and urinary tract infections, increase in liver enzymes

### DRUG INTERACTIONS

**Amphotericin B:** hypokalemia may occur if administered concurrently with glucocorticoids

**Angiotensin-converting enzyme (ACE) inhibitors:** phenothiazines, such as trimeprazine tartrate, may increase the effects of ACE inhibitors

**Antacids and antidiarrheal mixtures (e.g., kaolin/pectin, bismuth subsalicylate):** may reduce the absorption of oral phenothiazines

**Anticholinesterase agents (e.g., pyridostigmine, neostigmine):** concurrent use of glucocorticoids with these drugs may result in profound muscle weakness

**Aspirin:** salicylate blood levels may be reduced by glucocorticoids

**Cisapride:** risks for cardiac arrhythmias increase

**CNS depressant agents (e.g., barbiturates, narcotics, anesthetics):** CNS depression may be potentiated

**Cyclophosphamide:** the hepatic metabolism of cyclophosphamide may be inhibited by glucocorticoids

**Cyclosporine:** mutual inhibition of hepatic metabolism of cyclosporine and prednisolone may occur, leading to potential increase in blood levels of both drugs

**Diuretics, potassium-depleting (e.g., furosemide, thiazides):** hypokalemia may develop if these drugs are used concurrently with glucocorticoids

**Insulin:** insulin requirement may be increased when it is used concurrently with glucocorticoids

**Non-steroidal anti-inflammatory drugs (NSAIDs):** increased risk for gastrointestinal ulcers if used concurrently with glucocorticoids

**Paroxetine:** may increase phenothiazine plasma levels

**Phenobarbital, phenytoin, rifampin:** these drugs may increase the metabolism of glucocorticoids

#### MONITORING

- Efficacy and adverse effects
- The authors recommend performing serum chemistry profile, urinalysis and urine culture every 6–12 months when using long-term glucocorticoid therapy

## Vitamin A

**Trade/brand name:** *Liquid A Drops*® (US), many generics
**Classification:** Vitamin

#### INDICATIONS

**Dogs:** Sebaceous adenitis, vitamin-A-responsive dermatosis of cocker spaniels and other breeds, primary idiopathic seborrhea, or other primary keratinization disorders.

#### CONTRAINDICATIONS

Do not use in pregnant animals. Over-supplementation of vitamin A or excess liver in the diet for a long period of time may result in hypervitaminosis A or toxicity. Dosages as high as 10,000 IU/kg/day may be needed to cause toxicity. Avoid using topical and systemic formulations concurrently, to prevent toxicity.

#### MECHANISM OF ACTION

Vitamin A is an alcohol, all-trans retinol that is oxidized in the body to retinal and retinoic acid. These compounds play an important role in stimulating and maintaining normal growth and differentiation of keratinocytes through binding to specific nuclear receptors and altering gene transcription of various molecules such as proteins, inflammatory mediators, and growth factors. All retinoids have some antiproliferative, anti-inflammatory, and immunomodulatory effects.

#### DOSAGES

**Note:** Reported doses are variable and anecdotal.

**Dogs**

- Sebaceous adenitis: a recent retrospective study showed that sebaceous adenitis was fairly well controlled (>25% improvement) in most dogs treated with vitamin A and other adjunctive therapies (e.g., various topical treatments, fatty acids) (Lam *et al*. 2011). The dosage of vitamin A ranged from 380 IU/kg to

2667 IU/kg PO q24h, and it was administered for a minimum of 1 month. No side effects were reported, and there was no correlation between the dosage used and response to therapy, suggesting that the source of vitamin A was at least partially associated with the lack of response in some cases
- Vitamin-A-responsive dermatosis and primary idiopathic seborrhea: 625–800 IU/kg PO q24h or 10,000–50,000 IU per dog PO q24h with a fatty meal. It may take 4–8 weeks before any improvement can be seen

## FORMULATIONS

### Veterinary-labeled products
- Oral drops (as palmitate): 2000 IU/drop in 1.2 oz (15 mL) btl; *Liquid A Drops*® (inactive ingredient: extra virgin olive oil)

### Human-labeled products
- Oral capsules/softgels: 10,000 IU; generic
- Oral tablets: 10,000 IU, 25,000 IU, 50,000 IU; generic
- Oral solution: 5000 IU/0.1 mL; generic

**Note:** This list is not all inclusive. The amount of vitamin A may be expressed in units, retinol equivalents (RE), or mcg of retinol. One RE of vitamin A corresponds to 3.33 units or 1 mcg of retinol.

## SIDE EFFECTS

**Dogs:** dogs appear to tolerate natural retinoids well. Potential side effects associated with over-supplementation for long periods of time may include localized or generalized papules with a firm center, poor coat quality, alopecia, scaling, excessive bleeding, liver disease, keratoconjunctivitis sicca

**Note:** In humans, side effects are typically associated with doses higher than 100,000 IU/day and include various dermatologic signs (e.g., erythema, dry skin and mucosa, alopecia), gingivitis, anemia, coagulation disorders, neutropenia, liver cirrhosis, liver fibrosis, hepatotoxicity, osteoporosis, osteosclerosis, seizure, drowsiness, pseudotumor cerebri, diplopia, dyspnea, teratogenicity.

## DRUG INTERACTIONS

**Acitretin, bexarotene:** concurrent use may increase the risk for vitamin A toxicity

**Etretinate, isotretinoin:** concurrent use may increase the risk for vitamin A toxicity

**Minocycline:** concurrent use may increase the risk for pseudotumor cerebri (benign intracranial hypertension)

**Tretinoin:** concurrent use may increase the risk for vitamin A toxicity

**Warfarin:** concurrent use may cause an increased anticoagulant effect if high doses of vitamin A are used

## MONITORING
- Efficacy and adverse effects
- Baseline and periodic monitoring (q6–12 months) of liver enzymes and tear production (Schirmer tear test) in animals receiving high doses or long-term treatment

## Vitamin E

**Trade/brand name:** Many generics available
**Classification:** Vitamin

### INDICATIONS

**Dogs:** Vitamin E has been anecdotally used as adjunctive therapy for immune-mediated skin diseases such as discoid lupus erythematosus, dermatomyositis, and demodicosis.

**Cats:** Pansteatitis.

### CONTRAINDICATIONS

Use with caution in animals with coagulation disorders.

### MECHANISM OF ACTION

Vitamin E, also known as alpha-tocopherol, is an antioxidant with immunostimulatory and anti-inflammatory effects mediated by stabilization of lysosomes, reduction of prostaglandin $E_2$ synthesis, and increase in the production of IL-2. A deficiency of vitamin E results in T-cell dysfunction.

### DOSAGES

**Dogs:** 400–800 IU per dog PO q12h

**Cats:** 10 mg (13.5 IU)/kg PO q24h

### FORMULATIONS

**Veterinary-labeled products:** There are many brands containing vitamin E labeled for dogs presented in different formulations; however, these brands usually contain other vitamins and/or minerals.

**Human-labeled products:** This list is not all-inclusive

- Oral tablets: 100 IU, 200 IU, 400 IU, 500 IU, 800 IU; generic
- Oral capsules: 100 IU, 200 IU, 400 IU, 1000 IU; Mixed E 400 *Softgels®*, *d'Alpha E 1000 Softgels®*, *Vita-Plus E®*, generic
- Oral drops: 15 IU/0.3 mL in 12 mL and 30 mL; *Aquasol E®*, *Aquavit-E®*
- Oral liquid: 15 IU/0.3 mL in 30 mL, 60 mL, and 120 mL; 798 IU/30 mL in 473 mL; *Nutr-E-Sol®*, generic

### SIDE EFFECTS

**Dogs and cats:** vitamin E appears to be well tolerated in dog and cats.

**Note:** In humans, doses of vitamin E ≥ 1000 IU per day (15 IU/kg/day) can cause coagulation disorders. Coagulopathy results from a decrease in vitamin-K-dependent coagulation factors.

### DRUG INTERACTIONS

**Iron:** the hematologic response to iron therapy may be delayed in patients with iron deficiency taking large doses of vitamin E

**Mineral oil:** may decrease the absorption of orally administered vitamin E

**Vitamin A:** may enhance the absorption, utilization and storage of vitamin A

**Warfarin:** the anticoagulant effect of warfarin may be intensified

### MONITORING

- Efficacy and adverse effects

## Voriconazole

**Trade/brand name:** *Vfend*® (US, CA, UK) (Rx)
**Classification:** Antifungal (second-generation azole, triazole)

### INDICATIONS

Voriconazole is mainly recommended as primary or salvage therapy in infections caused by *Aspergillus*, *Scedosporium apiospermum* (asexual form of *Pseudallescheria boydii*), *Fusarium*, and *Candida* in people. Voriconazole is also effective against *Cryptococcus*, *Histoplasma*, *Blastomyces*, and *Trichosporon* species. Although it has very good efficacy against the majority of molds, the exception is zygomycetes. It penetrates the CNS barrier and eye.

### CONTRAINDICATIONS

Patients with known hypersensitivity to voriconazole or its excipients. Use cautiously in patients with liver disease and in pregnant animals. The intravenous formulation should be avoided in individuals with renal failure because the solubilizing agent (cyclodextrin) can accumulate in the body.

### MECHANISM OF ACTION

Voriconazole is a second-generation triazole antifungal similar in structure to fluconazole. The primary mechanism of action of voriconazole is the inhibition of fungal cytochrome P450-dependent 14-alpha-lanosterol demethylase, which is essential for the synthesis of ergosterol in the fungal cell wall. It also inhibits 24-methylene dehydrolanosterol demethylation in molds, explaining its good activity against these fungi.

### DOSAGES

These doses are extrapolated from humans.

**Dogs:** 6 mg/kg PO or IV q12h for the first 2 days (loading dose); thereafter 3–4 mg/kg PO q12h as needed (maintenance dose)

### FORMULATIONS

**Veterinary-labeled products:** None

**Human-labeled products**

- Oral tablets: 50 mg, 200 mg; *Vfend*®
- Powder for oral suspension: 45 g (40 mg/mL); *Vfend*®
- Powder for injection (voriconazole/sulfobutyl ether beta-cyclodextrin sodium): 200 mg/3200 mg per vial; *Vfend I.V.*®

### SIDE EFFECTS

Adverse effects in veterinary patients are unknown at this time because of limited use of this drug. In humans, reported side effects include dose-related

photosensitization, Stevens–Johnson syndrome (rare), other dermatologic reactions, photophobia, visual disturbances, nausea, vomiting, diarrhea, increased liver enzymes activity and rarely hepatotoxicity (jaundice, abnormal liver function tests), anaphylaxis with intravenous administration. Rarely anemia, leukopenia, thrombocytopenia, pancytopenia, QT interval prolongation, and nephrotoxicity.

### DRUG INTERACTIONS

Voriconazole is metabolized by the hepatic cytochrome P450 (CYP) enzymes CYP2C19, CYP2C9, and CYP3A4. It has highest affinity for CYP2C19, followed by CYP2C9, and has significantly lower affinity for CYP3A4. Inducers or inhibitors of these three enzymes may decrease or increase voriconazole plasma concentrations.

**Astemizole (CYP3A4 substrate):** may increase plasma concentrations of astemizole, resulting in serious cardiac arrhythmias if these drugs are used concurrently

**Benzodiazepines (CYP3A4 substrate):** may increase benzodiazepine levels

**Calcium channel blockers (amlodipine, diltiazem, verapamil):** serum concentrations of these drugs may be increased

**Carbamazepine and long-acting barbiturates such as phenobarbital and mephobarbital (potent CYP inducers):** these drugs may reduce serum concentrations of voriconazole

**Cisapride (CYP3A4 substrate):** may increase plasma concentrations of cisapride, resulting in serious cardiac arrhythmias

**Corticosteroids:** may increase AUC (area under the curve) for prednisolone

**Cyclosporine (CYP3A4 substrate):** increased serum concentration of cyclosporine; cyclosporine dose should be decreased

**Phenytoin (CYP2C9 substrate and potent CYP inducer):** phenytoin decreases serum concentration of voriconazole, and voriconazole can increase serum concentration of phenytoin

**Proton-pump inhibitors (omeprazole):** serum concentrations of omeprazole or proton-pump inhibitors may be increased

**Quinidine (CYP3A4 substrate):** may increase plasma concentrations of quinidine, resulting in serious cardiac arrhythmias

**Rifampin (potent CYP inducer), rifabutin:** these drugs decrease serum concentration of voriconazole

**Sulfonylureas (CYP2C9 substrates; e.g., tolbutamide, glipizide, and glyburide):** serum concentration of these drugs may be increased, with increased risk for hypoglycemia

**Terfenadine (CYP3A4 substrate):** may increase plasma concentrations of terfenadine resulting in serious cardiac arrhythmias

**Vincristine, vinblastine (CYP3A4 substrates):** may increase serum concentrations of vinca alkaloids

**Warfarin (CYP2C9 substrate):** warfarin effects may be potentiated

### MONITORING

- Efficacy and adverse effects
- Monitor liver enzymes periodically if voriconazole is used long-term

## Zinc

**Trade/brand name:** *Zinpro*® (US, CA), *Orazinc*® (US), many generics available
**Classification:** Nutritional supplement

### INDICATIONS

**Dogs:** Zinc-responsive dermatosis of malamutes and Siberian huskies (rarely other breeds) fed balanced diets (syndrome I) or young rapidly growing puppies fed diets low in zinc or high in phytates (e.g., cereal grains, soy-based or corn-based diets), or supplemented with high levels of minerals (e.g., calcium, iron, copper) that may bind zinc and interfere with its intestinal absorption (syndrome II). It can also be used as adjunctive therapy for superficial necrolytic dermatitis (metabolic epidermal necrosis, hepatocutaneous syndrome).

**Cats:** Superficial necrolytic dermatitis.

### CONTRAINDICATIONS

Patients sensitive to zinc.

### MECHANISM OF ACTION

Zinc is an integral part of over 200 metalloenzymes, and it is necessary for cell membrane, protein and nucleic acid syntheses, wound healing, cell division and growth, normal vision, taste acuity, sexual maturation and reproduction, and immune response.

### DOSAGES

**Dogs**

- Zinc-responsive dermatosis and superficial necrolytic dermatitis: 2 mg/kg PO q24h of elemental zinc; 5 mg/kg PO q24h of zinc gluconate; 10 mg/kg PO q24h or divided q12h of zinc sulfate

**Note:** Doses may need to be adjusted based on response to therapy. The addition of low-dose glucocorticoid therapy may benefit cases that do not respond solely to zinc supplementation. The authors typically start with 0.5–1.0 mg/kg/day of oral prednisone or prednisolone and reduce the dose to the lowest every-other-day dose required to maintain the disease under control (ideally ≤0.2 mg/kg once every other day). For syndrome I cases that do not respond to oral zinc supplementation and low-dose glucocorticoid therapy, slow IV or IM injections with sterile zinc sulfate solutions at 10–15 mg/kg weekly (maximum of 600 mg/month) for at least 1 month have been recommended. These cases may need to be maintained on injections every 1–6 months to prevent recurrences. Life-long therapy is required for syndrome I. In syndrome II, the zinc supplement can be discontinued when clinical signs have resolved and any dietary problem has been corrected.

**Cats:** Specific doses of zinc for superficial necrolytic dermatitis have not been reported; however, doses used in dogs can be possibly extrapolated for cats.

## FORMULATIONS

**Veterinary-labeled products:** Many vitamin/mineral supplements labeled for dogs and cats contain zinc. This is not a complete list

- Oral biscuits (zinc methionine): *Zinpro Dog Biscuits®* (flavored: original/beef, turkey and barley)
- Oral chewable tablets (zinc methionine): 13 mg/tablet, 180 tablets/btl; *Zinpro Chewable Tablets®* for dogs (also contains manganesium stearate, garlic, fish protein concentrate and natural cheese flavor)

**Human-labeled products:** This list is not all-inclusive

- Oral tablets (sulfate): 66 mg (15 mg zinc), 110 mg (25 mg zinc), 200 mg (45 mg zinc); *Zinc 15®*, *Orazinc®*, generic
- Oral capsules (sulfate): 220 mg (50 mg zinc); *Orazinc®*, *Verazinc®*, *Zinc–220®*, *Zincate®*, generic
- Injection (sulfate): 1 mg/mL in 10 mL and 30 mL vials; 5 mg/mL in 5 mL and 10 mL vials; *Zinca-Pak®*, generic

## SIDE EFFECTS

**Dogs and cats:** nausea, vomiting, decreased appetite. These side effects are most commonly seen with zinc sulfate supplementation and can be reduced if the dose is divided into twice-a-day administration and given with food (tablets can be crushed). Intravenous administration of zinc may cause cardiac arrhythmias if administered rapidly.

## DRUG INTERACTIONS

**Calcium, iron:** large doses may bind to zinc and inhibit its absorption

**Copper:** absorption may be reduced by large doses of zinc

**Fluoroquinolones:** the oral absorption of some fluoroquinolones may be reduced by zinc

**Penicillamine:** penicillamine may inhibit zinc absorption

**Phytates:** may bind to zinc and inhibit its absorption

**Tetracyclines:** zinc may bind to tetracyclines and impair their absorption

**Ursodiol:** ursodiol may inhibit zinc absorption

## MONITORING

- Efficacy and adverse effects

# Section 2
# Topical Agents

The following section lists many of the active ingredients and corresponding commercial products commonly used in veterinary medicine for their local action; however, it is not a complete list of all that is available. It includes both veterinary-labeled dermatological products and some potentially useful human-labeled products. Active ingredients are listed by therapeutic class. The list of ingredients includes all the active ingredients but may not include all the inactive ingredients. Refer to the complete label for additional information on each product.

## ANTIPRURITIC AGENTS, NON-CORTICOSTEROID

### Aluminum Acetate Solution (Burow's Solution or Modified Burow's Solution)

*For **otic** use, refer to the Otic section.*

#### INDICATIONS

Burow's solution can be used for adjunctive treatment of minor skin irritations such as insect-bite reactions, and localized inflamed and exudative skin conditions including acute moist dermatitis, intertrigo and contact dermatitis. It can also be used for the treatment of otitis externa (see Otic section).

#### MECHANISM OF ACTION

Burow's solution has astringent and acidifying properties and also has mild soothing, antipruritic, and antiseptic/antimicrobial effects. The pharmaceutical properties of the solution are not fully understood. All veterinary products containing Burrow's solution also contain hydrocortisone, which adds antipruritic and anti-inflammatory effects.

#### SUGGESTED USES/DOSAGES

Burow's solution (alone) is usually used topically as a wet compress, dressing, or soak. Application for 15–30 minutes is generally recommended, and the affected area is air-dried between applications. Use can be as often as necessary, but every 4–6 hours is often employed. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. The duration of administration depends on the condition being treated and the response to the medication. The veterinary-labeled products containing hydrocortisone can be directly applied. As Burow's solution products come in various dosage forms (powder or tablets for dissolving, liquid)

*Canine and Feline Dermatology Drug Handbook*, First Edition.
Sandra N. Koch, Sheila M.F. Torres and Donald C. Plumb.

Published 2012 by Blackwell Publishing Ltd.

refer to package directions for proper dilutions. Dilutions of 1:40, 1:20, or 1:10 are commonly used.

### PRECAUTIONS/ADVERSE EFFECTS

Do not use plastic or any occlusive dressing material to prevent evaporation. Use room-temperature water for dissolving and application. Soap reduces the astringent actions of aluminum acetate. Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. May cause dry skin and skin irritation in some patients. The long-term use of products containing glucocorticoids can cause skin atrophy and potentially iatrogenic Cushing's disease. For products containing hydrocortisone, at least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing.

### VETERINARY-LABELED ALUMINUM ACETATE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Cort/Astrin Solution®*** (Vedco) | **Solution:** Burow's solution 2% Hydrocortisone 1% | OTC | Water, propylene glycol base. Labeled for dogs and cats. 1 oz dropper btl, 16 oz |
| ***Corti-Derm Solution®*** (First Priority) | **Solution:** Burow's solution 2% Hydrocortisone 1% | OTC | Water, propylene glycol base. Labeled for dogs. 1 oz |
| ***Hydro-Plus®*** (Phoenix) ***Bur-O-Cort 2:1®*** (Q.A. Labs) ***Hydro-B 1020®*** (Butler) | **Solution:** Hydrocortisone 1% Burow's solution 2% | OTC | Propylene glycol base. Labeled for dogs. 1 oz, 2 oz, 16 oz |

### HUMAN-LABELED ALUMINUM ACETATE TOPICAL PRODUCTS

| Product (company) | Form: active ingredients | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Bluboro Powder®*** (Allergan) ***Domeboro Powder®*** (Miles) ***Pedi-Boro Soak Paks®*** (Pedinol Pharmacal) | **Powder packets:** Aluminum sulfate Calcium acetate | OTC | Packets of 12 or 100/box. One packet dissolved in 16 oz (480 mL) of water makes a 1:40 (2.5%) modified Burow's solution |

### HUMAN-LABELED ALUMINUM ACETATE TOPICAL PRODUCTS
(continued)

| Product (company) | Form: active ingredients | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Domeboro Tablets®*** (Miles) | **Effervescent tablets:** Aluminum sulfate Calcium acetate | OTC | Tablets of 12 or 100/box. One tablet dissolved in 16 oz (480 mL) of water makes a 1:40 (2.5%) modified Burow's solution |
| ***Burow's Solution*** (various generic) | **Solution:** Aluminum acetate | OTC | 480 mL btl |

## Colloidal Oatmeal

### INDICATIONS
Colloidal oatmeal provides temporary relief and soothing effect for itching and pain associated with allergic reactions.

### MECHANISM OF ACTION
Colloidal oatmeal is used topically as an anti-inflammatory and antipruritic, but the exact mechanism for this effect is not known. It is thought that as the concentration of oatmeal increases, both its drying and antipruritic effects increase. It has been suggested that it may inhibit prostaglandin synthesis.

### SUGGESTED USES/DOSAGES
If using spray: up to 2–3 times a day as needed for itching relief. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo or conditioner: daily to weekly baths/after baths according to the veterinarian's recommendations. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well. Refer to product label for details of individual use.

### PRECAUTIONS/ADVERSE EFFECTS
Other than the potential for increased drying of already dry skin, colloidal oatmeal is very safe. In humans, there are some reports of contact dermatitis associated with its use.

### VETERINARY-LABELED COLLOIDAL OATMEAL TOPICAL PRODUCTS
Products listed are those containing only colloidal oatmeal as the principal active ingredient. *For **other products containing colloidal oatmeal,** refer to Diphenhydramine, Lidocaine, Pramoxine, Hydrocortisone, Permethrin, and Pyrethrin listings*.

## VETERINARY-LABELED COLLOIDAL OATMEAL TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***DermAllay Oatmeal® Spray*** (Dechra) | **Leave-on spray:** 0.75% | Sold only through licensed veterinarians | Exfoliating alpha-hydroxy acids. Does not need to be shaken. Labeled for dogs and cats. 12 oz, 1 gal |
| ***DermAllay Oatmeal® Shampoo*** (Dechra) | **Shampoo:** 2% | Sold only through licensed veterinarians | Safflower oil, sodium lactate, glycerin. Labeled for dogs and cats. 12 oz, 1 gal |
| ***Epi-Soothe® Shampoo*** (Virbac) | **Shampoo:** 2% | Sold only through licensed veterinarians | *Spherulite*® microcapsules. Glycothecnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside) minimizes microbial colonization. Labeled for dogs and cats of any age. Shake well. 8 oz, 16 oz, 1 gal |
| ***Pearlyt® Shampoo*** (TEVA/DVM) | **Shampoo:** % not listed | OTC | Propylene glycol, paraben, fragrance. Soap-free. Labeled for dogs and cats. 12 oz, 1 gal |
| ***Hartz Groomer's Best Oatmeal Shampoo®*** (Hartz Mountain) | **Shampoo:** % not listed | OTC | Labeled for dogs. 18 oz |
| ***Hartz Soothing Botanicals Skin Moisturizing Shampoo®*** (Hartz Mountain) | **Shampoo:** % not listed | OTC | Aloe vera. Labeled for dogs. 15 oz |
| ***Vet Solutions Aloe & Oatmeal Shampoo®*** (Vetoquinol) | **Shampoo:** % not listed | OTC | Aloe vera. Labeled for dogs and cats. 16 oz, 1 gal |

## VETERINARY-LABELED COLLOIDAL OATMEAL TOPICAL PRODUCTS (continued)

| | | | |
|---|---|---|---|
| ***Foaming Silk Bath®*** (AAH) | **Shampoo:** % not listed | OTC | Aloe vera, vitamins A and E. Labeled for dogs and cats. 16 oz |
| ***Aloe & Oatmeal Shampoo®*** (Sogeval) | **Shampoo:** 2% | Sold only through licensed veterinarians | Aloe vera, chamomile, glycerin, coconut oil, almond oil, vitamins A, D and E. Soap free. Labeled for dogs and cats. 2 oz, 17 oz, 1 gal |
| ***DermAllay® Conditioner*** (Dechra) | **Conditioner:** 0.75% | Sold only through licensed veterinarians | Exfoliating alpha-hydroxy acids. Does not need to be shaken. Labeled for dogs and cats. 8 oz, 1 gal |
| ***Epi-Soothe® Cream Rinse*** (Virbac) | **Cream rinse:** 1% | Sold only through licensed veterinarians | Lactic acid, propylene glycol. Labeled for dogs and cats of any age. Shake well. 8, 16 oz |
| ***ResiSoothe® Leave-On Lotion*** (Virbac) | **Lotion:** % not listed | Sold only through licensed veterinarians | Omega 6 fatty acids (sunflower oil), vitamin E. Labeled for dogs and cats of any age. Shake well. 8 oz |
| ***Vet Solutions Aloe & Oatmeal Skin and Coat Conditioner®*** (Vetoquinol) | **Conditioner:** % not listed | OTC | Aloe vera gel, vitamins A, D and E, chamomile, cetearyl alcohol, glycerin, lactic acid. Labeled for dogs and cats. 16 oz, 1 gal |
| ***Aloe & Oatmeal Conditioner®*** (Sogeval) | **Shampoo:** 2% | Sold only through licensed veterinarians | Aloe vera, chamomile, glycerin, coconut oil, cetyl alcohol, vitamins A, D and E, propylene glycol, lactic acid, parabens. Labeled for dogs and cats. 17 oz, 1 gal |

### HUMAN-LABELED COLLOIDAL OATMEAL TOPICAL PRODUCTS

There are several human products available containing colloidal oatmeal, including creams, lotions and products to be added to the bath. Common trade names include *Aveeno®*, *Geri SS®*, *and Oatmeal Bath®*.

## Diphenhydramine Hydrochloride

*For **systemic** use, refer to Section 1: Systemic Drugs.*

### INDICATIONS

Provides temporary relief of itching and pain associated with allergic reactions.

### MECHANISM OF ACTION

Diphenhydramine hydrochloride (HCl), a first-generation antihistamine, is an $H_1$-receptor antagonist with anti-allergic properties inhibiting histamine-induced wheal and flare responses. It has some local anesthetic activity, which probably relates to its main antipruritic mechanism of action. Diphenhydramine may be absorbed in small amounts transdermally, but should not cause systemic side effects.

### SUGGESTED USES/DOSAGES

If using spray, lotion, gel, or cream: 1–3 times a day or as needed. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo or conditioner: daily to weekly baths/after baths according to the veterinarian's recommendations. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes or mucous membranes. Do not apply to blistered or draining/oozing areas of skin. At least 2-week withdrawal period is recommended prior to intradermal testing.

### VETERINARY-LABELED DIPHENHYDRAMINE HYDROCHLORIDE TOPICAL PRODUCTS

None. *Histacalm® Shampoo and Spray and ResiHist® Leave-on Lotion* have been discontinued by the manufacturer at the time of writing.

### HUMAN-LABELED DIPHENHYDRAMINE HYDROCHLORIDE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| Products include ***Benadryl®, Caladryl®, Dermamycin®, Ziradryl®*** (various manufacturers and | **Spray:** 1%, 2%<br>**Lotion:** 0, 1%, 1%<br>**Gel:** 1%, 2%<br>**Cream:** 1%, 2%, 4% | OTC | These products may also contain astringents (calamine, zinc acetate, zinc oxide), |

**HUMAN-LABELED DIPHENHYDRAMINE HYDROCHLORIDE TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| additional trade-name modifiers such as Maximum Strength, etc. may be found) | | | other antihistamines (pyrilamine), and/or counter-irritants (menthol, camphor). Various sizes available |

## Lidocaine ± Prilocaine

### INDICATIONS

Lidocaine is used topically as an anesthetic or antipruritic and is included in several products labeled for acute moist dermatitis and pruritic lesions. It can be used for temporary relief of pain from minor cuts, abrasions, minor burns, sunburns, insect bites/reactions, and irritant or contact dermatitis. When combined with prilocaine (commonly called EMLA cream), it may be useful for dermal anesthesia prior to invasive procedures (e.g., prior to wound debridement, catheter placement, etc.).

### MECHANISM OF ACTION

Lidocaine exerts its anesthetic properties via alteration of cell membrane ion permeability, thereby inhibiting conduction from sensory nerves.

### SUGGESTED USES/DOSAGES

A thin layer applied to affected areas every 3–4 hours or as needed for pain and/or pruritus. A thin layer applied prior to wound debridement and catheter replacement. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. For veterinary-labeled products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Side effects are related to amount and duration of use. Topical lidocaine may be absorbed systemically, but systemic toxicity is unlikely to occur unless it is used on a large body surface area, for prolonged periods of time, or at high concentrations. Be extra-vigilant in patients also receiving other class I antiarrhythmics (e.g., mexiletine or tocainide). Avoid contact with eyes and do not use in ears, unless specifically labeled for such. Clients should wash hands after application or wear gloves when applying. Hypersensitivity or skin irritation (burning, tenderness, etc.) are possible, but apparently occur uncommonly. Products containing prilocaine (EMLA) may be more prone to causing (rarely) methemoglobinemia or systemic toxicity.

## VETERINARY-LABELED LIDOCAINE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Allercaine®*** (Tomlyn) | **Spray:** 2.4% | OTC | Denatonium benzoate (bittering agent), benzalkonium chloride. Do not apply to entire body or to large areas of broken skin. Labeled for dogs. 4 oz, 12 oz |
| ***Allerspray®*** (Vetoquinol) | **Spray:** 2.4% | OTC | Denatonium benzoate (bittering agent), benzalkonium chloride, aloe vera gel, allantoin, PEG-75 lanolin. Labeled for dogs. 4 oz |
| ***Dermacool Spray w/ Lidocaine®*** (Virbac) | **Spray:** 1.5% | Rx | Colloidal oatmeal, lactic acid, parachlorometaxylenol, hamamelis extract, denatonium benzoate (bittering agent), propylene glycol. Alcohol-free. Labeled for dogs and cats. 4 oz |
| ***Hexa-Caine®*** (PRN Pharmacal) | **Spray:** 2.4% | OTC | Denatonium benzoate (*Bitrex®*, bittering agent), benzalkonium chloride, aloe vera gel, allantoin, lanolin. Labeled for dogs and cats. 4 oz, 8 oz, 16 oz |
| ***Biocaine®*** (Tomlyn) | **Lotion:** 2% | OTC | Denatonium benzoate (*Bittran®* II, bittering agent), myristalkonium chloride, urea, lanolin, allantoin, chloroxylenol. Labeled for dogs and cats. 2 oz, 4 oz |

## HUMAN-LABELED LIDOCAINE TOPICAL PRODUCTS

There are several topical OTC products listed for human use, including sprays (2–2.5%), liquids (2–4%), creams (0.5–2%), gels (0.5–2.5%), and topical patches.

### HUMAN-LABELED LIDOCAINE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***EMLA®*** (Astra) **Lidocaine/ Prilocaine Cream** (various generics) | **Cream:** Lidocaine 2.5% Prilocaine 2.5% | Rx | Depending on manufacturer: 5 g, 15 g, 30 g |

## Neutralized Zinc

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Can be used alone for mild itching or as an adjunctive treatment to provide soothing of more pruritic conditions, mild bacterial infections, or dry skin. It can be used for insect-bite reactions, acute moist dermatitis, acral lick dermatitis, fold dermatitis (intertrigo), feline acne, and post-surgery wounds.

### MECHANISM OF ACTION

The exact mechanism of action is unknown. Zinc plays a role in wound healing including extracellular matrix remodeling, connective tissue repair, inflammation, and cell proliferation. Zinc also has antiseptic and astringent properties.

### SUGGESTED USES/DOSAGES

May be applied to affected areas two times a day or as needed to relieve itching and soothe the skin. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to allow the medication to work. For veterinary-labeled products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Overall it appears to be safe. Not to be used in patients with known sensitivity or allergy to the ingredients. Avoid contact with eyes.

### VETERINARY-LABELED NEUTRALIZED ZINC TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Maxi/Guard® ZN7 Derm*** (Addison Biological Laboratory) | **Solution and spray:** Zinc gluconate 0.9–1.1% | OTC | Taurine, L-lysine, glycerin. pH range 6.8–7.2, alcohol-free. Labeled for dogs and cats. 2 oz |

### HUMAN-LABELED NEUTRALIZED ZINC TOPICAL PRODUCTS

There are several OTC zinc gluconate or zinc oxide products available for use in humans, and many of the products contain other ingredients. A common trade name is *Calamine®* lotion, which contains zinc oxide and 0.5% iron (III) oxide ($Fe_2O_3$).

## Pramoxine Hydrochloride

### INDICATIONS

Provides temporary relief of itching and pain associated with allergic reactions. It has been specifically shown to be useful as an adjunctive therapy for pruritus in dogs with atopic dermatitis. Pramoxine hydrochloride (HCl) is often combined with other topicals to help reduce pain and/or itching.

### MECHANISM OF ACTION

The exact mechanism of action is unknown. Pramoxine is a surface and local anesthetic to peripheral nerves shown to decrease nerve membrane permeability to sodium, inhibiting depolarization, and to antagonize histamine-mediated pruritus; it is not related structurally to procaine-type anesthetics. Pramoxine has antipruritic effects that appear to be from a mechanism other than its anesthetic effect. Peak local anesthetic effects occur within 3–5 minutes of application. Duration of action is short, and it becomes even less when used frequently and repetitively.

### SUGGESTED USES/DOSAGES

If using spray, lotion, gel, or cream: apply every 3–4 hours or as needed for itching/pain relief. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo or rinse: daily to weekly baths/after baths or according to the veterinarian's recommendations. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well. For veterinary-labeled products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes; pramoxine is too irritating for ophthalmic use. Depending on product labeling, clients should wash hands after application or wear gloves when applying. Adverse effects are unlikely, but localized dermatitis is possible. Due to its antagonizing effect on histamine-mediated pruritus, at least a 2-week withdrawal period prior to intradermal test is recommended.

### VETERINARY-LABELED PRAMOXINE HCL TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Dermal-Soothe® Spray*** (Vetoquinol) | **Spray:** 1% | OTC | Lactamide monoethanolamine, *Novasome®* microvesicles. Shake well and repeat as necessary. Labeled for dogs and cats. 12 oz |
| ***Relief® Spray*** (TEVA/DVM) | **Spray:** 1% | Sold only through licensed veterinarians | Colloidal oatmeal. Labeled for dogs and cats. 8 oz |

## VETERINARY-LABELED PRAMOXINE HCL TOPICAL PRODUCTS
(continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Relief® HC Spray*** (TEVA/DVM) | **Spray:** Pramoxine 1% Hydrocortisone 1% | Sold only through licensed veterinarians | Colloidal oatmeal. Labeled for dogs and cats. 8 oz |
| ***Pramoxine Anti-Itch® Spray*** (Davis) | **Spray:** 1% | OTC | Colloidal oatmeal. Labeled for dogs and cats. 8 oz |
| ***Pramosoothe® Spray*** (Sogeval) | **Spray:** 1% | Sold only through licensed veterinarians | Colloidal oatmeal, omega-6 essential fatty acids. Labeled for dogs and cats. 8 oz |
| ***Pramosoothe HC® Spray*** (Sogeval) | **Spray:** Pramoxine 1% Hydrocortisone 1% | Sold only through licensed veterinarians | Colloidal oatmeal, omega-6 essential fatty acids. Labeled for dogs and cats. 8 oz |
| ***Pramoxine Anti-Itch® Shampoo*** (Davis) | **Shampoo:** 1% | OTC | Colloidal oatmeal, emollients. Labeled for dogs, cats, puppies, kittens. 12 oz, 1 gal |
| ***Relief® Shampoo*** (TEVA/DVM) | **Shampoo:** 1% | OTC | Colloidal oatmeal, omega-6 essential fatty acids. Labeled for dogs and cats. 8, 12 oz, 1 gal |
| ***Pramosoothe® Shampoo + PS*** (Sogeval) | **Shampoo:** Pramoxine 1% Phytosphingosine salicyloyl 0.05% | Sold only through licensed veterinarians | Colloidal oatmeal, omega 6 essential fatty acids. Labeled for dogs and cats. 8, 16 oz, 1 gal |
| ***Dermal-Soothe® Cream Rinse*** (Vetoquinol) | **Rinse:** 1% | OTC | Colloidal oatmeal, *Novasome®* microvesicles, Skin respiratory factor. Labeled for dogs and cats. 12 oz, 1 gal |

## VETERINARY-LABELED PRAMOXINE HCL TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Pramoxine Anti-Itch® Creme Rinse*** (Davis) | **Rinse:** 1% | OTC | Colloidal oatmeal, emollients, omega-6 fatty acids. Labeled for dogs, cats, puppies, kittens. 12 oz, 1 gal |
| ***Relief® Creme Rinse*** (TEVA/DVM) | **Rinse:** 1% | OTC | Colloidal oatmeal, emollients, omega-6 fatty acids. Labeled for dogs and cats. 8, 12 oz, 1 gal |
| ***ResiProx® Leave-On Lotion*** (Virbac) | **Lotion:** 1.5% | Sold only through licensed veterinarians | Colloidal oatmeal, cetyl alcohol, stearyl alcohol base. Shake well. Labeled for dogs and cats. 8 oz |

## HUMAN-LABELED PRAMOXINE HCL TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***AmLactin® AP*** (UpsherSmith) | **Cream:** 1% | OTC | Ammonium lactate 12% (moisturizer). Usually used for extremely dry, painful or itchy skin in humans. 4.9 oz |
| ***Prax®*** (Ferndale) | **Cream:** 1%<br>**Lotion:** 1% | OTC | Cetyl alcohol. Usually used for extremely dry, painful or itchy skin in humans. 15, 120, 240 mL |
| ***Tronolane®*** (Abbott) | **Cream:** 1% | OTC | Cetyl alcohol, zinc oxide. Usually used for extremely dry, painful or itchy skin in humans. 1, 2 oz |
| ***Itch-X®*** (Ascher) | **Spray:** 1% | OTC | Benzyl alcohol 10%, aloe vera. 2 oz |
| ***Itch-X®*** (Ascher) | **Gel:** 1% | OTC | Benzyl alcohol 10%, aloe vera, propylene glycol. 1.25 oz |
| ***PrameGel®*** (GenDerm) | **Gel:** 1% | OTC | Menthol 0.5%, emollient base. 120 g |

# ANTI-INFLAMMATORY AGENTS

## CORTICOSTEROIDS

There are at least 20 chemical entities (plus a variety of salts) used in humans for topical corticosteroid therapy. The following section includes many veterinary topical products and some human products that may be of use in veterinary medicine.

### Betamethasone

*For **systemic** use, refer to Section 1: Systemic Drugs.*
*For **otic** use, refer to the Otic section.*

#### INDICATIONS

Considered a high-potency topical corticosteroid, betamethasone may be useful for adjunctive treatment of localized pruritic and/or inflammatory conditions that may be associated with bacterial and/or yeast skin infections (betamethasone and antimicrobial combination products). Because risks associated with betamethasone (e.g., hypothalamus–pituitary–adrenal axis suppression, systemic corticosteroid effects, skin atrophy) are greater than with hydrocortisone, betamethasone products are generally reserved for more severe localized pruritic conditions or when hydrocortisone is not effective. All veterinary-labeled products are in combination with gentamicin and many in combination with clotrimazole. The products containing bethametasone, gentamicin, and clotrimazole are labeled for otic use; however, they can also be used extra-label for yeast and/or bacterial skin infections sensitive to clotrimazole and gentamicin, when an anti-inflammatory effect is also needed. Sole-ingredient betamethasone topical forms are available with human labeling.

#### MECHANISM OF ACTION

Corticosteroids are non-specific anti-inflammatory agents. Amongst their various mechanisms of action, corticosteroids induce annexin I (i.e., phospholipase A2-alpha inhibitory protein) in cells, thereby blocking the release of arachidonic acid and its subsequent conversion to eicosanoids (i.e., leukotrienes, prostaglandins, prostacyclins, and thromboxanes). They also inhibit the synthesis of various inflammatory cytokines (e.g., IL-1, TNF-alpha) by inhibiting the pro-inflammatory transcription factor, NF-kB. Moreover, corticosteroids reduce DNA synthesis via an antimitotic effect on epidermal cells. Topically applied corticosteroids also inhibit the migration of leukocytes and macrophages to the area, reducing erythema, pruritus, and edema.

#### SUGGESTED USES/DOSAGES

Initially, topical corticosteroids are usually used sparingly 1–2 times per day, then tapered to less frequent use. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. Bethametasone formulations are best suited for focal (e.g., pedal) or multifocal lesions and for relatively short durations. However, clinicians must tailor the frequency and duration of application to the severity of clinical signs, being always mindful of the potential side effects associated with

frequent and prolonged use. For veterinary products, refer to individual product labeling for specific dosing and frequency recommendations.

### PRECAUTIONS/ADVERSE EFFECTS

Several veterinary topical products list tuberculosis of the skin and pregnancy as a contraindication. Use care when treating large areas, or when using on smaller patients. Increased risks of hypothalamic–pituitary–adrenal axis suppression, systemic corticosteroid effects (e.g., polydipsia/polyuria, Cushing's disease, gastrointestinal signs), cutaneous atrophy that can be associated with skin fragility, superficial follicular cysts (milia), and comedones may occur as product concentration and duration of treatment increase. Local skin reactions (burning, itching, redness) are possible but unlikely. Betamethasone may delay wound healing, particularly if used for longer than 7 days. Vomiting and diarrhea have been reported with the use of products containing betamethasone. Risks can be reduced by treating for only as long as necessary on as small an area as possible. Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. At least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing. Use caution when using medications containing gentamicin empirically, because of possible bacterial resistance.

### VETERINARY-LABELED BETAMETHASONE TOPICAL PRODUCTS

At the time of writing, there were no veterinary-labeled products in the US containing betamethasone as the sole active ingredient.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Gentocin Topical Spray®*** (Intervet/Schering-Plough)<br>***Gentaspray®*** (Butler)<br>***Betagen Topical Spray®*** (Med-Pharmex)<br>***Gentamicin Topical Spray®*** (RXV)<br>***Gentaved Topical Spray®*** (Vedco) | **Spray** (all products listed)<br>Gentamicin 0.57 mg/mL<br>Betamethasone valerate 0.284 mg/mL | Rx (all products listed) | All products listed are labeled for dogs and contain propylene glycol, isopropyl alcohol and parabens<br>All products listed are available in 3 different sizes 60 mL, 120 mL, 240 mL, except for *Gentocin Topical Spray®* available in 72 mL and *Gentamicin Topical Spray®* available in 60 mL and 120 mL |

## VETERINARY-LABELED BETAMETHASONE TOPICAL PRODUCTS
(continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Otomax®*** ***Ointment*** (Intervet/ Schering-Plough) ***Vetromax®*** ***Ointment*** (Dechra) ***MalOtic®*** ***Ointment*** (Vedco) | **Ointment (otic)** (all products listed) Gentamicin 3 mg/g Betamethasone valerate 1 mg/g Clotrimazole 10 mg/g | Rx or sold only through licensed veterinarians (all products listed) | Mineral-oil based All products listed are approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected lesions on the skin, e.g., bacterial skin lesions or *Malassezia* dermatitis. 15 g, 30 g tb (*Otomax®*) 7.5 g, 15 g tb (*Vetromax®*, *MalOtic®*) |
| ***Fuciderm Gel®*** (Dechra) | **Gel:** Bethametasone valerate 0.1% Fusidic acid 0.5% | Sold only through licensed veterinarians (not available in US, only in EU and CA) | Labeled for dogs. Can be used extra-label in cats. 15 g, 30 g tb |

## HUMAN-LABELED BETAMETHASONE TOPICAL PRODUCTS

Partial listing. There are also topical brand products (two common trade names are *Diprosone®* and *Maxivate®*) available with betamethasone dipropionate. Do not confuse products containing augmented betamethasone dipropionate (*Diprolene®*, etc.) with betamethasone dipropionate. Augmented betamethasone dipropionate is not equivalent to betamethasone dipropionate, as it is more potent. For more information on human-labeled betamethasone products, refer to a comprehensive human drug reference (e.g., *Facts and Comparisons* or *Micromedex*) or contact a pharmacist.

### HUMAN-LABELED BETAMETHASONE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Betamethasone Dipropionate** (generic) | **Ointment:** 0.05%<br>**Cream:** 0.05%<br>**Lotion:** 0.05% | Rx | 15 g, 45 g<br>15 g, 45 g<br>20 mL, 30 mL, 60 mL |
| ***Maxivate***® (Schering-Plough) | **Ointment:** 0.05%<br>**Cream:** 0.05%<br>**Lotion:** 0.05% | Rx | 100 g<br>100 g<br>100 mL |
| ***Diprosone***® (Westwood Squibb) | **Aerosol spray:** 0.1%<br>**Ointment:** 0.05%<br>**Cream:** 0.05%<br>**Lotion:** 0.05% | Rx | Spray: isopropyl alcohol, mineral oil. 85 g<br>Ointment: isopropyl alcohol. 20 mL, 60 mL<br>Cream: propylene glycol. 15 g, 45 g<br>Lotion: isopropyl alcohol. 30 mL, 75 mL |
| **Clotrimazole & Betamethasone Dipropionate** (Fougera)<br>***Lotrisone***® (Schering-Plough) | **Cream:** Betamethasone dipropionate 0.05% Clotrimazole 1%<br>**Lotion:** Betamethasone dipropionate 0.05% Clotrimazole 1% | Rx | Clotrimazole & Betamethasone Dipropionate is available in sizes 15 g and 45 g tb<br>*Lotrisone*® is available in 30 mL tb |

## Hydrocortisone

### INDICATIONS

Considered a low-potency topical corticosteroid, hydrocortisone may be useful for adjunctive treatment of localized pruritic and/or inflammatory conditions. Because risks associated with hydrocortisone are significantly less when compared to higher-potency corticosteroids, hydrocortisone is a reasonable first choice, particularly when treating large areas, or when using on smaller patients. Some products also contain other ingredients, which may have additional antipruritic effects.

### MECHANISM OF ACTION

Corticosteroids are non-specific anti-inflammatory agents. Amongst their various mechanisms of action, corticosteroids induce annexin I (i.e. phospholipase A2-alpha inhibitory protein) in cells, thereby blocking the release of arachidonic acid and its subsequent conversion to eicosanoids (i.e., leukotrienes, prostaglandins, prostacyclins, and thromboxanes). They also inhibit the synthesis of various inflammatory cytokines (e.g., IL-1, TNF-alpha) by inhibiting the pro-inflammatory transcription factor, NF-kB. Moreover, corticosteroids reduce DNA synthesis via an antimitotic effect on epidermal cells. Topically applied

corticosteroids also inhibit the migration of leukocytes and macrophages to the area, reducing erythema, pruritus, and edema.

### SUGGESTED USES/DOSAGES

Initially, topical corticosteroids are usually used sparingly 1–2 times per day, then tapered to less frequent use. Do not allow the animal to lick or chew at treated sites for at least 20–30 minutes after application, to prevent ingestion and allow the medication to work. Hydrocortisone formulations are best suited for focal (e.g., pedal) or multifocal lesions and for relatively short durations. However, clinicians must tailor the frequency and duration of application to the severity of clinical signs, being mindful of the potential side effects associated with frequent and prolonged use. If shampoo or conditioner: daily to weekly baths/after baths according to veterinarian's recommendations. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well. For veterinary-labeled products, refer to individual product labeling for specific dosing/frequency recommendations.

### PRECAUTIONS/ADVERSE EFFECTS

Several veterinary topical products list tuberculosis of the skin and pregnancy as contraindications. Although systemic absorption is rare with topical hydrocortisone, long-term use may lead to hypothalamic–pituitary–adrenal axis suppression. Increased risks of systemic corticosteroid effects (e.g., polydipsia/polyuria, Cushing's disease, gastrointestinal signs), cutaneous atrophy that can be associated with skin fragility, superficial follicular cysts (milia), and comedones may occur as product concentration and duration of use increase. Local skin reactions (burning, itching, redness) are possible but unlikely. Risks can be reduced by treating for only as long as necessary on as small an area as possible. Clients should wash hands after application or wear gloves when applying Avoid contact with eyes. At least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing.

### VETERINARY-LABELED HYDROCORTISONE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Corticalm Lotion®*** (TEVA/DVM) | **Lotion:** 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 6 oz |
| ***Sulfodene HC Anti-Itch Lotion®*** (Farnam) | **Lotion:** 0.5% | OTC | Labeled for dogs and cats. 1.5 oz |
| ***Zymox Topical Cream®*** (PKB Animal Health) | **Cream:** Hydrocortisone 1% Active bio-enzymes: lactoperoxidase, lysozyme, lactoferrin | Sold only through licensed veterinarians | Labeled for dogs and cats. 1 oz |

## VETERINARY-LABELED HYDROCORTISONE TOPICAL PRODUCTS
(continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Malacetic HC Wipes®*** (Dechra) | **Wipes:** Hydrocortisone 1% Acetic acid 1% Boric acid 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 25 count jar |
| ***Relief® HC Spray*** (TEVA/DVM) | **Spray:** Hydrocortisone 1% Pramoxine 1% | Sold only through licensed veterinarians | Colloidal oatmeal. Labeled for dogs and cats. 8 oz |
| ***Pramosoothe HC® Spray*** (Sogeval) ***Pramoderm HC® Spray*** (Butler) | **Spray:** Hydrocortisone 1% Pramoxine 1% | Sold only through licensed veterinarians | Coloidal oatmeal, essential fatty acids. Labeled for dogs and cats. 8 oz |
| ***CortiSpray®*** (TEVA/DVM) | **Spray:** 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 2 oz |
| ***Dermacool HC Spray®*** (Virbac) | **Spray:** 1% | Rx | Colloidal oatmeal, hamamelis extract, lactic acid, PCMX, propylene glycol. Labeled for dogs and cats. 2 oz, 4 oz |
| ***Hartz Hydrocortisone Spray w/Aloe®*** (Hartz) | **Spray:** 0.5% | OTC | Aloe. Labeled for dogs and cats. 5 oz |
| ***Zymox Topical Spray®*** (PKB Animal Health) | **Spray:** Hydrocortisone 1% Active bio-enzymes: lactoperoxidase, lysozyme, lactoferrin | Sold only through licensed veterinarians | Labeled for dogs and cats. 2 oz |
| ***Malacetic Ultra Spray®*** (Dechra) | **Spray:** Hydrocortisone 1% Ketoconazole 0.15% Acetic acid 1% Boric acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |

## VETERINARY-LABELED HYDROCORTISONE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Cort/Astrin Solution®*** (Vedco) | **Solution:** Hydrocortisone 1% Burow's solution 2% | OTC | Propylene glycol base. Labeled for dogs and cats, 1 oz dropper btl, 16 oz |
| ***Corti-Derm Solution®*** (First Priority) | **Solution:** Hydrocortisone 1% Burow's solution 2% | OTC | Propylene glycol base. Labeled for dogs. 1 oz |
| ***Hydro-Plus®*** (Phoenix) ***Bur-O-Cort 2:1®*** (Q.A. Labs) ***Hydro-B 1020®*** (Butler) | **Solution:** Hydrocortisone 1% Burow's solution 2% | OTC | Propylene glycol base. Labeled for dogs. 1 oz, 2 oz, 16 oz |
| ***Cortisoothe Shampoo®*** (Virbac) | **Shampoo:** Hydrocortisone 1% Colloidal oatmeal 1% | Rx | Labeled for dogs and cats. 8 oz, 16 oz |
| ***Chlorhexidine® 4% HC Shampoo*** (Sogeval) | **Shampoo:** Hydrocortisone 1% Chlorhexidine 4% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz |
| ***Malacetic Ultra Shampoo®*** (Dechra) | **Shampoo:** Hydrocortisone 1% Ketoconazole 0.15% Acetic acid 1% Boric acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Resicort Leave-On Lotion®*** (Virbac) | **Lotion:** 1% | Rx | *Spherulite®* microcapsules, chitosanide. Labeled for dogs and cats. 8 oz, 16 oz |

### HUMAN-LABELED HYDROCORTISONE TOPICAL PRODUCTS

Partial listing. There are many brand products available with hydrocortisone; these are listed only when they have relatively unique formulations and concentrations. For more information on human-labeled hydrocortisone products, refer to a comprehensive human drug reference (e.g., *Facts and Comparisons* or *Micromedex*) or contact a pharmacist.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Hydrocortisone** (various generics) | **Ointment:** 0.5, 1% – 15 g, 20 g, 28.4 g, 30 g, 60 g, 120 g, 454 g | OTC/Rx (status determined by labeling) | 15 g, 20 g, 28.4 g, 30 g, 60 g, 120 g, 454 g |
| | **Ointment:** 2.5% – 20 g, 30 g | | 20 g, 30 g |
| | **Cream:** 0.5, 1%–1 g pkts, 15 g, 20 g, 28.4 g, 30 g, 60 g, 120 g, 454 g | | 1 g pkt, 15 g, 20 g, 28.4 g, 30 g, 60 g, 120 g, 454 g |
| | **Cream:** 2.5%–15 g, 20 g, 30 g, 60 g, 240 g, 454 g | | 15 g, 20 g, 30 g, 60 g, 240 g, 454 g |
| | **Lotion:** 0.5, 1%–30 mL, 60 mL, 120 mL | | 30 mL, 60 mL, 120 mL |
| | **Lotion:** 2.5%–60 mL, 120mL | | 60 mL, 120 mL |
| ***Alcortin A®*** (Primus) | **Gel:** 2% | Rx | Iodoquinol (provides antimicrobial effect), aloe. 2 g |
| ***Texacort®*** (JSJ) | **Solution:** 1%, 2.5% | Rx | 30 mL |
| ***Penecort®*** (Allergan) | **Solution:** 1%<br>**Cream:** 1%<br>**Gel:** 1% | Rx | 30 mL, 60 mL<br>30 g, 60 g<br>30 g, 60 g |
| ***Scalpicin®*** (Combe) | **Liquid:** 1% | OTC | Aloe, propylene glycol, menthol, alcohol, coneflower extract, tea tree oil. 45 mL, 75 mL |

**HUMAN-LABELED HYDROCORTISONE TOPICAL PRODUCTS**
(continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***T/Scalp®*** (Neutrogena) | **Liquid:** 1% | OTC | 60 mL, 600 mL |
| ***Proctor®*** (Roberts) | **Spray:** 1% | OTC | 45 mL |
| ***Cortizone-10 Quick shot®*** (Pfizer) | **Spray:** 1% | OTC | 44 mL |
| ***Maximum Strength Cortaid®*** (Pharmacia Upjohn) | **Pump spray:** 1% | OTC | 45 mL |

## Hydrocortisone aceponate

*Hydrocortisone aceponate is not currently available in the US. It is available in EU.*
*For **otic** use, refer to the Otic section.*

### INDICATIONS

Hydrocortisone aceponate (HCA) is labeled for symptomatic treatment of various inflammatory and/or pruritic dermatoses in dogs. A pilot study showed that HCA may be a good treatment option for pedal dermatitis in atopic dogs (Bryden *et al*. 2008). Moreover, a placebo-controlled study showed that HCA was an effective treatment for canine atopic dermatitis, with clinical response occurring within 14–28 days (Nuttall *et al*. 2009). Another recent randomized single-blinded controlled study showed that HCA spray and oral cyclosporine were equally effective for the treatment of canine atopic dermatitis for the 84-day study duration (Nuttall *et al*. 2011). A controlled clinical trial conducted in dogs with experimentally induced flea-allergy dermatitis showed a potential benefit for this condition (Bonneau *et al*. 2009). Anecdotal reports also suggest potential benefit for canine pyotraumatic dermatitis.

More recently, a small open-label pilot study showed that HCA appears to be effective (with significant improvement in clinical lesions and pruritus) and safe for the management of presumed feline allergic dermatitis, including cases of eosinophilic granuloma complex, although it is not licensed for use in cats (Schmidt *et al*. 2011).

## MECHANISM OF ACTION

HCA, a diester glucocorticoid, is a pro-drug that is biotransformed in the epidermis to its active form, hydrocortisone-17-propionate. Diester glucocorticoids have minimal suppression of IL-1 and IL-6 on dermal fibroblasts but marked suppression of epidermal IL-1. Diesters are also very lipophilic, so penetrate the subcutaneous tissue well. In addition, it is metabolized entirely in the skin, and is not absorbed into the systemic circulation, thus sparing the hypothalamic–pituitary–adrenal axis.

## SUGGESTED USES/DOSAGES

The recommended dosage is 1.52 mcg of HCA per $cm^2$ of affected skin per day. This dosage can be achieved with two pump sprays 10 cm away from the area to be treated equivalent to a square of 10 cm × 10 cm (e.g., palm-sized area of skin). Total area treated should not exceed one-third of the body surface. No massage is required after application. Labeled to be applied once daily for 7 consecutive days, but clinicians must tailor the frequency and duration of application to the severity of clinical signs, being mindful of potential side effects. A 70-day placebo-controlled study in canine atopic dermatitis showed that the frequency of application necessary to maintain the disease under control varied from daily (3/21 dogs), to every other day (7/21 dogs), or twice weekly (6/21 dogs) (Nuttall *et al*. 2009). Some of the dogs (5/21 dogs) received additional therapy. The same study also showed that clinical signs may improve in 14 days, but full clinical remission may be seen only around 28 days. Coat length did not appear to influence the response to treatment. In a pilot study in cats with presumed allergic dermatitis, the cats received two sprays per 100 $cm^2$ of affected skin once daily for 28–42 days (Schmidt *et al*. 2011). It was possible to reduce the frequency of application to every other day, but not further. Most of the clinical improvement reported was evident in 14 days, but full clinical remission occurred around 28 days.

## PRECAUTIONS/ADVERSE EFFECTS

Do not use on cutaneous ulcers. In the case of concurrent microbial disease or parasitic infestation, the dog should receive appropriate treatment for such conditions. HCA is reported to be well tolerated in dogs. Tolerance studies using 3 and 5 times the recommended dosage for twice the recommended treatment duration resulted in a reduced capacity for production of cortisol that is fully reversible within 7–9 weeks after the end of treatment. Systemic absorption appears to be negligible. A placebo-controlled study in canine atopic dermatitis showed that HCA was safe when used once daily during the 70-day study duration, despite not being licensed for long-term treatment (Nuttall *et al*. 2009). One study showed no local cutaneous reactions or histopathological changes with daily applications of HCA for over 2 months in healthy beagle dogs (Rème and Dufour 2010); however, another study in atopic Maltese-beagle dogs showed a significant decrease in dermal thickness at treated sites after 14 days of daily therapy (Bizikova *et al*. 2010). Care should be taken to avoid spraying into the eyes of the animal or the person applying the product.

The safety of this product has not been established during pregnancy and lactation. In the absence of information, it is recommended not to apply other topical preparations simultaneously on the treated lesions.

At least a 2-week withdrawal period has been proposed for HCA prior to intradermal testing (Bizikova *et al*. 2010). The effect of HCA on allergy serum test results is currently unknown. HCA is a flammable product (keep treated animals away from fires, other sources of heat, and surfaces likely to be affected by the excipient propylene glycol methyl ether) for at least 30 minutes following spraying or until the hair is totally dry.

### VETERINARY-LABELED HYDROCORTISONE ACEPONATE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Cortavance***® (Virbac) | **Spray:** 0.584 mg/mL | Rx (not available in US; available in EU) | Propylene glycol methyl ether (volatile carrier). Labeled for dogs. 76 mL btl |
| ***Easotic***® (Virbac) | **Suspension (otic):** Hydrocortisone aceponate 1.11 mg/mL Gentamicin sulfate 1505 IU/mL Miconazole nitrate 15.1 mg/mL | Rx (not available in US; available in EU) | Oily suspension. Paraffin. Labeled for otic use in dogs. May be used extra-label to treat skin infections (e.g., bacterial and/or *Malassezia* dermatitis) associated with inflammation in dogs and cats. 10 mL |

### HUMAN-LABELED HYDROCORTISONE ACEPONATE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Size(s) |
|---|---|---|---|
| ***Efficort Cream***® (Galderma) ***Efficort Lipocream***® (Galderma) | **Cream:** 0.127% | Rx (not available in US; available in EU) | 30 g |

## Isoflupredone Acetate

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Considered a high-potency topical corticosteroid, isoflupredone in combination with neomycin and tetracaine may be useful for adjunctive topical treatment of localized skin or otic pruritic or inflammatory conditions that may be associated with bacterial infection and pain. Because risks associated with isoflupredone (suppression of the hypothalamic–pituitary–adrenal axis, systemic corticosteroid effects, skin atrophy) are greater than with hydrocortisone, these products are generally reserved for more severe localized pruritic and/or inflammatory conditions or when hydrocortisone is not effective. All veterinary products (*Tritop® Ointment* and *Neo-Predef w/Tetracaine Powder®*) have labeled indications that include conditions associated with neomycin-susceptible organisms and/or allergy, or as a superficial dressing applied to minor cuts, wounds, lacerations, abrasions, and for post-surgical pain application where reduction in pain and in inflammatory response is deemed desirable. In addition, *Tritop® Ointment* is labeled for acute (and possibly chronic) otitis externa, acute moist dermatitis, and anal sac inflammation/infection, and Neo-*Predef w/ Tetracaine Powder®* for acute otitis externa, acute moist dermatitis, and interdigital dermatitis in dogs and cats.

### MECHANISM OF ACTION

Corticosteroids are non-specific anti-inflammatory agents. Amongst their various mechanisms of action, corticosteroids induce annexin I (i.e., phospholipase A2-alpha inhibitory protein) in cells, thereby, block the release of arachidonic acid and its subsequent conversion to eicosanoids (i.e., leukotrienes, prostaglandins, prostacyclins, and thromboxanes). They also inhibit the synthesis of various inflammatory cytokines (e.g., IL-1, TNF-alpha) by inhibiting the pro-inflammatory transcription factor, NF-kB. Moreover, corticosteroids reduce DNA synthesis via an antimitotic effect on epidermal cells. Topically applied corticosteroids also inhibit the migration of leukocytes and macrophages to the area, reducing erythema, pruritus, and edema.

### SUGGESTED USES/DOSAGES

Labeled dose for *Tritop®* when used on skin or mucous membranes surfaces is: cleanse area, apply a small amount, and spread and rub in gently. Involved area may be treated 1–3 times daily and continued in accordance with clinical response. Labeled dose for *Neo-Predef w/Tetracaine Powder®* is: cleanse area, apply by compressing bottle with short, sharp squeezes; once daily application usually sufficient, but may use 1–3 times as required. It is important to closely monitor for side effects that may develop when using glucocorticoid-containing products frequently and for long periods of time. Do not allow the animal to lick or chew at treated sites for at least 20–30 minutes after application, to prevent ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Several veterinary topical products containing corticosteroids list tuberculosis of the skin and pregnancy as a contraindication. Use care when treating large areas or when using on small patients. Risks can be reduced by treating for only as

long as necessary on as small an area as possible. Hypothalamic–pituitary–adrenal axis suppression, systemic corticosteroid effects (polydipsia/polyuria, Cushing's disease, gastrointestinal signs), cutaneous atrophy that can be associated with skin fragility, alopecia, localized pyoderma, superficial follicular cysts (milia), and comedones may occur with long-term, frequent use. Local skin reactions (burning, itching, redness) are possible but unlikely. Hypersensitivity reactions to neomycin and/or tetracaine are possible. Clients should wash hands after application or wear gloves when applying. Avoid contact with eyes. Isoflupredone may delay wound healing, particularly if used for longer than 7 days. At least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing.

#### VETERINARY-LABELED ISOFLUPREDONE ACETATE TOPICAL PRODUCTS

At the time of writing, there were no veterinary-labeled sole active ingredient isoflupredone acetate products in the US.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Tritop***® (Pharmacia & Upjohn) | **Ointment:** Isoflupredone acetate 0.1% Neomycin sulfate 0.5% Tetracaine hydrochloride 0.5% | Rx | Labeled for dogs and cats. 10 g tb |
| ***Neo-Predef w/Tetracaine Powder***® (Pharmacia & Upjohn) | **Powder:** Isoflupredone acetate 0.1% Neomycin sulfate 0.5% Tetracaine hydrochloride 0.5% | Rx | Myristyl-gamma-picolinium chloride (germicidal surfactant) 0.2 mg/g. Store in dry place, do not allow tip of bottle to contact moisture. Labeled for dogs and cats. Also labeled for ears. 15 g plastic insufflator btl |

#### HUMAN-LABELED ISOFLUPREDONE ACETATE TOPICAL PRODUCTS

None.

## Mometasone Furoate Monohydrate

*For **otic** use, refer to the Otic section.*

#### INDICATIONS

Considered a high-potency topical corticosteroid, mometasone furoate monohydrate may be useful for adjunctive treatment of pruritic and/or inflammatory

conditions that are associated with bacterial and/or yeast skin infections (mometasone and antimicrobial combination). Because risks associated with mometasone (e.g., suppression of the hypothalamic–pituitary–adrenal axis, Cushing's disease, skin atrophy) are greater than with hydrocortisone, mometasone-containing products are generally reserved for more severe pruritic conditions or when hydrocortisone is not effective. Mometasone is present in two veterinary-labeled suspensions for otic use in dogs (*Mometamax*® and *Posatex*®) in combination with an antibiotic and an antifungal. These medications can also be used extra-label for yeast and/or bacterial skin infections sensitive to the antimicrobials included, when a strong anti-inflammatory effect is also needed.

### MECHANISM OF ACTION

Corticosteroids are non-specific anti-inflammatory agents. Amongst their various mechanisms of action, corticosteroids induce annexin I (i.e. phospholipase A2-alpha inhibitory protein) in cells, thereby blocking the release of arachidonic acid and its subsequent conversion to eicosanoids (i.e., leukotrienes, prostaglandins, prostacyclins, and thromboxanes). They also inhibit the synthesis of various inflammatory cytokines (e.g., IL-1, TNF-alpha) by inhibiting the pro-inflammatory transcription factor, NF-kB. Moreover, corticosteroids reduce DNA synthesis via an antimitotic effect on epidermal cells. Topically applied corticosteroids also inhibit the migration of leukocytes and macrophages to the area, reducing erythema, pruritus, and edema.

### SUGGESTED USES/DOSAGES

Initially, topical corticosteroids are usually used 1–2 times per day, then tapered to less frequent use. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. Mometasone formulations are best suited for focal (e.g., pedal) or multifocal lesions and for relatively short durations. However, clinicians must tailor the frequency and duration of application to the severity of clinical signs, being always mindful of the potential side effects associated with frequent and prolonged use. For veterinary-labeled products, refer to individual product labeling for specific dosing and frequency recommendations.

### PRECAUTIONS/ADVERSE EFFECTS

Several veterinary topical products list tuberculosis of the skin and pregnancy as a contraindication. Use care when treating large areas, or when using on small patients. Risks can be reduced by treating for only as long as necessary on as small an area as possible. Increased risks of hypothalamic–pituitary–adrenal axis suppression, systemic corticosteroid effects (polydipsia/polyuria, Cushing's disease, gastrointestinal signs), cutaneous atrophy that can be associated with skin fragility, alopecia, localized pyoderma, superficial follicular cysts (milia), and comedones occur as product concentration and duration of use increase. Local skin reactions (burning, itching, redness) are possible but unlikely. Mometasone may delay wound healing, particularly if used for longer than 7 days. Clients should wash hands after application or wear gloves when applying. Avoid contact with eyes. At least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing. Use caution if recommending these medications empirically, because of possible bacterial resistance to gentamicin and orbifloxacin.

## VETERINARY-LABELED MOMETASONE FUROATE MONOHYDRATE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Mometamax® Otic Suspension*** (Intervet/ Schering-Plough) | **Suspension (otic):** Mometasone 1 mg Gentamicin 3 mg Clotrimazole 10 mg | Rx | Mineral-oil based. Approved for otic use (once daily) in dogs. Extra-label use in dogs and cats with localized inflamed and/or infected cutaneous lesions, e.g., bacterial skin lesions or *Malassezia* dermatitis. 7.5 g, 15 g, 30 g, 215 g tb |
| ***Posatex® Otic Suspension*** (Intervet/ Schering-Plough) | **Suspension (otic):** Mometasone 0.1% Posaconazole 0.1% Orbifloxacin 1% | Rx | Approved for otic use (once daily) in dogs. Extra-label use in dogs and cats with localized inflamed and/or infected cutaneous lesions, e.g., bacterial skin lesions or *Malassezia* dermatitis. 7.5 g, 15 g, 30 g |

## HUMAN-LABELED MOMETASONE FUROATE MONOHYDRATE TOPICAL PRODUCTS

Partial listing. For more information on human-labeled mometasone-containing products, refer to a comprehensive human drug reference (e.g., *Facts and Comparisons* or *Micromedex*) or contact a pharmacist.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Mometasone Furoate** (generic) ***Elocon®*** (Schering-Plough) | **Cream, ointment and lotion**: 0.1% | Rx | Cream: stearyl alcohol. 15 g, 45 g Ointment: 15 g, 45 g Lotion: propylene glycol, isopropyl alcohol. 30 mL, 60 mL |
| ***Nasonex®*** (Schering-Plough) | **Nasal spray:** 50 mcg/100 mg suspension | Rx | Glycerin, citric acid. 17 g btl |

## Triamcinolone Acetonide

*For **systemic** use, refer to Section 1: Systemic Drugs.*
*For **otic** use, refer to the Otic section.*

### INDICATIONS

Considered a medium-potency topical corticosteroid when used at concentrations <0.5%, triamcinolone acetonide may be useful for adjunctive treatment of pruritic and/or inflammatory conditions. Because risks associated with triamcinolone (e.g., suppression of the hypothalamic–pituitary–adrenal axis, skin atrophy) are greater than with hydrocortisone, triamcinolone acetonide products should be reserved for more severe pruritic/inflammatory conditions or when hydrocortisone is not effective. Triamcinolone can be found as sole agent in a veterinary-labeled cream (*Medalone®*) or spray (*Genesis®*). It is also available in combination with antibiotics and anti-yeast ingredients in several veterinary products (e.g., *Panolog®*) particularly labeled for otic use; however, these products can be used extra-label to treat bacterial and yeast skin infections including pododermatitis and anal sac disease caused by bacteria and fungal/yeast sensitive to gentamicin and nystatin, when a strong anti-inflammatory effect is also needed.

### MECHANISM OF ACTION

Corticosteroids are non-specific anti-inflammatory agents. Amongst their various mechanisms of action, corticosteroids induce annexin I (i.e. phospholipase A2-alpha inhibitory protein) in cells, thereby blocking the release of arachidonic acid and its subsequent conversion to eicosanoids (i.e., leukotrienes, prostaglandins, prostacyclins, and thromboxanes). They also inhibit the synthesis of various inflammatory cytokines (e.g., IL-1, TNF-alpha) by inhibiting the pro-inflammatory transcription factor, NF-kB. Moreover, corticosteroids reduce DNA synthesis via an antimitotic effect on epidermal cells. Topically applied corticosteroids also inhibit the migration of leukocytes and macrophages to the area, reducing erythema, pruritus, and edema.

### SUGGESTED USES/DOSAGES

Initially, topical corticosteroids are usually used sparingly 1–2 times per day, then tapered to less frequent use. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. Triamcinolone formulations are best suited for focal (e.g., pedal) or multifocal lesions and for relatively short durations. However, clinicians must tailor the frequency and duration of application to the severity of clinical signs, being always mindful of the potential side effects that may occur with frequent and prolonged use. For veterinary-labeled products, refer to individual product labeling for specific dosing and frequency recommendations.

### PRECAUTIONS/ADVERSE EFFECTS

Several veterinary topical products list tuberculosis of the skin and pregnancy as a contraindication. Use care when treating large areas, or when using on small patients. Risks can be reduced by treating for only as long as necessary on as small an area as possible. Increased risks of hypothalamic–pituitary–adrenal axis suppression, systemic corticosteroid effects (polydipsia/polyuria, Cushing's disease, gastrointestinal signs), cutaneous atrophy that may be associated with

skin fragility, alopecia, localized pyoderma, superficial follicular cysts (milia), and comedones occur as product concentration and duration of use increase. Local skin reactions (burning, itching, redness) are possible but unlikely. Triamcinolone may delay wound healing, particularly if used for longer than 7 days.

Because the veterinary products contain polyethylene glycol, nephrotoxicity may potentially develop if they are used on extensive areas associated with eroded/ulcerated skin surfaces. Anecdotally, very rarely, renal toxicity has been reported. Should use caution in conditions where absorption of large quantities of polyethylene glycol is possible, especially if there is evidence of renal impairment. Clients should wash hands after application or wear gloves when applying. Avoid contact with eyes. At least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing. Use caution if recommending empirically the products also containing an antibiotic, because of possible bacterial resistance.

### VETERINARY-LABELED TRIAMCINOLONE ACETONIDE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Medalone Cream®*** (Med-Pharmex) | **Cream:** 0.1% | Rx | Polyethylene glycol. Labeled for dogs. Indications include allergic dermatitis and summer eczema. Bacterial skin infection needs to be resolved prior to use or treated concurrently. 7.5 g, 15 g tb |
| ***Genesis Spray®*** (Virbac) | **Spray:** 0.015% | Rx | Propylene glycol, denatured alcohol. Approved for dogs. Indicated for control of pruritus associated with allergic dermatitis. Bacterial skin infection needs to be resolved prior to use. Should be administered twice daily for 7 days, once daily for the next 7 days, then every other day for an additional 14 days (28 days total). Strongly recommend referring to the package insert information for maximum allowable dosages, etc. 8 oz, 16 oz btl |

## VETERINARY-LABELED TRIAMCINOLONE ACETONIDE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Panolog Cream®*** (Fort Dodge) ***Cortalone Cream®*** (Vedco) ***Derma-Vet Cream®*** (Med-Pharmex) ***Animax Cream®*** (Dechra) | **Cream:** Triamcinolone 1 mg Nystatin 100,000 units Neomycin sulfate 2.5 mg Thiostrepton 2500 units | Rx or sold only through licensed veterinarians | Cetearyl alcohol and propylene glycol (*Panolog®* and *Cortalone®*). Cetearyl alcohol and polyethylene glycol (*Derma-Vet Cream®*). Alcohol ether, propylene glycol (*Animax®*). Provides four basic therapeutic effects: anti-inflammatory, antipruritic, antifungal and antibacterial. *Panolog®*, *Derma-Vet®* and *Animax®* labeled for dogs and cats. *Cortalone®* is labeled for dogs only. 7.5 g, 15 g tb |
| ***Panolog Ointment®*** (Fort Dodge) ***Animax Ointment®*** (Dechra) ***Quadritop Ointment®*** (Butler) ***Derma-Vet Ointment®*** (Med-Pharmex) ***Dermalog Ointment®*** (RXV) ***Dermalone Ointment®*** (Vedco) ***Entederm Ointment®*** (VetOne) | **Ointment:** Triamcinolone 1 mg Nystatin 100,000 units/g Neomycin sulfate 2.5 mg Thiostrepton 2500 units | Rx or sold only through licensed veterinarians | Polyethylene glycol. Labeled for dogs and cats. Also approved for otic use in dogs and cats. Depending on product: 7.5 mL, 15 mL, 30 mL, 240 mL tb |

### HUMAN-LABELED TRIAMCINOLONE ACETONIDE TOPICAL PRODUCTS

Partial listing. There are several topical brand products containing triamcinolone (two common trade names are *Aristocort*® and *Kenalog*®). For more information on human-labeled triamcinolone products, refer to a comprehensive human drug reference (e.g., *Facts and Comparisons* or *Micromedex*) or contact a pharmacist.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Triamcinolone Acetonide** (generic) | **Ointment:** 0.025, 0.1, 0.5%<br><br>**Cream:** 0.025, 0.1, 0.5%<br><br>**Lotion:** 0.025, 0.1% | Rx | 15 g, 20 g, 28.4 g, 30 g, 60 g, 120 g, 454 g<br>15 g, 20 g, 30 g, 60 g, 120 g, 240 g, 454 g<br>15 mL, 60 mL |
| ***Kenalog***® (Westwood Squibb) | **Aerosol spray:** 0.2% | Rx | 10.3% alcohol. 23 g, 63 g |
| **Nystatin-Triamcinolone Acetonide** (various)<br>***Mycogen II***® (Goldline)<br>***Mycolog-II***® (Bristol Meyers Squibb)<br>***Myco-Triacet II***® (Lemmon)<br>***Myconel***® (Marnel)<br>***Myco-Biotic II***® (Moore) | **Cream/ointment:** Triamcinolone 0.1% Nystatin 100,000 units/g | Rx | Depending on product: 1 g, 1.5 g, 15 g, 30 g, 60 g, 100 g, 120 g, 454 g |

## NON-CORTICOSTEROIDS

## Essential Fatty Acids

*For **systemic** use, refer to Section 1: Systemic Drugs.*

### INDICATIONS

Essential fatty acids are indicated primarily as adjunctive therapy for pruritic and inflammatory conditions such as atopic dermatitis and sebaceous adenitis, and keratinization disorders such as seborrhea. They may also be used to improve

coat quality and ameliorate dry skin. Some of these products may contain other active ingredients, including other natural oils.

### MECHANISM OF ACTION

The exact mechanism of action of essential fatty acids is not well known. However, by competing with arachidonic acid for the enzymes lipoxygenase and cyclooxygenase, they decrease the synthesis of inflammatory leukotrienes and prostaglandins in the body, thereby potentially reducing inflammation and pruritus.

### SUGGESTED USES/DOSAGES

If using spray: up to 2–3 applications a day or as needed. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to allow the medication to work. If spot-on: treatment may vary from weekly to every 2 weeks or monthly. If shampoo or conditioner: daily to weekly baths/after baths or according to the veterinarian's recommendations. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well. Refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

No specific precautions or adverse effects were located for these products.

### VETERINARY-LABELED ESSENTIAL FATTY ACIDS TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Dermoscent® Atop7*** (Aventix Animal Dermo-Care) | **Spray:** *Capparis spinosa* extract, essential fatty acids from hamp and neen, essential oils of cajputi and melaleuca | Sold only through licensed veterinarians | 100% natural ingredients. Indicated for itchy or allergy prone skin. May be used once or several times a day. Labeled for dogs. 75 mL |
| ***Dermoscent® Cicafolia*** (Aventix Animal Dermo-Care) | **Spray:** Cajputi essential oil and Amazonian *Croton lechleri* sap extract, peptids, Margosa's essential fatty acids, gamma oryzanol and silicon | Sold only through licensed veterinarians | 100% natural ingredients. Indicated for pruritus, irritations, superficial lesions, first-degree burns and for post-surgical use. It also has antiseptic and barrier-restoring properties. May be used as needed. Labeled for dogs and cats. 30 mL |

**VETERINARY-LABELED ESSENTIAL FATTY ACIDS TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***HyLyt® EFA Bath Oil*** (TEVA/DVM) | **Spray:** Omega 6 fatty acids (safflower oil) | Sold only through licensed veterinarians | Sodium lactate, mineral oil, diazolidinyl urea, lanolin oil, parabens. Labeled for dogs and cats. 8 oz |
| ***Dermoscent® Essential 6 Spot-On*** (Aventix Animal Dermo-Care) | **Spot-on:** Essential oils of rosemary, lavender, melaleuca, cedar, oregano, essential fatty acids from hemp grain and neem, vitamin E | Sold only through licensed veterinarians | 100% natural ingredients. Smoothing and purifying agents, bio-diffusing vector. Indicated for mild pruritus. Also has antimicrobial, sebo-regulating, deodorizing and barrier restoring properties. Directions: 1 pipette every week for an initial treatment of 2 consecutive months followed by a regular and continuous treatment at one pipette every 2 weeks. Labeled for dogs and cats<br>Cats: 4 pipettes of 0.4 mL<br>Dogs 0–10 kg: 4 pipettes of 0.6 mL<br>Dogs 10–20 kg: 4 pipettes of 1.2 mL<br>Dogs 20–40 kg: 4 pipettes of 2.4 mL |
| ***Dermoscent® Essential Mousse*** (Aventix Animal Dermo-Care) | **Mousse:** Oils and polyunsatured fatty acids as well as soothing Cucurbitine® | Sold only through licensed veterinarians | 100% natural ingredients. Soap free. Indicated as a mild antipruritic, as well as an antiseptic, deodorizing and skin barrier-restoring. Labeled for dogs and cats. 150 mL |

## VETERINARY-LABELED ESSENTIAL FATTY ACIDS TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***HyLyt® EFA Shampoo*** (TEVA/DVM) | **Shampoo:** Omega 6 fatty acids (safflower oil) | Sold only through licensed veterinarians | Sodium lactate, sodium chloride, lanolin, glycerin, hydrolyzed collagen. Soap free. Labeled for dogs and cats. 8 oz, 12 oz, 1 gal |
| ***Dermoscent® EFA Treatment Shampoo*** (Aventix Animal Dermo-Care) | **Shampoo:** Essential fatty acids from hemp grain, cucurbitine (lichen plant extract), Niaouli essential oil | Sold only through licensed veterinarians | 100% natural ingredients. Soap free. Indicated for mild to moderate pruritus. Labeled for dogs and cats. 200 mL |
| ***DermaLyte® Shampoo*** (Dechra) | **Shampoo:** Omega 6 fatty acids Vitamin E Coconut oil | Sold only through licensed veterinarians | 100% natural ingredients. Soap free. Indicated for dogs and cats with sensitive skin. May help reduce itching. 1 oz pouch, 12 oz, 1 gal |
| ***Hyliderm® Shampoo*** (Sogeval) | **Shampoo:** Omega 6 fatty acids | Sold only through licensed veterinarians | Soap-free. Labeled for dogs and cats. 2 oz, 8 oz, 16 oz, 1 gal |
| ***Allermyl® Shampoo*** (Virbac) | **Shampoo:** Omega 6 fatty acids (linoleic acid) Ceramides 1, 3, 6 Cholesterol | Sold only through licensed veterinarians | Glycotechnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside) minimizes microbial colonization. Fragrance free. Indicated for control of pruritus, specifically labeled for management of allergic skin conditions in dogs and cats. Also has skin barrier-restoring properties. 8 oz, 16 oz |

**VETERINARY-LABELED ESSENTIAL FATTY ACIDS TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Allerderm Spot-on®*** (Virbac) | **Spot-on:** Free fatty acids, Ceramides 1, 3 and 6 Cholesterol | Sold only through licensed veterinarians | Indicated specifically for allergic dermatitis, contact allergies, keratinization disorders and chronic microbial infections. May also be used for the treatment of sebaceous adenitis. 2 mL, 4 mL |
| ***HyLyt® EFA Creme Rinse*** (TEVA/DVM) | **Creme rinse:** Omega 6 fatty acids (safflower oil) | Sold only through licensed veterinarians | Cetearyl alcohol, quaternarium-18, polysorbate 60, sodium lactate, hydrolyzed collagen, glycerin. Labeled for dogs and cats. 8 oz, 1 gal |

### HUMAN-LABELED ESSENTIAL FATTY ACIDS TOPICAL PRODUCTS

Several human OTC products containing essential fatty acids are available in the US, but they may contain other ingredients and are generally not used in dogs and cats.

## Phytosphingosine Salicyloyl

*For **other products containing phytosphingosine combined with other active ingredients**, refer to other main active ingredients in Section 2.*

### INDICATIONS

Phytosphingosine *Douxo® Calm* line is indicated for localized or generalized inflammatory skin conditions that may be associated with pruritus, including allergic diseases such as atopic dermatitis. *Douxo® Calm Gel* is also indicated as a liquid wound dressing for localized inflammation and after surgery (can be sprayed on sutures).

### MECHANISM OF ACTION

Phytosphingosine salicyloyl is a modified pro-ceramide with salicylic acid and a key molecule in the natural defense mechanism of the skin. Ceramides comprise 40–50% of the main lipids responsible for maintaining the cohesion of the stratum corneum, the skin lipid barrier controlling local flora (antibacterial and antifungal effects) and maintaining the correct moisture balance. It is also anti-inflammatory as it has anti-IL-1 activity, impairs the production of prostaglandin $E_2$ and inhibits protein kinase C.

### SUGGESTED USES/DOSAGES

If using spray or gel: up to 2–3 times a day as needed for itching relief. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to allow the medication to work. If shampoo: daily to weekly baths according to the veterinarian's recommendations. It is important to leave the shampoo in contact with the skin for at least 10 minutes prior to rinsing well. Refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Phytosphingosine-containing products are typically well tolerated. Skin redness or irritation may occur.

### VETERINARY-LABELED PHYTOSPHINGOSINE SALICYLOYL TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Douxo® Calm Gel*** (Sogeval) | **Gel:** Phytosphingosine salicyloyl 0.1% Hinokitiol 0.2% | Sold only through licensed veterinarians | Raspberry seed oil, natural tocopherol, extract of creosote bush (Larrea tridentate), glycerin, pemulen, glycofilm. Labeled for dogs and cats. 2 oz |
| ***Douxo® Calm Micro-emulsion Spray*** (Sogeval) | **Spray:** Phytosphingosine salicyloyl 0.05 % Hinokitiol 0.1% | Sold only through licensed veterinarians | Raspberry seed oil, cetearyl and cetylstearyl alcohol, castor oil, sodium cetearyl sulfate, dypropylene glycol, glycerin. Labeled for dogs and cats. 6.8 oz |
| ***Douxo® Calm Shampoo*** (Sogeval) | **Shampoo:** Phytosphingosine salicyloyl 0.05% Hinokitiol 0.1% | Sold only through licensed veterinarians | Raspberry seed oil, allantoin, lipidure C. Labeled for dogs and cats. 6.8 oz, 16.9 oz, 3 L |

### HUMAN-LABELED PHYTOSPHINGOSINE SALICYLOYL TOPICAL PRODUCTS

There are several OTC human cosmetic products containing phytosphingosine in the US. These products target mostly lipid barrier restoration and include *Epionce Extreme Barrier Cream®*, *Kronos Phyx Overnight Repair Mask®*, *Skinceuticals Age Interruptor®*, *Darphin Lipid Replenishing Soothing Balm®*.

# ANTIMICROBIALS

## ANTIBACTERIAL AGENTS

*Refer also to the **Sulfur** listing in the Antiseborrheic Agents section.*

### Acetic Acid/Boric Acid

#### INDICATIONS

Indicated for the treatment of skin infections caused by bacteria including *Staphylococcus* and *Pseudomonas* and yeast such as *Malassezia*. Also indicated for fold dermatitis, acute moist dermatitis, pododermatitis, and seborrhea. Products may contain other antimicrobials such as chlorhexidine and ketoconazole, or hydrocortisone for antipruritic effect.

#### MECHANISM OF ACTION

Acetic and boric acids have antibacterial and antifungal properties and a rapid killing effect. They also possess ceruminolytic, keratolytic, keratoplastic, and astringent activities.

#### SUGGESTED USES/DOSAGES

If using spray or wipes: up to 2–3 times a day. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo: daily to weekly baths according to the veterinarian's recommendations. It is important to leave the shampoo in contact with the skin for at least 10 minutes prior to rinsing well. Refer to product for individual label directions.

#### PRECAUTIONS/ADVERSE EFFECTS

Skin redness and irritation may occur.

#### VETERINARY-LABELED ACETIC ACID AND BORIC ACID TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Malacetic Ultra Spray®*** (Dechra) | **Spray:** Acetic acid 1% Boric acid 2% Ketoconazole 0.15% Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Malacetic Spray®*** (Dechra) | **Leave-on spray:** Acetic acid 2% Boric acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz |

## VETERINARY-LABELED ACETIC ACID AND BORIC ACID TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Mal-A-Ket Wipes®*** (Dechra) | **Wipes:** Acetic acid 2% Chlorhexidine 2% Ketoconazole 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 50 count jar |
| ***Malacetic HC Wipes®*** (Dechra) | **Wipes:** Acetic acid 1% Boric acid 1% Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 25 count jar |
| ***Malacetic Wet Wipes®*** (Dechra) | **Wipes:** Acetic acid 1% Boric acid 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. Indicated for anal sac expression, skin folds and cleaning of ears. 25 and 100 count jars and 25 count brick pack |
| ***Malacetic Shampoo®*** (Dechra) | **Shampoo:** Acetic acid 2% Boric acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 12 oz, 16 oz, 1 gal |
| ***Malacetic Ultra Shampoo®*** (Dechra) | **Shampoo:** Acetic acid 1% Boric acid 2% Ketoconazole 0.15% Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Mal-A-Ket® Shampoo*** (Dechra) | **Shampoo:** Acetic acid 2% Chlorhexidine 2% Ketoconazole 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 1 oz pouch, 8 oz, 1 gal |

## HUMAN-LABELED ACETIC ACID AND BORIC ACID TOPICAL PRODUCTS

There are several OTC human products available containing acetic acid and/or boric acid (alone or containing other ingredients). For more information on human-labeled acetic acid or boric acid products, refer to a comprehensive human drug reference (e.g., *Facts and Comparisons* or *Micromedex*) or contact a pharmacist.

## Bacitracin

### INDICATIONS

Bacitracin is labeled in humans for topical use to treat superficial skin infections caused by susceptible organisms, and to prevent infection after minor skin injuries such as dermal lacerations, scrapes, or burns. However, the authors recommend the use of bacitracin in dogs and cats only for confirmed local bacterial skin infections, as bacterial resistance may occur if it is used to prevent infection.

### MECHANISM OF ACTION

Bacitracin is a polypeptide antibiotic that acts by inhibiting cell wall synthesis of susceptible bacteria, and it is either bactericidal or bacteriostatic depending on drug concentration and bacterial susceptibility. It is active in low concentrations against Gram-positive bacteria, including *Staphylococcus* and *Streptococcus*, and some Gram-negative cocci, but Gram-negative bacilli are highly resistant. Bacitracin activity is not impaired by blood, pus, necrotic tissue, or large inocula. Bacterial resistance has been described.

### SUGGESTED USES/DOSAGES

Bacitracin may be applied 1–3 times daily and covered by a suitable dressing if needed. Use is usually not recommended for more than 1 week. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Bacitracin topical ointment labeled for skin should not be used in or around eyes, or in patients known to be hypersensitive to it. There have been anecdotal reports of cats developing fatal anaphylactic reactions after administered ophthalmic "triple" antibiotic ointments. Deep puncture wounds, animal bites, or deep cutaneous infections may require systemic antibiotic therapy. While topical administration generally results in negligible systemic levels, if used over large areas of the body or on severe burns or puncture wounds, measurable absorption and potential toxicity may occur. Bacitracin is contraindicated for the treatment of ulcerated lesions. Clients should wash hands after application or wear gloves when applying. Use caution when recommending bacitracin empirically, mainly for long-term use, because of possible bacterial resistance.

### VETERINARY-LABELED BACITRACIN TOPICAL PRODUCTS

Veterinary bacitracin formulations are not labeled specifically for dermatological use; however, ophthalmic preparations such as *Vetropolycin Ophthalmic® Ointment* (bacitracin–neomycin–polymyxin) and *Vetropolycin HC Ophthalmic® Ointment* (bacitracin–neomycin–polymyxin with hydrocortisone acetate 1%), both from Dechra Veterinary Products, are available and can be used extra-label for the treatment of ear and skin infections.

### HUMAN-LABELED BACITRACIN TOPICAL PRODUCTS

Bacitracin ointment is available alone as 500 units/g in various tube sizes. There are many OTC human products available with formulas containing bacitracin, neomycin, and polymyxin B. A well-known trade name is *Neosporin®*, or it is available generically as Triple Antibiotic Ointment. When combined with only polymyxin B, a common trade name is *Polysporin®*.

### HUMAN-LABELED BACITRACIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Bacitracin** (various generics) | **Ointment:** 500 units/g | OTC | Depending on manufacturer: white petrolatum, mineral oil. 14 g, 28 g, 120 g tb, 1 lb jar |

## Benzoyl Peroxide

### INDICATIONS

Benzoyl peroxide products are used topically as either gels or shampoos. Shampoos are generally used for oily and scaly skin (seborrhea oleosa), superficial and deep pyodermas, crusty pyodermas (such as seborrheic dermatitis/pyoderma commonly seen in cocker spaniels), and as adjunctive therapy for generalized demodicosis and schnauzer comedo syndrome. Gels may be useful for treating localized superficial and deep pyodermas, fold pyodermas, chin acne, and localized demodectic lesions.

### MECHANISM OF ACTION

Benzoyl peroxide possesses antimicrobial (especially antibacterial), keratolytic, comedolytic ("follicular flushing"), and degreasing actions. Benzoyl peroxide's antimicrobial activity is due to the formation of oxidative benzoyl peroxy radicals that disrupt cell membranes.

### SUGGESTED USES/DOSAGES

Gels are usually recommended for use once to twice daily, and shampoos once daily to weekly according to the veterinarian's recommendation. When using gel, it is important to not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. It is important to leave the shampoo in contact with the skin for at least 10 minutes prior to rinsing well. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes or mucous membranes. Clients should wash hands after application or wear gloves when applying benzoyl peroxide, as it will bleach colored fabrics, jewelry, clothing, or carpets and may bleach the patient's hair. Clients should be advised to keep treated animals away from fabrics during treatment. Benzoyl peroxide can be drying or irritating (causing erythema, pruritus, pain) in some patients, particularly at higher (>5%) concentrations. Use of emollients after bathing, using shampoos with moisturizing microvesicles, or reducing the frequency of baths may alleviate or prevent this problem. Benzoyl peroxide shampoos do not lather well.

## VETERINARY-LABELED BENZOYL PEROXIDE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Pyoben Gel®*** (Virbac) | **Gel:** 5% | Rx | Labeled for dogs and cats. For once or twice daily use after cleaning. 1 oz |
| ***Oxydex Gel®*** (TEVA/DVM) | **Gel:** 5% | Sold only through licensed veterinarians | Labeled for dogs and cats. For once or twice daily use after cleaning. Rub in well so that no residue remains. 1 oz |
| ***Micro-Pearls Advantage Benzoyl-Plus®*** (Vetoquinol) | **Shampoo:** 2.5% | Rx | *Novasome®* microvesicles. Labeled for dogs and cats. Shake well; wear gloves. May be used up to once daily as directed. 12 oz, 1 gal |
| ***Benzoyl Peroxide Shampoo®*** (Davis) | **Shampoo:** 2.5% | OTC | Labeled for dogs, cats, puppies and kittens. 12 oz, 1 gal |
| ***OxyDex Shampoo®*** (TEVA/DVM) | **Shampoo:** 2.5% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8, 12 oz, 1 gal |
| ***SulfOxyDex Shampoo®*** (TEVA/DVM) | **Shampoo:** Benzoyl peroxide 2.5% Sulfur (micronized) 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. Shake well. May be used as needed or as directed by veterinarian. 8, 12 oz, 1 gal |
| ***DermaBenSs® Shampoo*** (Dechra) | **Shampoo:** Benzoyl peroxide 2.5% Sulfur 1% Salicylic acid 1% | Sold only through licensed veterinarians | Moisturizing factors, vitamin E, coconut oil. Soap free. Labeled for dogs and cats. 12 oz, 1 gal |
| ***Pyoben Shampoo®*** (Virbac) | **Shampoo:** 3% | Rx | *Spherulite®* microcapsules, chitosanide. Labeled for dogs and cats. Use initially 2–3 times/week, then once a week or as directed. 8, 16 oz |

### VETERINARY-LABELED BENZOYL PEROXIDE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Oxiderm®*** ***Shampoo*** + ***PS*** (Sogeval) | **Shampoo:** Benzoyl peroxide 3% Sulfur (micronized) 2% Salicylic acid 2% Phytosphyngosine hydrochloride 0.05 % | Sold only through licensed veterinarians | Soap-free. Labeled for dogs and cats. 8 oz, 16 oz |
| ***Vet Solutions BPO–3®*** Shampoo (Vetoquinol) | **Shampoo:** 3% | Rx | Labeled for dogs and cats. 16 oz, 1 gal |

### HUMAN-LABELED BENZOYL PEROXIDE TOPICAL PRODUCTS

There are many human products available containing benzoyl peroxide (from 2.5% to 10% formulations). If using human products, avoid concentrations higher than 3% for shampoos or 5% for gels, as risks for skin irritation may increase. Benzoyl peroxide 5% gel can be labeled as either Rx or OTC depending on product, and it is available as generics or with the trade names *Benzac®*, *Desquam-X®*, or *PanOxyl®*.

## Clindamycin

*For **systemic** use, refer to Section 1: Systemic Drugs.*

### INDICATIONS

Topical clindamycin may be used for the treatment of feline acne or other localized skin infections caused by bacteria susceptible to clindamycin. The only available veterinary-labeled product (*ClinzGard®*) is indicated for the treatment of anal sac and tissue abscesses, puncture wounds, and surgical incisions. The authors recommend using clindamycin when other topical antibiotics (such as gentamicin) have failed and based on culture and sensitivity results, because of the potential for rapid occurrence of bacterial resistance.

### MECHANISM OF ACTION

Clindamycin inhibits bacterial protein synthesis by binding to the 50S ribosome. Its primary activity is against anaerobic and Gram-positive aerobic bacteria.

### SUGGESTED USES/DOSAGES

When used for feline acne, topical clindamycin is generally applied in a thin film once daily; however, the authors recommend twice-daily applications. *ClinzGard®* is used as a single application that has sustained release over 7–10 days. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. Must be applied to cleaned and debrided (if necessary) surfaces.

### PRECAUTIONS/ADVERSE EFFECTS

Topical clindamycin should not be used in patients with a history of hypersensitivity to clindamycin or lincomycin. Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. Contact reactions (pain, burning erythema, itching, drying, peeling) are possible. Clindamycin lotions and gels may cause less burning than the topical solutions or foams. As clindamycin can be absorbed through the skin, systemic adverse effects are possible. Antibiotic-associated diarrheas are potentially possible, but severe, life-threatening diarrheas (so-called pseudomembranous colitis) are thought to occur very rarely in animal patients and only when clindamycin is used systemically.

### VETERINARY-LABELED CLINDAMYCIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***ClinzGard*®** (TriLogic Pharma) | **Gel:** Clindamycin hydrochloride 1% | Rx | Indicated for anal sac and tissue abscesses, puncture wounds, and surgical incisions. Single dose with sustained release over 7–10 days. Must be applied to cleaned and debrided (if necessary) surfaces. Labeled for dogs and cats. Sterile single-dose syringes (box with 4 units) |

### HUMAN-LABELED CLINDAMYCIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Clindamycin Phosphate** (various generics) | **Lotion:** 1%<br>**Gel:** 1%<br>**Solution:** 1% | Rx | 30 g, 60 g<br>30 g, 60 g<br>30 mL, 60 mL |
| ***Cleocin T*®** (Pharmacia Upjohn) | **Lotion:** 1% | Rx | Cystostearyl alcohol, glycerin, methylparaben. 60 mL |
| ***Clindamax*®** (PharmaDerm) | **Lotion:** 1% | Rx | Cystostearyl alcohol, glycerin, methylparaben. 60 mL |
| ***Cleocin T*®** (Pharmacia Upjohn) | **Gel:** 1% | Rx | Methylparaben. 30 g, 60 g |
| ***Clindagel*®** (Galderma) | **Gel:** 1% | Rx | Methylparaben. 7.5 g, 42 g, 77 g |

**HUMAN-LABELED CLINDAMYCIN TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Clindamax®*** (PharmaDerm) | **Gel:** 1% | Rx | Methylparaben. 30 g, 60 g |
| ***Cleocin T®*** (Pharmacia Upjohn) | **Solution:** 1% | Rx | Isopropyl alcohol 50%. Single-use pledgets. 30 mL, 60 mL |
| ***Clindets®*** (Stiefel) | **Pledgets:** 1% | Rx | Isopropyl alcohol 52%. 1 mL pledgets |
| ***Evoclin®*** (Connetics) | **Aerosol foam:** 1% | Rx | Cetyl alcohol, ethanol 58%, stearyl alcohol, propylene glycol. 50 g |

## Fusidic Acid

*This product is not currently available in the US. It is available in EU and CA.*

### INDICATIONS

Fusidic acid is labeled for the topical treatment of surface pyoderma in dogs such as acute moist dermatitis and intertrigo (skin fold dermatitis), and it may also be used for superficial pyoderma and resistant bacterial skin infections. Fusidic acid is highly effective against *Staphylococcus pseudintermedius*, which plays a pivotal role in surface and superficial pyoderma in dogs. *Fuciderm®* contains betamethasone valerate in addition to fusidic acid, adding anti-inflammatory and antipruritic properties to the product.

### MECHANISM OF ACTION

Fusidic acid is a bacteriostatic antibiotic that belongs to a group of its own, fusidanes, and exerts an antibacterial action by interfering with bacterial protein synthesis. Fusidic acid exhibits in-vitro activity against most coagulase-positive and coagulase-negative staphylococci, beta-hemolytic streptococci, *Corynebacterium* species, and most *Clostridium* species. In addition, almost all strains of methicillin-resistant *Staphylococcus aureus* and *S. pseudintermedius* demonstrate in-vitro sensitivity to fusidic acid. Fusidic acid has the ability to penetrate both intact and damaged skin.

### SUGGESTED USES/DOSAGES

Apply to affected area(s) twice daily for 5–7 days. It may be applied longer if determined by the veterinarian. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. For veterinary-labeled products, refer to individual product labeling for specific dosing/frequency recommendations.

### PRECAUTIONS/ADVERSE EFFECTS

Prolonged treatment or treatment of large surface areas (mostly if using *Fuciderm®*) should be avoided. Discontinue use if hypersensitivity develops to the product. Local

hypersensitivity reactions to fusidic acid are uncommon and include mild stinging, skin irritation, contact dermatitis, and urticaria. Gastrointestinal side effects are possible if ingestion occurs. With products containing betamethasone (*Fuciderm*®), increased risks of hypothalamic–pituitary–adrenal axis suppression, systemic corticosteroid effects (polydipsia/polyuria, Cushing's disease, gastrointestinal signs), cutaneous atrophy that can be associated with skin fragility, superficial follicular cysts (milia), and comedones may occur as product concentration and duration of treatment increase. Betamethasone may delay wound healing, particularly if used for longer than 7 days. Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. If product contains betamethasone, at least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing. Despite the small number of reports of bacterial resistance with fusidic acid, caution should be used with inappropriate use.

### VETERINARY-LABELED FUSIDIC ACID TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Fuciderm Gel***® (Dechra) | **Gel:** Fusidic acid 0.5% Bethametasone valerate 0.1% | Sold only through licensed veterinarians (not available in US, available in EU and CA) | Labeled for dogs. Can be used extra-label in cats. 15 g, 30 g tb |

### HUMAN-LABELED FUSIDIC ACID TOPICAL PRODUCTS

None available in the US.

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***Fucidin***® (Leo Pharma) | **Ointment/cream:** Fusidic acid 2% Fusidate sodium 2% | Rx (not available in US, available in EU and CA) | 15 g, 20 g, 30 g, 60 g tb |
| ***Fucidin H***® (Leo Pharma) | **Cream:** Fusidic acid 2% Hydrocortisone acetate 1% | Rx (not available in US. Available in EU and CA) | 15 g, 20 g, 30 g, 60 g tb |
| ***Fucicort***® (Leo Pharma) | **Cream:** Fusidic acid 2% Bethametasone valerate 0.1% | Rx (not available in US, available in EU and CA) | 15 g |
| ***Fucicort Lipid***® (Leo Pharma) | **Cream:** Fusidic acid 2% Bethametasone valerate 0.1% | Rx (not available in US, available in EU and CA) | Contains lipids/ moisturizer. 15 g |

## Gentamicin Sulfate

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Gentamicin can be useful for treating bacterial skin infections caused by organisms susceptible to gentamicin. Some commercial products also indicate prophylactic use after lacerations/abrasions or after minor surgery. However, the authors recommend the use of topical gentamicin to treat only confirmed bacterial skin infections, as resistance may occur. Gentamicin can be used in combination with the corticosteroid betamethasone to treat skin infections where an anti-inflammatory or antipruritic effect is needed. It has activity against many *Streptococcus*, *Staphylococcus* (coagulase-negative/positive and some penicillinase-producing strains) and Gram-negative bacteria including many *Klebsiella*, *Escherichia coli*, and *Pseudomonas* (often becomes resistant to gentamicin). All veterinary-labeled products are in combination with bethametasone (or mometasone) and many are also in combination with clotrimazole. The products containing bethametasone or mometasone and clotrimazole are labeled for otic use; however, they can also be used extra-label for bacterial and/or yeast skin infections sensitive to gentamicin and clotrimazole, when a strong anti-inflammatory or antipruritic effect is also needed. Topical formulations containing gentamicin as the sole ingredient are available as veterinary ophthalmic solutions and with human labeling.

### MECHANISM OF ACTION

Gentamicin is an aminoglycoside with bactericidal activity. It binds to the bacterial 30S ribosomal subunit and inhibits protein synthesis.

### SUGGESTED USES/DOSAGES

Topical gentamicin/betamethasone sprays are labeled for use 2–4 times daily for up to 7 days. Topical gentamicin creams and ointments are generally applied to affected areas 1–2 times daily. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. Creams are generally used for secondary or oily/exudative infections and ointments for dry skin infections.

### PRECAUTIONS/ADVERSE EFFECTS

Topical gentamicin may be absorbed systemically if used on ulcerated, burned, or denuded skin. Systemic toxicity is unlikely to occur unless it is used on a large body area or for prolonged periods of time. Creams are more likely to be absorbed than ointments. Potential side effects associated with gentamicin products include skin irritation, erythema, burning, and photosensitivity. It is contraindicated in patients with hypersensitivity to gentamicin or its class. Prolonged use, or use over large areas with products also containing corticosteroids (betamethasone or mometasone), may cause adrenal suppression. Increased risks of hypothalamic–pituitary–adrenal axis suppression, systemic corticosteroid effects (e.g., polydipsia/polyuria, Cushing's disease, gastrointestinal signs), cutaneous atrophy that can be associated with skin fragility, superficial follicular cysts (milia), and comedones may occur as product concentration and duration of use increase. Vomiting and diarrhea have been reported with use of the products containing betamethasone. Avoid contact

with eyes. Clients should wash hands after application or wear gloves when applying. Use caution when using these products empirically, because of possible bacterial resistance to gentamicin. For products containing glucocorticoids, at least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing.

### VETERINARY-LABELED GENTAMICIN TOPICAL PRODUCTS

Veterinary-labeled formulations containing gentamicin as the sole ingredient are not available specifically for dermatological use; however, ophthalmic preparations such as *Vetro-Gen Ophthalmic® Ointment*, from Dechra Veterinary Products, are available and labeled for dogs and cats and can be used extra-label for the treatment of skin and ear infections.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Gentocin Topical Spray®*** (Intervet/ Schering-Plough)<br>***Gentaspray®*** (Butler)<br>***Betagen Topical Spray®*** (Med-Pharmex))<br>***Gentamicin Topical Spray®*** (RXV)<br>***GentaVed Topical Spray®*** (Vedco)<br>***GenOne® Spray*** (VetOne)<br>***Gentamicin® Topical Spray*** (Priority Care 1) | **Spray** (all products listed): Gentamicin 0.57 mg/mL Betamethasone valerate 0.284 mg/mL | Rx (all products listed) | All products listed contain isopropyl alcohol, propylene glycol and parabens and are labeled for dogs<br>All products listed, except for *Gentocin Topical Spray®* and *GenOne® Spray*, are available in 3 different sizes: 60, 120, 240 mL<br>*Gentocin Topical Spray®* is available in 72 mL and *GenOne® Spray* is available in 60 mL and 120 mL |
| ***Otomax® Ointment*** (Intervet/ Schering-Plough)<br>***DVMAX® Ointment*** (IVX)<br>***Vetromax® Ointment*** (Dechra) | **Ointment (otic)** – all products listed: Gentamicin 3 mg/g Betamethasone (as valerate) 1 mg/g Clotrimazole 10 mg/g | Rx or sold only through licensed veterinarians (all products listed) | All products listed are mineral-oil based and approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected lesions on the skin, e.g., bacterial skin lesions or *Malassezia* dermatitis |

## VETERINARY-LABELED GENTAMICIN TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| | | | 7.5 g, 15 g, 30 g tb (*Otomax*®)<br>7.5 g, 15 g tb (*Vetromax*®)<br>10 g, 20 g, 215 g btl (*DVMax*®) |
| ***Mometamax*® *Otic Suspension*** (Intervet/ Schering-Plough) | **Suspension (otic):** Gentamicin 3 mg/g Mometasone 1 mg/g Clotrimazole 10 mg/g | Rx | Mineral-oil base. Approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected cutaneous lesions, e.g., bacterial skin lesions or *Malassezia* dermatitis. 7.5 g, 15 g, 30 g, 215 g tb |
| ***Easotic*®** (Virbac) | **Suspension (otic):** Gentamicin sulfate 1505 IU/mL Hydrocortisone aceponate 1.11 mg/mL Miconazole nitrate 15.1 mg/mL | Rx (not available in US, available in EU) | Labeled for otic use in dogs. May be used extra-label to treat skin infections (e.g., bacterial and/or *Malassezia* dermatitis) associated with inflammation in dogs and cats. 10 mL pump btl |

## HUMAN-LABELED GENTAMICIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Gentamicin** (various generics). Commonly used brand names: ***G-Myticin*®** ***Garamycin*®** ***Gentamar*®** | **Cream:** 0.1% (as base)<br>**Ointment:** 0.1% (as base) | Rx or OTC depending on product | **Cream** may contain propylene glycol and parabens. 15 g tb<br>**Ointment** may contain white petrolatum and parabens. 15 g tb |

## Mupirocin (Pseudomonic Acid)

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Mupirocin is approved for treating skin infections in dogs (e.g., superficial pyoderma, fold pyoderma, interdigital cysts/draining tracts, acne, pressure point pyodermas) caused by susceptible strains of *Staphylococcus aureus* or *S. pseudintermedius*, including beta-lactamase-producing and methicillin-resistant strains. It may also be used for feline acne cases complicated with staphylococcal infection.

### MECHANISM OF ACTION

Mupirocin is produced from *Pseudomonas fluorescens*, and it is chemically unrelated to any other antibiotic. It exerts a bacteriostatic action (although the high concentrations applied to the skin may be bactericidal) against sensitive organisms by binding specifically to bacterial isoleucyl transfer-RNA synthetase and inhibiting bacterial protein synthesis. Despite its broad spectrum, its main activity is mostly against Gram-positive cocci (*Staphylococcus* and *Streptococcus*). It also shows activity against other Gram-positive pathogens: *Corynebacterium*, *Clostridium*, *Proteus*, and *Actinomyces*. Mupirocin also has activity against some Gram-negative bacteria, but is not used clinically for infections caused by those bacteria. Moreover, it has been reported to have little efficacy against *Candida* and *Trychophyton mentagrophytes*. A possible effect against *Malassezia* in dogs and cats has been anecdotally reported. *Pseudomonas* species are particularly resistant to mupirocin. While bacterial resistance is rare, resistant strains of *Staphylococcus aureus* have been identified and resistance transference is thought to be plasmid-mediated. It is thought that resistance occurs more frequently when mupirocin is used over a prolonged period and over larger areas of skin; therefore, it may be best to use mupirocin for short-term treatment and on small localized areas. Cross-resistance with other antimicrobials has not been identified. Mupirocin is not significantly absorbed into the systemic circulation, but does penetrate well into granulomatous deep lesions. It is not suitable for application to burns.

### SUGGESTED USES/DOSAGES

Mupirocin is labeled for twice-daily application on dogs and 10 minutes contact time to the skin is required in order to be active. Do not let the dog lick or chew at affected areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. In cats with chin acne, once- to twice-daily applications have been shown to be efficacious in treating the secondary infection.

### PRECAUTIONS/ADVERSE EFFECTS

Mupirocin is contraindicated in patients with a history of hypersensitivity to mupirocin or other ointments containing polyethylene glycols. Avoid contact with eyes. Because the ointment has a polyethylene glycol base, the manufacturer warns that nephrotoxicity may potentially develop if it is used on extensive deep lesions. Anecdotally, very rare cases of renal toxicity have been reported. Should use caution in conditions where absorption of large quantities of polyethylene glycol is possible, especially if there is evidence of renal impairment. Mupirocin appears to be very well tolerated; however, contact reactions rarely

reported in humans include pain, itching, erythema, and dryness of the skin. Erythema has been reported in dogs. Overgrowth of non-susceptible organisms (superinfection) is also possible with prolonged use. Despite low potential for bacterial resistance, overuse, mostly over prolonged period of time, should be avoided. Safety in pregnant or breeding animals has not been determined.

### VETERINARY-LABELED MUPIROCIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Muricin® Ointment*** (Dechra) | **Ointment:** 2% | Sold only through licensed veterinarians | Polyethylene glycol base. Labeled for dogs. Extra-label use in cats. 15 g |

### HUMAN-LABELED MUPIROCIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Mupirocin** (various generics) | **Ointment:** 2% | Rx | Polyethylene glycol base. 15 g, 22 g, 30 g |
| ***Bactroban® Ointment*** (GlaxoSmithKline) | **Ointment:** 2% | Rx | Polyethylene glycol base. 15 g, 30 g |
| ***Centany®*** (OrthoNeutrogena) | **Ointment:** 2% | Rx | Propylene glycol, castor oil, oleyl alcohol, hard fat base. 15 g, 30 g |
| ***Bactroban® Cream*** (GlaxoSmithKline) | **Cream:** 2% | Rx | Benzyl alcohol, cetyl alcohol, stearyl alcohol, phenocyethanol, mineral oil/water base. 15 g, 30 g |

## Nitrofurazone

### INDICATIONS

Nitrofurazone can be used for treating bacterial skin infections associated with *Escherichia coli* or *Staphylococcus aureus*, among other bacteria. Clinical evidence demonstrating efficacy in the treatment of minor burns or bacterial skin infections is apparently unavailable.

### MECHANISM OF ACTION

Nitrofurazone is a nitrofuran antibacterial. It is bactericidal and thought to inhibit bacterial enzymes that primarily degrade glucose and pyruvate.

### SUGGESTED USES/DOSAGES

Apply once to twice daily until lesions resolve or as directed by the veterinarian. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

The soluble dressing contains polyethylene glycol, and if it is used on large areas of denuded skin significant amounts of polyethylene glycol could be absorbed and cause nephrotoxicity. Avoid contact with eyes or mucous membranes if product is not labeled for eyes. Clients should wash hands after application or wear gloves when applying. Avoid exposure to sunlight, strong fluorescent lighting, excessive heat, or alkaline materials. Topical nitrofurazone appears to be well tolerated; however, hypersensitivity or skin reactions (pain, erythema, itching) are possible, but thought to occur rarely. Overgrowth of non-susceptible organisms (superinfection) is also possible with prolonged use. There is some concern with potential carcinogenic effects, from previous reports in rats.

### VETERINARY-LABELED NITROFURAZONE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Nitrofurazone Soluble Dressing** (Generic; Med-Pharmex, AgriLabs, Vedco, etc.). Also available under a variety of trade names. | **Ointment (soluble):** 0.2% | OTC | Water-soluble and polyethylene glycol base. Some brands are labeled for dogs and cats. 1 lb jars |
| ***NFZ® Puffer*** (AgriLabs, Durvet, Aspen, etc.) | **Soluble powder:** 0.2% | OTC | Water-soluble base. Labeled for surface wounds, cuts, and abrasions in dogs and cats. Also labeled for eye and ear infections. Shake or rotate to loosen powder. Restricted drug in California. 45 g |

### HUMAN-LABELED NITROFURAZONE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Nitrofurazone** (various) | **Solution:** 0.2% | Rx | 1 pt, 1 gal |
| ***Furacin®*** (Roberts) | **Solution:** 0.2% | Rx | 1 pt |
| **Nitrofurazone** (various) | **Ointment (soluble):** 0.2% | Rx | 1 lb |
| ***Furacin®*** (Roberts) | **Ointment (soluble):** 0.2% | Rx | Polyethylene glycol base. 28 g, 56 g, 454 g |
| ***Furacin®*** (Roberts) | **Cream:** 0.2% | Rx | Water-miscible base, cetyl alcohol, mineral oil. 28 g |

## Silver Sulfadiazine

### INDICATIONS

Topical silver sulfadiazine (SSD) is labeled for prophylactic use and treatment of wounds and second- and third-degree burns. However, the authors recommend its use only for confirmed cases of localized bacterial skin infections, to avoid bacterial resistance. It is useful in treating localized pyodermas caused by *Pseudomonas* or other susceptible bacteria.

### MECHANISM OF ACTION

SSD acts by disrupting microbial cell membranes and cell walls; this differs from the antibacterial actions of silver nitrate or sodium sulfadiazine. SSD has extensive antimicrobial activity and is bactericidal for yeast and many Gram-negative and Gram-positive bacteria. It enhances epithelialization but retards granulation (avoid use in non-granulated wounds).

### SUGGESTED USES/DOSAGES

When used for burns, SSD is applied once to twice daily at a thickness of approximately 1/16 of an inch (1.5 mm). Dressings may be applied over the cream. When used for wounds or localized pyodermas apply the cream once to twice daily. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Patients hypersensitive to sulfonamides may also react to SSD. Risks of continued treatment must be weighed against the risks of not treating with SSD. Patients with significant hepatic or renal dysfunction may accumulate drug, particularly when used over large areas. Avoid contact with eyes. Clients should wash hands

after application or wear gloves when applying. Adverse effects associated with sulfonamides (e.g., keratoconjunctivitis sicca in dogs, blood dyscrasias in dogs and cats, etc.) are possible, particularly when used over large areas or for extended periods. *Refer to Sulfadiazine/Sulfamethoxazole + Trimethoprim in Section 1 (Systemic Drugs) for more information*.

### VETERINARY-LABELED SILVER SULFADIAZINE TOPICAL PRODUCTS

There are no topical products labeled for veterinary patients. An otic preparation (*Baytril Otic®*) contains SSD. *Refer to the Otic section for more information*.

### HUMAN-LABELED SILVER SULFADIAZINE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Silvadene®*** (Hoechst MR) | **Cream:** 1% | Rx | Water-miscible base containing white petrolatum, cetyl alcohol, propylene glycol, stearyl alcohol, methylparaben. 50 g, 85 g, 400 g, 1000 g |
| ***SSD AF Cream®*** (Boots) ***Thermazene®*** (Sherwood) | **Cream:** 1% | Rx | Water-miscible base containing white petrolatum, stearyl alcohol, methylparaben. 50 g, 400 g, 1000 g |
| ***SSD Cream®*** (Boots) | **Cream:** 1% | Rx | Water-miscible base containing cetyl alcohol, white petrolatum, stearyl alcohol, methylparaben. 25 g, 50 g, 85 g, 400 g, 1 kg |

## Three Point Enzyme System

*For **otic** use, refer to the Otic section*.

### INDICATIONS

Labeled for various types of bacterial and fungal skin infections and some specific conditions such as impetigo, fold pyoderma, anal sac abscesses, pyotraumatic dermatitis, and dermatophytosis. The manufacturer claims that it is effective against *Staphylococcus*, *Pseudomonas*, *Malassezia*, *Candida albicans*, and *Microsporum*. Can also be used alone for mild itching or as an adjunctive treatment to provide soothing of more pruritic conditions such as atopic dermatitis, especially if using products that also contain hydrocortisone.

### MECHANISM OF ACTION

The Three Point Enzyme System includes milk-derived enzymes such as lactoperoxidase, lysozyme, and lactoferrin that are reported to be effective against

bacterial, fungal, and viral microorganisms. Lactoperoxidase, when combined with hydrogen peroxide, thiocyanate, and/or iodide, produces a potent antibacterial system known as the lactoperoxidase system. The hypohalous ions produced are either the hypothiocyanate ion or the hypoiodite ion. Both are bactericidal substances. Hypoiodite is also a known fungicidal agent. The antibacterial property of the lactoperoxidase system is based upon inhibition of vital bacterial metabolic enzymes brought on by their oxidation by hypothiocyanate or hypoiodite. Lysozyme kills bacteria by disrupting the formation of a glycosidic bond between the two components of peptidoglycan, a constituent of the bacterial cell wall. Lactoferrin is bacteriostatic against a wide range of microorganisms including Gram-negative (coliforms) and Gram-positive (*Staphylococcus*) bacteria. It has the potential to inhibit the growth of bacteria and kills the bacteria by depriving them of iron, which is vital for growth.

### SUGGESTED USES/DOSAGES

If using spray, cream, or wipes: 1–2 times a day application. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo or rinse: daily to weekly baths/after baths according to the veterinarian's recommendations. It is important to leave the shampoo in contact with the skin for at least 10 minutes prior to rinsing well. Refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Overall appears to be safe. No reported side effects.

### VETERINARY-LABELED THREE POINT ENZYME SYSTEM TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Zymox Topical Spray®*** (PKB Animal Health) | **Spray:** Lactoperoxidase, lysozyme, lactoferrin Available with and without Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 2 oz |
| ***Zymox Topical Cream®*** (PKB Animal Health) | **Cream:** Lactoperoxidase, lysozyme, lactoferrin Available with and without Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 1 oz |

**VETERINARY-LABELED THREE POINT ENZYME SYSTEM TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Zymox Topical Wipes®*** (PKB Animal Health) | **Wipes:** Lactoperoxidase, lysozyme, lactoferrin Available with and without hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 30 wipes |
| ***Zymox Enzymatic Shampoo®*** (PKB Animal Health) | **Shampoo:** Lactoperoxidase, lysozyme, lactoferrin | Sold only through licensed veterinarians | Labeled for dogs and cats. 12 oz |
| ***Zymox Enzymatic Rinse®*** (PKB Animal Health) | **Rinse:** Lactoperoxidase, lysozyme, lactoferrin | Sold only through licensed veterinarians | Labeled for dogs and cats. 12 oz |

**HUMAN-LABELED THREE POINT ENZYME SYSTEM TOPICAL PRODUCTS**

None.

# ANTISEPTIC AGENTS

## Chlorhexidine Gluconate

**INDICATIONS**

Chlorhexidine, a topical antiseptic, is generally used as adjunctive therapy for bacterial skin infections caused by Gram-positive and Gram-negative bacteria, with no predictable activity against *Pseudomonas* or *Serratia*. It may also be used as adjunctive therapy for fungal skin diseases. Veterinary products are available in many different forms (solutions, shampoos, scrubs, ointments, sprays, etc.). Because it causes less drying and is usually less irritating than benzoyl peroxide, it is sometimes used in patients that cannot tolerate benzoyl peroxide. However, it does not have the keratolytic, comedolytic, or degreasing effects of benzoyl peroxide. Chlorhexidine possesses some residual effects and can remain active

on skin after rinsing. Chlorhexidine products may also contain other ingredients such as antifungals (ketoconazole and miconazole), salicylic acid, and phytosphingosine.

### MECHANISM OF ACTION

Chlorhexidine is a phenol-related bisbiguanide. It is an important antiseptic, disinfectant, and preservative. At usual concentrations, chlorhexidine acts by damaging bacterial cytoplasmic membranes. Antifungal activity can be obtained with 2% or higher concentrations. Chlorhexidine has residual activity and works in organic debris.

### SUGGESTED USES/DOSAGES

For wound irrigation or foot soaking, 0.05–0.1% dilution in water is recommended. If using spray or wipes/pads: 1–2 times a day or according to the veterinarian's recommendation. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo or conditioner: daily to weekly baths/after baths according to the veterinarian's recommendation. It is important to leave the shampoo in contact with the skin for at least 10 minutes prior to rinsing well. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Keep away from eyes, as chlorhexidine products can damage eyes. Clients should wash hands after application or wear gloves when applying. Safe in cats, although irritation and corneal ulcers have been reported. Hypersensitivity and local skin irritant reactions are possible. Likelihood of irritation increases with increased concentrations. Chlorhexidine may retard wound healing; not recommended for long-term use, particularly on granulating lesions.

### VETERINARY-LABELED CHLORHEXIDINE TOPICAL PRODUCTS

There are several trade names used for chlorhexidine products, including *Nolvasan®*, *Chlorhexiderm®*, *Dermachlor®*, *Chlorasan®*, *Chloradine®*, *Privasan®*, and *Chlorhex®*.

## VETERINARY-LABELED CHLORHEXIDINE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Chlorhexidine Spray** (various manufacturers and trade names) | **Spray:** 4% | OTC | Aloe. Shake well. Labeled for dogs and cats. 8 oz |
| ***Douxo® Chlorhexidine PS Micro-emulsion Spray*** (Sogeval) | **Spray:** Chlorhexidine 3% Phytosphingosine salicyloyl 0.05% | Sold only through licensed veterinarians | Spray the product by holding the pump approximately 12 inches from the pet's body and do not over apply. 1 spray/10 lb. Number of sprays can be doubled for long-haired dogs. Twice weekly applications are usually recommended. Labeled for dogs and cats. 6.8 oz |
| ***Ketoseb-D® Spray*** (Sogeval) | **Spray:** Chlorhexidine 2% Ketoconazole 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Mal-A-Ket Plus TrizEDTA Spray®*** (Dechra) | **Leave-on spray:** Chlorhexidine 2% Ketoconazole 1% TrizEDTA | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***TrizChlor 4® Spray*** (Dechra) | **Leave-on spray:** Chlorhexidine 4% TrizEDTA | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 1 gal |
| ***Chlorhex 2X 4%® Spray*** (Vedco) | **Spray:** 4% | OTC | 4% Isopropyl alcohol. Labeled for dogs and cats. 8 oz |

(continued)

## VETERINARY-LABELED CHLORHEXIDINE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***ChlorhexiDerm® Spray*** (TEVA/DVM) | **Spray:** 4% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Malaseb® Spray*** (TEVA/DVM) | **Spray:**<br>Chlorhexidine 2%<br>Miconazole nitrate 2% | Rx | Alcohol 30%. Labeled for dogs and cats. 8 oz |
| **Chlorhexidine Solution** (various manufacturers and trade names) | **Solution:** 2% | OTC | May be labeled for dogs and cats. 16 oz, 1 gal |
| **20% Chlorhexidine Concentrate Gluconate Additive** (Davis) | **Solution for dilution:** 20% | OTC | For 1%: Dilute 6 oz into 1 gal water or shampoo; for 2%: 12 oz into one gal. Labeled for dogs and cats. 32 oz |
| ***Douxo® Chlorhexidine 3% PS Pads*** (Sogeval) | **Medicated pads:**<br>Chlorhexidine 3%<br>Climbazole 0.5%<br>Phytosphingosine salicyloyl 0.05% | Sold only through licensed veterinarians | Alcohol-free. Labeled for dogs and cats. 30 count jar |
| ***Ketoseb-D® Wipes*** (Sogeval) | Wipes:<br>Chlorhexidine 2%<br>Ketoconazole 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 50 count jar |
| ***Mal-A-Ket® Wipes*** (Dechra) | **Wipes:**<br>Chlorhexidine 2%<br>Ketoconazole 1%<br>Acetic acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 50 count jar |
| ***TrizChlor® 4 Wipes*** (Dechra) | **Wipes:**<br>Chlorhexidine 4%<br>TrizEDTA | Sold only through licensed veterinarians | Labeled for dogs and cats. 50 count jar |

## VETERINARY-LABELED CHLORHEXIDINE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Malaseb® Pledgets*** (TEVA/DVM) | **Pledgets:**<br>Chlorhexidine 20 mg<br>Miconazole nitrate 17.4 | Sold only through licensed veterinarians | Alcohol 30%. Labeled for dogs and cats. 60 count jar |
| ***Malaseb® Towelettes*** (TEVA/DVM) | **Towelettes:**<br>Chlorhexidine 72 mg<br>Miconazole nitrate 63 mg | Sold only through licensed veterinarians | Polypropylene 60%, Alcohol 30%. Labeled for dogs and cats. 12 and 60 count jars |
| **Chlorhexidine Flush** (various manufacturers and trade names) | **Flush:** depending on product, concentration may not be listed | OTC | 4 oz, 12 oz |
| ***TrizChlor® Flush*** (Dechra) | **Flush:**<br>Chlorhexidine 0.15%<br>TrizEDTA | Sold only through licensed veterinarians | A multicleanse flush for cleaning and/or alkalinizing and/or pre-treatment. pH 8. Labeled for dogs and cats. 4 oz |
| ***Mal-A-Ket Plus TrizEDTA® Flush*** (Dechra) | **Flush:**<br>Chlorhexidine 0.15%<br>Ketoconazole 0.15%<br>TrizEDTA | Sold only through licensed veterinarians | A multicleanse flush to aid in the treatment of bacterial and fungal (dermatophytosis and *Malassezia*) infections. pH 8. Labeled for dogs and cats. 4 oz, 12 oz |
| ***Dermachlor Flush with Lidocaine®*** (Butler)<br>***Dermachlor Flush Plus®*** (Butler) | **Flush:**<br>Chlorhexidine 0.2%<br>Lidocaine 0.5% | OTC | Propylene glycol, malic acid, benzoic acid, salicylic acid, glycerin. Dermachlor Flush Plus® also contains Bitrex® (bitter-tasting substance to discourage licking). Labeled for dogs and cats. 4 oz, 16 oz |
| ***Hexadene Flush®*** (Virbac) | **Flush:**<br>Chlorhexidine 0.25%<br>Triclosan (% not listed) | Sold only through licensed veterinarians | *Spherulite®* microcapsules, chitosanide, propylene glycol, fragrance. Labeled for dogs and cats. 12 oz |

## VETERINARY-LABELED CHLORHEXIDINE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Malaseb® Flush*** (TEVA/DVM) | **Flush:** Chlorhexidine 0.2% Miconazole nitrate 0.2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 4 oz, 12 oz |
| ***ChlorhexiDerm® Flush*** (TEVA/DVM) | **Flush:** 0.22% | Sold only through licensed veterinarians | Labeled for dogs and cats. 4 oz, 12 oz |
| ***Chlorhexidine 0.2% Solution®*** (Sogeval) | **Flush:** Chlorhexidine 0.2% | Sold only through licensed veterinarians | Isopropyl alcohol, glycerin, castor oil. Labeled for dogs and cats. 4 oz, 8 oz, 16 oz |
| ***Ketoseb-D® Flush*** (Sogeval) | **Flush:** Chlorhexidine 0.2% Ketoconazole 0.2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 4 oz, 16 oz |
| **Chlorhexidine Ointment** (various manufacturers and trade names) | **Ointment:** 1% | OTC | 1 oz, 7 oz, 1 lb |
| **Chlorhexidine Ointment 1%** (Vedco) | **Ointment:** 1% | OTC | Labeled for dogs and cats. 1 oz, 7 oz, 16 oz |
| ***Nolvasan Shampoo®*** (Fort Dodge) | **Shampoo:** 0.5% | OTC | Labeled for dogs and cats. 8 oz, 1 gal |
| **Chlorhexidine Shampoo 2%** (various manufacturers and trade names) | **Shampoo:** 2% | OTC | 8 oz, 16 oz, 1 gal |
| ***Ketochlor Shampoo®*** (Virbac) | **Shampoo:** Chlorhexidine 2.3% Ketoconazole 1% | Rx | *Spherulite®* microcapsules. Glycotechnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside), chitosanide. Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |

## VETERINARY-LABELED CHLORHEXIDINE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Mal-A-Ket® Shampoo*** (Dechra) | **Shampoo:**<br>Chlorhexidine 2%<br>Ketoconazole 2%<br>Acetic acid 2% | Sold only through licensed veterinarians | 1 oz pouch, 8 oz, 1 gal |
| ***ChlorhexiDerm® 2% Shampoo*** TEVA/DVM) | **Shampoo:** 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |
| ***Malaseb® Shampoo*** (TEVA/DVM) | **Shampoo:**<br>Chlorhexidine 2%<br>Miconazole nitrate 2% | OTC | Labeled for dogs and cats. 250 mL, 500 mL |
| ***Douxo® Chlorhexidine PS*** + ***Climbazole Shampoo*** (Sogeval) | **Shampoo:**<br>Chlorhexidine 3%<br>Climbazole 0.5%<br>Phytosphingosine salicyloyl 0.05%<br>Lipacide® C8G 2.5% | Sold only through licensed veterinarians | Citric acid, pH 7. Labeled for dogs and cats. 6.8 oz, 16.9 oz, 3 L |
| ***Hexadene® Shampoo*** (Virbac) | **Shampoo:** 3% | Sold only through licensed veterinarians | *Spherulite*® microcapsules. Glycotechnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside), chitosanide. Labeled for dogs and cats. 8 oz, 16 oz |
| **Chlorhexidine Shampoo 4%** (various manufacturers and trade names) | **Shampoo:** 4% | OTC | 12 oz |

## VETERINARY-LABELED CHLORHEXIDINE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***ChlorhexiDerm® 4% Shampoo*** (TEVA/DVM) | **Shampoo:** 4% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 12 oz, 1 gal |
| ***Chlorhexidine® 4% Shampoo*** (Sogeval) | **Shampoo:** 4% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |
| ***ChlorhexiDerm® HC Shampoo*** (TEVA/DVM) | **Shampoo:** Chlorhexidine 4% Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |
| ***Chlorhexidine® 4% HC Shampoo*** (Sogeval) | **Shampoo:** Chlorhexidine 4% Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz |
| ***TrizChlor 4® Shampoo*** (Dechra) | **Shampoo:** Chlorhexidine 4% TrizEDTA | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 1 gal |
| ***Malaseb® Concentrate Rinse*** (TEVA/DVM) | **Rinse:** Chlorhexidine 5.9% Miconazole nitrate 5.2% | Sold only through licensed veterinarians | Labeled for dogs and cats. Must be diluted before use. 32 oz |
| ***ResiKetoChlor Leave-On Conditioner®*** (Virbac) | **Conditioner:** Chlorhexidine 2.3% Ketoconazole 1% | Rx | *Spherulite®* microcapsules. Glycotechnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside), chitosanide. Labeled for dogs and cats. 8 oz |
| **Chlorhexidine Scrub** (various) | **Scrub:** 2%, 4% | OTC | 1 gal |
| ***ChlorhexiDerm® Plus Scrub*** (TEVA/DVM) | **Scrub:** 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 1 gal |

### HUMAN-LABELED CHLORHEXIDINE TOPICAL PRODUCTS

There are several topical skin cleansers available in the 2–4% range. Trade names include: *BactoShield®*, *Betasept®*, *Dyna-Hex®*, *Exidine®*, *Hibiclens®*, and *Hibistat®*.

## Chloroxylenol (PCMX)

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Chloroxylenol is an antimicrobial disinfectant with demonstrated efficacy against Gram-negative and Gram-positive bacteria, in addition to a wide variety of fungal organisms, and against RNA and DNA viruses. Can be used in presurgical preparation of skin, for cleaning wounds, and in the treatment of bacterial, fungal, and yeast skin infections.

### MECHANISM OF ACTION

Chloroxylenol, also known as parachlorometoxylenol (PCMX), is a chlorinated phenolytic antiseptic. Its antibacterial action is due to disruption of bacterial cytoplasmic membranes blocking production of adenosine triphosphate.

### SUGGESTED USES/DOSAGES

If using spray or wipes/pads: 1–2 times a day or according to patient's needs. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If using shampoo: daily to weekly baths according to the veterinarian's recommendations. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well. Refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Overall safe for dogs and cats. May cause skin irritation.

### VETERINARY-LABELED CHLOROXYLENOL TOPICAL PRODUCTS

This list contains only products where chloroxylenol is one of the main active ingredients. ***For more products containing chloroxylenol (PCMX)**, refer to other topicals mentioned elsewhere in Section 2.*

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Chloroxylenol® Scrub*** (Vedco) | **Scrub:** 2% | OTC | Propylene glycol, citric acid. Used for surgical scrub and preoperative skin preparation. Use full strength. Do not dilute. Labeled for dogs and cats. 1 gal |
| ***Pharmaseb® Wipes*** (Animal Pharmaceuticals) | **Wipes:** Chloroxylenol 0.3% Ketoconazole 0.3% | OTC | Water-based. Labeled for dogs and cats. 60 count |

## VETERINARY-LABELED CHLOROXYLENOL TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Pharmaseb® Flush*** (Animal Pharmaceuticals) | **Flush:** Chloroxylenol 0.3% Ketoconazole 0.3% | OTC | Water-based. Propylene glycol, benzyl alcohol. Can be used as a cleanse agent for skin and ears. Labeled for dogs and cats. 4 oz, 8 oz |
| ***Pharmaseb® Spray*** (Animal Pharmaceuticals) | **Spray:** Chloroxylenol 0.3% Ketoconazole 0.3% | OTC | Water-based. Propylene glycol, benzyl alcohol. Labeled for dogs and cats. 4 oz, 8 oz |
| ***Medicated Shampoo*** (Sogeval) | **Shampoo:** Chloroxylenol 2% Salicylic acid 2% Sodium thiosulfate 2% (source of sulfur) | Sold only through licensed veterinarians | Propylene glycol, citric acid. Also has antiseborrheic effect (keratolytic and keratoplastic). Labeled for dogs and cats. 16 oz, 1 gal |
| ***Vet Solutions Sebozole® Shampoo*** (Vetoquinol) | **Shampoo:** Chloroxylenol 1% Miconazole nitrate 1% | OTC | Also has antimycotic effect. Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |
| ***Vet Solutions Universal Medicated®*** *Shampoo* (Vetoquinol) | **Shampoo:** Chloroxylenol 2% Salicylic acid 2% Sodium thiosulfate 2% (source of sulfur) | OTC | Propylene glycol, citric acid. Also has antiseborrheic effect (keratolytic and keratoplastic). Labeled for dogs and cats. 16 oz |
| ***VPS Medicated® Shampoo*** (Jeffers) | **Shampoo:** Chloroxylenol 2% Salicylic acid 2% Sodium thiosulfate 2% (source of sulfur) | OTC | Propylene glycol. Also has antiseborrheic effect (keratolytic and keratoplastic). Labeled for dogs and cats. 16 oz, 1 gal |
| ***Pharmaseb® Shampoo*** (Animal Pharmaceuticals) | **Shampoo:** Chloroxylenol 2% Ketoconazole 1% | OTC | Labeled for dogs and cats. 8 oz, 16 oz, gal |

### HUMAN-LABELED CHLOROXYLENOL TOPICAL PRODUCTS

There are several topical products available containing chloroxylenol, usually combined with other ingredients such as hydrocortisone, menthol, pramoxine, and benzocaine. They are presented in different forms (creams, ointments, lotions, and shampoos), but these are not commonly used in dogs and cats. Trade names include *Aurinol®*, *Calamycin®*, *Cortamox®*, *Cortane-B®*, *Dermacoat®*, and *Foille®*, including some otic products as well.

## Ethyl Lactate

### INDICATIONS

Indicated for bacterial skin infections including surface and superficial pyodermas. It also has a keratoplastic effect that provides antiseborrheic activity.

### MECHANISM OF ACTION

Ethyl lactate is a very lipid-soluble compound that rapidly penetrates hair follicles and sebaceous glands, where it is hydrolyzed by bacterial lipases into lactic acid and ethanol, and the free lactic acid lowers the skin pH, thereby producing an antibacterial activity. Ethanol makes fat soluble and lowers sebaceous secretions. It is not as active as benzoyl peroxide against staphylococcal organisms, but is less irritating and drying.

### SUGGESTED USES/DOSAGES

Daily to weekly baths according to the patient's needs. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well. Refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. Adverse effects are unlikely, but local effects (erythema, pain, itching) are possible.

### VETERINARY-LABELED ETHYL LACTATE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Etiderm Shampoo®*** (Virbac) | **Shampoo:** 10% | Sold only through licensed veterinarians | *Spherulite®* microcapsules, chitosanide benzalkonium chloride (in encapsulated form), lactic acid and propylene glycol in a shampoo base. Shake well. Labeled for dogs and cats. 8 oz |

### HUMAN-LABELED ETHYL LACTATE TOPICAL PRODUCTS

None.

## Hypochlorous Acid

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Hypochlorous acid is indicated for the management of wounds, abscesses, cuts, abrasions, skin irritations, ulcers, post-surgical incision sites, and burns, as it can accelerate the healing process. It may be used for prevention of bacterial skin infections or as an adjunctive topical therapy for bacterial skin infections, including methicillin-resistant *Staphylococcus* and *Pseudomonas*. Hypochlorous acid also has antifungal and antiviral properties. Also reported to reduce inflammation, pain and itching. *Veterycin*® is a proprietary formulation based upon the *Microcyn*® technology platform.

### MECHANISM OF ACTION

Broad-spectrum antimicrobial with rapid activity against Gram-positive and Gram-negative bacteria and fungal/yeast organisms. It may also be effective against viruses. *Veterycin*® and *Microcyn*® contain oxychlorine compounds and have neutral pH. Its mode of action against microorganisms mimics that of neutrophils in the body. Specifically, the hypochlorous acid that is generated through the oxidative burst process of neutrophils acts as a potent antimicrobial agent which attacks only single-cell pathogens. As a strong oxidant, hypochlorous acid is known to react through a variety of pathways with biomolecules. However, the main route of attack against microorganisms is the disruption of the cellular membrane. It has also demonstrated the ability to speed healing through increase of oxygen and blood flow to a wound site as well as reduction of inflammation.

### SUGGESTED USES/DOSAGES

Clip hairs if necessary and apply spray or gel to affected areas up to three times a day. It may be used with dressing applications in wounds. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. No rinsing required. Skin may become red after application due to increased blood flow to lesional site, which will speed healing. Safe to use around eyes, nose, and mouth. Refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

No precautions or adverse effects reported. Considered as safe as saline. It is non-toxic, and does not sting or irritate the skin. Because of its unique mode of action, neither antibiotic-resistant bacteria nor viruses and fungi can develop an immunity to it. Clients should be warned about possible bleaching/staining of carpets, clothing, jewelry, etc.

## VETERINARY-LABELED HYPOCHLOROUS ACID TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Vetericyn® VF*** (Innovacyn) | **Spray/liquid:** Hypochlorous acid <0.1% Sodium phosphate <0.2% Sodium chloride < 0.05% Sodium hypochlorite 0.001% Electrolyzed water 99.8% | Sold only through licensed veterinarians | Veterinary formula. Nearly doubles the potency and provides 3–4 times the efficacy of the OTC product. Labeled for dogs and cats, including puppies and kittens. 4 oz, 8 oz, 16 oz |
| ***Vetericyn® VF Hydrogel*** (Innovacyn) | **Spray/gel:** Hypochlorous acid <0.1% Sodium hypochlorite 0.001% Sodium magnesium fluorosilicate 3% Boric acid 0.5% Sodium sulfate 0.3% Electrolyzed water 96.2% | Sold only through licensed veterinarians | Veterinary formula. Nearly doubles the potency and provides 3–4 times the efficacy of the OTC product. Labeled for dogs and cats, including puppies and kittens. 4 oz, 8 oz, 16 oz |
| ***Vetericyn® Wound and Infection Treatment*** (Innovacyn) ***Vetericyn® Hot Spot Spray*** (Innovacyn) | **Spray/liquid (all products contain the same formula):** Hypochlorous acid <0.01% Sodium hypochlorite 0.001% Sodium phosphate <0.01% Sodium chloride <0.01% Electrolyzed water 99.97% | OTC | Labeled for all animals. May be used in very young animals. 4 oz Labeled for dogs and cats. May be used in puppies and kittens. 4 oz pump spray btl |

## VETERINARY-LABELED HYPOCHLOROUS ACID TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Vetericyn® Hydrogel Spray*** (Innovacyn) | **Spray/gel:** Hypochlorous acid <0.1% Sodium hypochlorite 0.001% Sodium magnesium fluorosilicate 3% Boric acid 0.5% Sodium sulfate 0.3% Electrolyzed water 96.3% | OTC | Labeled for dogs and cats. 4 oz |

## HUMAN-LABELED HYPOCHLOROUS ACID TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **All products manufactured by** Oculus Innovative Sciences: | **All forms contain:** Hypochlorous acid 0.008% Sodium magnesium fluorosilicate 3% Sodium phosphate 0.4% Sodium chloride 0.066% Sodium hypochlorite 0.002% Electrolyzed water 97.524% | | Indicated for relief of itch and pain associated with skin lesions, injuries and ulcers. 1.5 oz |
| ***Microcyn® Skin & Wound HydroGel*** | | OTC/Rx | Indicated for the management of exudating wounds, burns and wound debridement. 1.76 oz, 4 oz |
| ***Microcyn® Dermatology HydroGel*** | | Rx | Indicated for the management of skin infections. 4 oz |
| ***Microcyn® Dermatology Spray*** | | Rx | Indicated for the management via debridement of post-surgical wounds. 500 mL, 990 mL btl |
| ***Microcyn® Solution with Preservatives*** | | Rx | |

**HUMAN-LABELED HYPOCHLOROUS ACID TOPICAL PRODUCTS**
(continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Microcyn® Skin & Wound Care***<br>***Microcyn® Negative -Pressure Wound Therapy Solution***<br>***Puracyn® Wound and Skin Care*** | | Rx<br>Rx<br>OTC | Indicated for debridement of wounds. 8 oz spray, 8.5 oz, 500 mL dosing btl<br>Indicated for the irrigation and management of wounds via negative-pressure wound therapy systems. Within pH ranges of 6–7.8. 500 mL, 990 mL btl |
| ***Myclyns® 0.0025% Spray*** (Union Spring Pharmaceuticals) | Hypochlorous acid 0.00025%<br>Sodium chloride 0.0111%<br>Oxidized water 99.99%<br>Sodium hypochlorite 0.0036% | OTC | pH: 6.2–7.8. 2 oz |

## Povidone Iodine

### INDICATIONS

Povidone iodine is used as a topical presurgical skin cleanser/antiseptic and may be used for superficial pyoderma and *Malassezia* dermatitis; however, it is infrequently used in small animal dermatology due to its drying, irritant, and staining effects.

### MECHANISM OF ACTION

Povidone iodine (PI) is iodine complexed with polyvinylpyrrolidone nitrogen. PI is an antiseptic that works by iodinating and oxidizing sulfhydryl compounds, peptides, proteins, enzymes, vitamins, lipids, and cytosine found in the cytoplasm and cytoplasmic membranes. PI has a wide spectrum of in-vitro activity against Gram-positive and Gram-negative bacteria (bactericidal), fungi, and viruses at proper concentrations. Povidone acts by slowly releasing iodine to tissues. It has

prolonged action (4–6 hours), but not as long as chlorhexidine. PI also has mild degreasing and debriding activity.

### SUGGESTED USES/DOSAGES

For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Povidone may be drying, irritant, and staining to the skin, hair, and fabrics. Can be extremely irritant to the scrotal skin and external ears. If used with emollients, the drying effects may be alleviated. Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. Systemic absorption can result in renal and thyroid dysfunction.

### VETERINARY-LABELED POVIDONE IODINE TOPICAL PRODUCTS

There are several trade names for povidone iodine labeled for large and small animals, including *Betadine®*, *Poviderm®*, *Povidine®*, *Prodine®*, *Lanodine®*, *Vetadine®*, and *Viodine®*. ***Note:*** *10% povidone iodine yields 1% titratable iodine. Labels may be confusing.*

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Poviderm® Medicated Shampoo*** (Butler) | **Shampoo:** 5% | OTC | 8 oz, 1 gal |
| ***Viodine® Medicated Shampoo*** (Farnam) | **Shampoo:** 5% | OTC | 1 pt |
| **Povidone Iodine Solution** (various manufacturers and trade names) | **Solution:** 10% | OTC | 1 qt, 1 gal |
| **Povidone Iodine Ointment** (various manufacturers and trade names) | **Ointment:** 10% | OTC | 1 lb |
| **Povidone Iodine Surgical Scrub** (various manufacturers and trade names) | **Scrub:** 7.5% | OTC | 1 gal |

### HUMAN-LABELED POVIDONE IODINE TOPICAL PRODUCTS

There are several trade names for povidone iodine products, including *Betadine®*, *Betagen®*, *Biodine®*, *Efodine®*, *Iodex®*, *Mallisol®*, *Minidyne®*, *Polydine®*, and

*Povidine*®. There are also (not listed) vaginal gels, swabs, and foaming skin cleansers available.

### HUMAN-LABELED POVIDONE IODINE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| **Povidone Iodine Solution** (various manufacturers and trade names) | **Solution:** 1%, 10% | OTC | 15 mL, 30 mL, 120 mL, 1 pt, 1 qt, 1 gal |
| **Povidone Iodine Spray** (various manufacturers and trade names) | **Spray:** 10% **Aerosol:** 5% | OTC | 30 mL, 60 mL, 1 pt, 1 gal 89 mL |
| **Povidone Iodine Surgical Scrub** (various manufacturers and trade names) | **Scrub:** 5.5–7.5% | OTC | 15 mL, 1 pt, 1 gal |
| **Povidone Iodine Ointment** (various manufacturers and trade names) | **Ointment:** 10% | OTC | 1 g, 30 g, 120 g, 1 lb |

## Triclosan (Irgasan)

### INDICATIONS

Triclosan is found in several products, often with other active ingredients. Its antibacterial effects may be useful in treating superficial pyodermas.

### MECHANISM OF ACTION

Triclosan is a halogenated bis-phenol bactericidal disinfectant and antiseptic. It has activity against a wide range of organisms, including Gram-positive and Gram-negative bacteria, and acts via inhibiting bacterial fatty acid synthesis, leading to disruption of cell membrane integrity and resulting in apoptosis in vitro. Triclosan reportedly is not effective against *Pseudomonas* and may be less effective against *Staphylococcus* than either chlorhexidine or ethyl lactate.

### SUGGESTED USES/DOSAGES

Daily to weekly baths according to the patient's needs. It is important to leave the shampoo in contact with the skin for at least 10 minutes prior to rinsing well. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Triclosan should not be used on burned or denuded skin, or on mucous membranes. Avoid contact with eyes. Triclosan is not recommended as a surgical scrub. Clients should wash hands after application or wear gloves when applying. Allergic contact reactions may occur.

#### VETERINARY-LABELED TRICLOSAN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; size(s); comments |
|---|---|---|---|
| ***Sebalyt® Shampoo*** (TEVA/DVM) | **Shampoo:** Triclosan 0.5% Sulfur 2% Salicylic acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 12 oz, 1 gal |
| ***Seborex® Shampoo*** (TEVA/DVM) | **Shampoo:** Triclosan 0.5% Sulfur 2% Salicylic acid 3% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 12 oz, 1 gal |
| ***Triclosan Deodorizing® Shampoo*** (Davis) | **Shampoo:** % not listed | OTC | Labeled for dogs and cats. 12 oz, 1 gal |

#### HUMAN-LABELED TRICLOSAN TOPICAL PRODUCTS

There are several human triclosan-containing products labeled as hand, face, or body washes for acne treatment. Trade names include *Septisoft®*, *Clearasil Antibacterial®*, *Clearasil Daily Face Wash®*, *Stri-Dex®*, *Oxy Medicated Soap®*, and *ASC®*.

## ANTIFUNGAL AGENTS

## Clotrimazole

*For **otic** use, refer to the Otic section.*

#### INDICATIONS

Topical clotrimazole has activity against dermatophytes and yeast; it may be particularly useful for localized lesions associated with *Malassezia*. Most available veterinary products also contain gentamicin and betamethasone and are labeled for otic use; however, these products are often used extra-label for bacterial and yeast skin infections and concurrent inflamed/pruritic skin.

#### MECHANISM OF ACTION

Clotrimazole, like other azoles, inhibits the biosynthesis of ergosterol, an essential component of fungal cell membranes, leading to increased membrane permeability and allowing leakage of intracellular components.

#### SUGGESTED USES/DOSAGES

For sprays, twice-daily applications are usually recommended. Ointments are generally applied to affected areas up to four times daily. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to

avoid ingestion and allow the medication to work. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Skin irritation is possible but unlikely. For products containing betamethasone, tuberculosis of the skin and pregnancy are listed as a contraindication. Use care when treating large areas with products containing betamethasone, or when using on small patients. Risks can be reduced by treating for only as long as necessary on as small an area as possible. *See Betamethasone for details on potential side effects*. Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. At least a 2-week withdrawal period is recommended for products containing betamethasone prior to intradermal or allergy serum testing. Use caution when using products containing gentamicin empirically, to avoid bacterial resistance.

### VETERINARY-LABELED CLOTRIMAZOLE TOPICAL PRODUCTS

There are other products containing clotrimazole for otic use; *refer to the Otic section for more information*.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Vet Solutions® Clotrimazole Solution*** (Vetoquinol) | **Spray and dropper:** 1% | Rx | Propylene glycol, chloroxylenol, alcohol. Labeled for dogs and cats. 1 oz |
| ***Otomax® Ointment*** (Intervet/ Schering-Plough) | **Ointment (otic):** Clotrimazole 10 mg/g Gentamicin 3 mg/g Betamethasone valerate 1 mg/g | Rx | Mineral-oil based. Approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected lesions on the skin, e.g., bacterial skin lesions or *Malassezia* dermatitis. 15 g, 30 g |
| ***DVMax® Ointment*** (TEVA/DVM) | **Ointment (otic):** Clotrimazole 10 mg/g Gentamicin 3 mg/g Betamethasone valerate 1 mg/g | Sold only through licensed veterinarians | Mineral-oil based. Approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected lesions on the skin, e.g., bacterial skin lesions or *Malassezia* dermatitis. 10 g, 20 g, 215 g btl |

## VETERINARY-LABELED CLOTRIMAZOLE TOPICAL PRODUCTS
(continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Vetromax®* *Ointment*** (Dechra) | **Ointment (otic):** Clotrimazole 10 mg/g Gentamicin 3 mg/g Betamethasone valerate 1 mg/g | Sold only through licensed veterinarians | Mineral-oil based. Approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected lesions on the skin, e.g., bacterial skin lesions or *Malassezia* dermatitis. 7.5 g, 15 g tb |
| ***MalOtic®* *Ointment*** (Vedco) | **Ointment (otic):** Clotrimazole 10 mg/g Gentamicin 3 mg/g Betamethasone valerate 1 mg/g | Rx | Mineral-oil based. Approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected lesions on the skin, e.g., bacterial skin lesions or *Malassezia* dermatitis. 7.5 g, 15 g tb |
| ***Aurizon®*** (Vetoquinol) | **Suspension (otic):** Clotrimazole 3 mg Dexamethasone acetate 0.9 mg Marbofloxacin 3 mg | Rx (not available in US, available in CA and EU) | Propyl gallate. Approved for otic use in dogs. Extra-label use in dogs and cats with localized inflamed or infected lesions on the skin, e.g., bacterial skin lesions or *Malassezia* dermatitis. 10 mL, 20 mL |

## HUMAN-LABELED CLOTRIMAZOLE TOPICAL PRODUCTS

In addition to the products listed below, there are vaginal creams and suppositories, and oral 10 mg troches.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Clotrimazole** (various) ***Lotrimin®*** (Schering-Plough) ***Lotrimin AF®*** (Schering-Plough) | **Solution:** 1% | OTC/Rx status determined by labeling | Depending on product: 10, 30 mL, 105–113 mL |

**HUMAN-LABELED CLOTRIMAZOLE TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Lotrimin®*** (Schering-Plough) ***Lotrimin AF®*** (Schering-Plough) | Lotion: 1% | OTC | 20 mL |
| **Clotrimazole & Betamethasone** (Fougera) ***Lotrisone®*** (Schering-Plough) | **Lotion:** Clotrimazole 1% Betamethasone dip. 0.05% | Rx | 30 mL |
| **Clotrimazole** (various) ***Desenex®*** (Novartis) ***Lotrimin®*** (Schering-Plough) ***Lotrimin AF®*** (Schering-Plough) | **Cream:** 1% | OTC/Rx status determined by labeling | Depending on product: 12 g, 15 g, 20 g |
| **Clotrimazole & Betamethasone** (Fougera) ***Lotrisone®*** (Schering-Plough) | **Cream:** Clotrimazole 1% Betamethasone dip. 0.05% | Rx | 15 g, 45 g |

## Enilconazole

### INDICATIONS

Although no products are currently commercially available for topical use in the US, enilconazole can be compounded as a rinse and used topically for the treatment of dermatophytosis in small animals. A topical rinse, *Imaverol®* 10%, is commercially available for the treatment of canine dermatophytosis in EU and CA. Intranasal instillation of enilconazole after plaque debridement has also been shown useful in treating nasal aspergillosis in small animals. Use of topical enilconazole on cats with dermatophytosis is somewhat controversial as there are currently no products with feline labeling available. There are reports of safety and efficacy in using enilconazole on cats with dermatophytosis as a sole therapy or in combination with oral itraconazole. A poultry environmental disinfectant product (*Clinafarm EC®*) is available in the US. This formulation has been used off-label to treat feline dermatophytosis associated with *Microsporum canis*. However, it is technically illegal to use this product other than as labeled, as it is an EPA-licensed product in the US.

### MECHANISM OF ACTION

Enilconazole, like other azoles, inhibits the biosynthesis of ergosterol, an essential component of fungal cell membranes, leading to increased membrane permeability and allowing leakage of intracellular components.

### SUGGESTED USES/DOSAGES

Hairs may need to be clipped/shaved prior to application to remove as much infected hair as possible and allow better topical effect. If used to treat feline dermatophytosis, concurrent systemic antifungal medication is recommended. *Imaverol*®: dilute as directed and wash or dip four times at 3-day intervals, or until two negative fungal cultures are obtained at 2-week intervals. Refer to product label for details on dilution or individual use. *Clinafarm EC*® [extra-label use (Hnilica and Medleau 2002)]: apply to dry hair coat 100 mL of 0.2% enilconazole solution (diluted from *Clinafarm EC*® as follows: 14.5 mL of the 13.8% concentrate added to 1 L of water) every 3 days until two negative fungal cultures are obtained at 2-week intervals. After each application the cat may be placed in a kennel and blown dry with cool air. Oral ingestion should be prevented.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes. Clients should wear gloves and use eye protection when applying. When used topically in cats, hypersalivation, vomiting, anorexia/weight loss, muscle weakness, and a slight increase in the liver enzyme ALT serum levels have been reported.

### VETERINARY-LABELED ENILCONAZOLE TOPICAL PRODUCTS

*Imaverol*® is not currently available in the US. It is available in EU and CA.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Imaverol***® (Janssen) | **Concentrate:** 10% | Rx (not available in US, available in EU and CA) | Polysorbate 20, sorbitan monolaurate (surfactants). Concentrate is diluted to 0.2% (1 part concentrate to 50 parts water). Labeled for dogs: dilute as directed and wash 4 times, at 3-day intervals; may also use as dip. Not approved for use in cats. 100 mL |
| ***Clinafarm EC***® (Schering Plough/ Intervet) | **Emulsifiable concentrate:** 13.8% | OTC<br>EPA Pesticide | Benzyl alcohol, alchyl sulfosuccinate (surfactants). Labeled for the control of Aspergillus fumigates contamination in poultry hatchery equipment. |

### VETERINARY-LABELED ENILCONAZOLE TOPICAL PRODUCTS
(continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Clinafarm EC®*** (Schering Plough/ Intervet) | | | Extra-label use for feline dermatophytosis. Corrosive. Undiluted solution may cause irreversible eye damage. Labeling includes several warnings on ingestion or exposure. Proper precautions (safety glasses and gloves) should be taken to limit human exposure. 750 mL |

### HUMAN-LABELED ENILCONAZOLE TOPICAL PRODUCTS
None.

## Ketoconazole

*For **systemic** use, refer to Section 1: Systemic Drugs.*
*For **otic** use, refer to the Otic section.*

### INDICATIONS
Topical ketoconazole has activity against dermatophytes and yeast, being especially useful for the treatment of *Malassezia* dermatitis. Topical ketoconazole shampoos are generally ineffective (or minimally effective) when used alone for dermatophytosis.

### MECHANISM OF ACTION
Ketoconazole, like other azoles, inhibits the biosynthesis of ergosterol, an essential component of fungal cell membranes, leading to increased membrane permeability and allowing leakage of intracellular components.

### SUGGESTED USES/DOSAGES
If using spray or wipes/pads: 1–2 times a day or according to patient's needs. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo or conditioner: daily to weekly baths/after baths according to patient's needs. It is important to leave the shampoo in contact with the skin for at least 10 minutes prior to rinsing well. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS
Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying. Skin irritation is possible.

## VETERINARY-LABELED KETOCONAZOLE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Ketochlor® Shampoo*** (Virbac) | **Shampoo:** Ketoconazole 1% Chlorhexidine 2.3% | Rx | *Spherulite*® microcapsules. Glycotechnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside), chitosanide. Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |
| ***Mal-A-Ket® Shampoo*** (Dechra) | **Shampoo:** Ketoconazole 2% Chlorhexidine gluconate 2% Acetic acid 2% | Sold only through licensed veterinarians | 1 oz pouch, 8 oz, 1 gal |
| ***Pharmaseb® Shampoo*** (Animal Pharmaceuticals) | **Shampoo:** Ketoconazole 1% Chloroxylenol 2% | OTC | Labeled for dogs and cats. 8 oz, 16 oz, gal |
| ***Malacetic Ultra® Shampoo*** (Dechra) | **Shampoo:** Ketoconazole 0.15% Acetic acid 1% Boric acid 2% Hydrocortisone 1% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***ResiKetochlor® Leave-on Conditioner*** (Virbac) | **Conditioner:** Ketoconazole 1% Chlorhexidine gluconate 2.3% | Rx | *Spherulite*® microcapsules. Glycotechnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside), chitosanide. Labeled for dogs and cats. 8 oz |

## VETERINARY-LABELED KETOCONAZOLE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Malacetic Ultra® Spray*** (Dechra) | **Spray:** Ketoconazole 0.15% Hydrocortisone 1% Acetic acid 1% Boric acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Mal-A-Ket Plus TrizEDTA® Spray*** (Dechra) | **Spray:** Ketoconazole 0.15% Chlorhexidine gluconate 0.15% TrizEDTA | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Ketoseb-D® Spray*** (Sogeval) | **Spray:** Ketoconazole 1% Chlorhexidine gluconate 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz |
| ***Pharmaseb® Spray*** (Animal Pharmaceuticals) | **Spray:** Ketoconazole 0.3% Chloroxylenol 0.3% | OTC | Water-based. Propylene glycol, benzyl alcohol. Labeled for dogs and cats. 4 oz, 8 oz |
| ***Pharmaseb® Wipes*** (Animal Pharmaceuticals) | **Wipes:** Ketoconazole 0.3% Chloroxylenol 0.3% | OTC | Water-based. Labeled for dogs and cats. 60 count |

## VETERINARY-LABELED KETOCONAZOLE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Ketoseb-D® Wipes*** (Sogeval) | **Wipes:** Ketoconazole 1% Chlorhexidine gluconate 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 50 count jar |
| ***Mal-A-Ket® Wipes*** (Dechra) | **Wipes:** Ketoconazole 1% Chlorhexidine gluconate 2% Acetic acid 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 50 count jar |
| ***T8 Keto® Flush*** (TEVA/DVM) | **Flush:** Ketoconazole 0.1% TrizEDTA | Sold only through licensed veterinarians | Indicated as cleansing for skin and ears. Labeled for dogs and cats. 4 oz, 12 oz |
| ***TrizUltra + Keto®*** (Dechra) | **Flush:** Ketoconazole 0.15% TrizEDTA | Sold only through licensed veterinarians | Indicated as cleansing for skin and ears. Labeled for dogs and cats. 4 oz, 12 oz |
| ***Ketoseb-D® Flush*** (Sogeval) | **Flush:** Ketoconazole 0.2% Chlorhexidine 0.2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 4 oz, 16 oz |
| ***Pharmaseb® Flush*** (Animal Pharmaceuticals) | **Flush:** Ketoconazole 0.3% Chloroxylenol 0.3% | OTC | Water-based. Propylene glycol, benzyl alcohol. Can be used as a cleanse agent for skin and ears. Labeled for dogs and cats. 4 oz, 8 oz |

### HUMAN-LABELED KETOCONAZOLE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Nizoral A-D®*** (McNeil) | **Shampoo:** 1% | OTC | 60 mL, 120 mL, 210 mL |
| **Ketoconazole** (Clay-Park) | **Shampoo:** 2% | Rx | 118 mL |
| **Ketoconazole** (Teva)<br>**Ketoconazole** (Fougera) | **Cream:** 2% | Rx | Aqueous vehicle containing cetyl alcohol, stearyl alcohol, sodium sulfite. 15 g, 30 g, 60 g |
| ***Nizoral®*** (McNeil) | **Cream:** 2% | Rx | 15 g, 30 g, 60 g |

## Lime Sulfur (Sulfurated Lime Solution)

### INDICATIONS

Lime sulfur applications are very effective and relatively inexpensive as a generalized topical treatment for dermatophytosis. Both lime sulfur and enilconazole are thought to have the best topical activity against *Microsporum canis*. For feline dermatophytosis, it should be used as an adjunct to systemic antifungal therapy. Lime sulfur is anecdotally reported as the most efficacious treatment of surface demodicosis (*Demodex gatoi*) in cats. It can also be useful in the adjunctive treatment of *Malassezia* dermatitis, cheyletiellosis, chiggers, notoedric mange, fur mites, lice, canine demodicosis, and sarcoptic mange.

### MECHANISM OF ACTION

Lime sulfur has antibacterial and antifungal/anti-yeast properties secondary to the formation of pentathionic acid and hydrogen sulfide after application. Lime sulfur may also have keratolytic, keratoplastic, antiparasitic, and antipruritic effects.

### SUGGESTED USES/DOSAGES

Labeled dose for *LymDyp®* and *Vet Solutions Lime Sulfur Dip®*: Shake well; dilute 4 oz of concentrate in 1 gal of water. Mix well. Apply as a dip at 5–7 day intervals. Do not rinse. For more chronic or resistant cases, may be used at 8 oz per gal. Labeled dose for *LimePlus Dip®* and *Lime Sulfur Dip®*: Pour 4 oz of concentrate in 1 gal of water. Mix well. Bathe animal prior to application. Rinse off shampoo. Apply as a dip the entire content of diluted *LimePlus Dip®* onto pet and work into skin. Allow to dry on the animal. Do not rinse. Repeat the application every 5–7 days. When used for dermatophytosis, once- to twice-weekly treatments have been recommended until two consecutive negative cultures are obtained. When used for confirmed cases of feline surface demodicosis, applications are recommended every 5–7 days for a total of 6–8 treatments. If using lime sulfur as a treatment trial (i.e., mites are not found on skin scrapings) for surface demodicosis, three applications should be performed, and if there is significant improvement in clinical signs 3–5 more applications are performed to complete

treatment. If no significant improvement is seen after three applications, demodicosis should be ruled out and other diagnoses should be considered.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes and mucous membranes. Lime sulfur has a very unpleasant smell. Can stain porous surfaces (e.g., concrete, porcelain) or permanently discolor jewelry. Clients should wear gloves and protect skin and eyes from solution. Application should be performed in a well-ventilated area or clients should wear a protective (respirator-type) mask. While reasonably non-toxic, lime sulfur may cause skin irritation or drying. Adding mineral oil to the solution may reduce its drying effects. Lime sulfur can (temporarily) stain light-colored fur and rarely cause hair loss on the pinnae in cats. Lime sulfur's odor may persist on treated animals, but generally is tolerable once the patient dries. Oral ingestion can rarely cause nausea and oral ulcers, mainly in cats; the use of an Elizabethan collar until the solution dries may help prevent these adverse effects.

### VETERINARY-LABELED LIME SULFUR TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***LymDyp®*** (TEVA/DVM) | **Concentrate:** 76.9% | Sold only through licensed veterinarians | Labeled for dogs, puppies, kittens and cats. Shake well and dilute before use (see dosages above). 16 oz, 1 gal |
| ***LimePlus Dip®*** (Dechra) | **Concentrate:** 97.8% | Sold only through licensed veterinarians | Labeled for dogs, puppies, kittens and cats. Shake well and dilute before use (see dosages above). 4, 16 oz, 1 gal |
| ***Vet Solutions Lime Sulfur Dip®*** (Vetoquinol) | **Concentrate:** 97.8% | OTC | Labeled for dogs, puppies, kittens and cats. Shake well and dilute before use (see dosages above). 4, 16 oz |
| ***Lime Sulfur Dip®*** (Davis) | **Concentrate:** 97.8% | OTC | Labeled for dogs, puppies, kittens and cats. Shake well and dilute before use (see dosages above). 16 oz |

### HUMAN-LABELED LIME SULFUR TOPICAL PRODUCTS

None.

## Miconazole Nitrate

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Topical miconazole has activity against dermatophytes and yeast; it is especially effective for the treatment of *Malassezia* dermatitis. Patients with severe, generalized infections may require systemic therapy. Lotions, sprays, and creams are generally used for localized lesions associated with *Malassezia* or dermatophytes. Topical miconazole products are generally ineffective (or minimally effective) when used alone for dermatophytosis; adjunctive systemic treatment is usually required.

### MECHANISM OF ACTION

Miconazole's actions are a result of altering the permeability of fungal cellular membranes and interfering with peroxisomal and mitochondrial enzymes, leading to intracellular necrosis. Miconazole products are fungicidal with repeated application.

### SUGGESTED USES/DOSAGES

If using spray, creams, lotions or wipes/pads: application once or twice a day or according to the patient's needs. Do not let the animal lick or chew at treated areas for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. If shampoo or conditioner: daily to weekly baths/after baths according to the patient's needs. It is important to leave medicated shampoos in contact with the skin for at least 10 minutes prior to rinsing well. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Skin irritation is unlikely to occur, but in very inflamed, eroded to ulcerated skin, the pledgets/wipes, towelettes, and spray containing alcohol (e.g., *Malaseb*®) can be severely irritant. Avoid contact with eyes. Clients should wash hands after application or wear gloves when applying.

### VETERINARY-LABELED MICONAZOLE NITRATE TOPICAL PRODUCTS

Miconazole nitrate is the salt generally used in pharmaceutical products. While, technically, a 1% concentration of miconazole nitrate contains <1% miconazole, the following products are rounded to the closest full percent regardless of how much miconazole base is actually in each product.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s); |
|---|---|---|---|
| ***Micro-Pearls Advantage Miconazole® Spray*** (Vetoquinol) | **Spray:** 1% | Rx | Labeled for dogs and cats. 4 oz |
| ***Conofite® Spray 1%*** (Intervet/Schering-Plough) ***Micaved® Spray 1%*** (Vedco) | **Spray:** 1% | Rx | Labeled for dogs and cats. 60 mL |

**VETERINARY-LABELED MICONAZOLE NITRATE TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s); |
|---|---|---|---|
| ***Malaseb® Spray*** (TEVA/DVM) | **Spray:** Miconazole 2% Chlorhexidine 2% | Sold only through licensed veterinarians | Alcohol 30%. Labeled for dogs and cats. 8 oz |
| ***Micazole® Spray*** (Butler) | **Spray:** 1% | Sold only through licensed veterinarians. | Labeled for dogs and cats. 120 mL, 240 mL |
| ***Priconazole® Spray 1%*** (First Priority) | **Spray:** 1% | Rx | Polyethylene glycol, ethyl alcohol. Labeled for dogs and cats. 120 mL, 240 mL |
| ***Malaseb® Flush*** (TEVA/DVM) | **Flush:** Miconazole 0.2% Chlorhexidine 0.2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 4 oz, 12 oz |
| ***Malaseb® Concentrate Rinse*** (TEVA/DVM) | **Rinse:** Miconazole 0.2% Chlorhexidine 0.2% | Sold only through licensed veterinarians | Labeled for dogs and cats. Must be diluted before use. 8 oz, 32 oz |
| ***Malaseb® Pledgets*** (TEVA/DVM) | **Pledgets:** Miconazole 20 mg Chlorhexidine 20 mg | Sold only through licensed veterinarians | Alcohol 30%. Labeled for dogs, and cats. 60 count jar |
| ***Malaseb® Towelettes*** (TEVA/DVM) | **Towelettes:** Miconazole 20 mg Chlorhexidine 20 mg | Sold only through licensed veterinarians | Alcohol 30%. Labeled for dogs, and cats. 12 and 60 count jars |
| ***Conofite Cream® 2%*** (Intervet/Schering-Plough) | **Cream:** 2% | Rx | Labeled for dogs and cats. 15 g |
| ***ResiZole Leave-On Lotion®*** (Virbac) | **Lotion:** 2% | Rx | Labeled for dogs and cats. 8 oz |
| ***Miconosol Lotion® 1%*** (Med-Pharmex) | **Lotion:** 1% | Rx | Polyethylene glycol, ethyl alcohol. Labeled for dogs and cats. 60 mL |
| ***Micaved Lotion® 1%*** (Vedco) | **Lotion:** 1% | Rx | Polyethylene glycol, ethyl alcohol. Labeled for dogs and cats. 60 mL |

**VETERINARY-LABELED MICONAZOLE NITRATE TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s); |
|---|---|---|---|
| ***Micazole Lotion® 1%*** (Butler) | **Lotion:** 1% | Rx | Polyethylene glycol, ethyl alcohol. Labeled for dogs and cats. 60 mL |
| ***Priconazole Lotion® 1%*** (First Priority) | **Lotion:** 1% | Rx | Polyethylene glycol, ethyl alcohol. Labeled for dogs and cats. 60 mL |
| ***Vet Solutions Sebazole® Shampoo*** (Vetoquinol) | **Shampoo:** Miconazole 2% Chloroxylenol 2% Salicylic acid 2% Sodium thiosulfate 2% | Rx | Labeled for dogs and cats. 8 oz, 12 oz, 1 gal |
| ***Dermazole® Shampoo*** (Virbac) | **Shampoo:** Miconazole 2% Salicylic acid 2% | Rx | Labeled for dogs and cats. 8, 16 oz |
| ***Malaseb® Shampoo*** (TEVA/DVM) | **Shampoo:** Miconazole 2% Chlorhexidine 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8, 12 oz, 1 gal |
| ***Surolan® Otic Suspension*** (Vetoquinol) | **Suspension (otic):** Miconazole 23 mg/mL Polymyxin B sulfate 0.5293 mg/mL Prednisolone acetate 5 mg/mL | Rx | For otic use in dogs only. Extra-label use for skin lesions associated with bacterial and/or fungal skin infections and inflammation. 15 mL, 30 mL |
| ***Easotic®*** (Virbac) | **Suspension (otic):** Hydrocortisone aceponate 1.11 mg/mL Gentamicin sulfate 1505 IU/mL Miconazole nitrate 15.1 mg/mL | Rx (not available in US, available in EU) | Labeled for otic use in dogs. May be used extra-label to treat skin infections (e.g., bacterial and/or *Malassezia* dermatitis) associated with inflammation in dogs and cats. 10 mL |

### HUMAN-LABELED MICONAZOLE NITRATE TOPICAL PRODUCTS

In addition to the products listed below, there are 2% topical vaginal creams, vaginal suppositories, powders, and spray powders available. Most human-labeled products are OTC.

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Micatin***® (Pharmacia and Upjohn)<br>***Neosporin AF***® (Pfizer)<br>***Prescription Strength Desenex***® (Ciba) | **Spray:** 2% | OTC | Depending on product: 90 mL, 115 mL |
| ***Tetterine***® (SSS Co.) | **Ointment:** 2% | | 30 mL |
| ***Zeosorb-AF***® (Stiefel) | **Gel:** 2% | OTC | 24 g |
| **Miconazole Nitrate** (Taro)<br>***Micatin***® (Pharmacia and Upjohn)<br>***Monistat-Derm***® (Orto)<br>***Neosporin AF***® (Pfizer) | **Cream:** 2% | OTC | Depending on product: 15 g, 30 g, 90 g |

## Nystatin

*For **otic** use, refer to the Otic section.*

### INDICATIONS

Because of limited dosage forms and other alternative anti-yeast medications readily available, nystatin is not usually used alone in small animal medicine. The combination products (e.g., *Panolog*®) can be useful for localized yeast skin infections and have been used for ear infections for many years.

### MECHANISM OF ACTION

Nystatin has efficacy against yeast (e.g., *Candida* and *Malassezia*) and molds (e.g., *Aspergillus*). It is fungistatic in vitro. Similar to other polyene antifungal agents, nystatin binds to ergosterol in the fungal cell membranes, thereby increasing membrane permeability and resulting in leakage of intracellular components and eventual cell death. Nystatin does not have activity against bacteria.

### SUGGESTED USES/DOSAGES

Treatment of focal yeast skin infections and otitis externa associated with yeast. Re-evaluate the patient before discontinuing treatment. For skin lesions apply 1–2 times daily or according to the patient's needs. The veterinary-labeled products contain triamcinolone; therefore, duration of treatment, especially for

the skin, should be short to avoid potential corticosteroid side effects including skin atrophy. Do not let the animal lick or chew at treated area(s) for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. When using to treat infectious otitis, apply the medication twice daily and re-evaluate the patient before discontinuing treatment. Treatment of otitis should be continued until 1 week after negative cytology.

### PRECAUTIONS/ADVERSE EFFECTS

Nystatin alone is very safe, although hypersensitivity reactions are possible. The combination veterinary products are usually well tolerated when used on skin; however, neomycin can cause localized sensitivity. Use combination products containing glucocorticoids carefully because of the potential side effects, including cutaneous atrophy. Because some of the products contain polyethylene glycol, nephrotoxicity may potentially develop if they are used on extensive deep lesions. Anecdotally, very rarely, renal toxicity has been reported. Should use caution in conditions where absorption of large quantities of polyethylene glycol is possible, especially if there is evidence of renal impairment. Clients should wash hands after application or wear gloves when applying. Avoid contact with eyes. At least a 2-week withdrawal period is recommended prior to intradermal or allergy serum testing for products containing corticosteroids such as triamcinolone. Use caution when using the medications containing antibiotic such as neomycin empirically, to avoid bacterial resistance.

### VETERINARY-LABELED NYSTATIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Animax®* *Ointment*** (Dechra)<br>***Derma Vet®* *Ointment*** (Med-Pharmex)<br>***Dermalog®* *Ointment*** (RXV)<br>***Dermalone®* *Ointment*** (Vedco)<br>***Quadritop®* *Ointment*** (Butler)<br>***Panolog®* *Ointment*** (Fort Dodge)<br>***Entederm®* *Ointment*** (VetOne) | **Ointment:** Nystatin 100,000 units Triamcinolone acetonide 1 mg Neomycin sulphate 2.5 mg Thiostrepton 2500 units | Rx (*Animax®* is sold only through licensed veterinarians) | All products listed contain polyethylene glycol, are labeled for dogs and cats, and are also approved for otic use in dogs and cats. 7.5 mL, 15 mL, 30 mL, 240 mL (*Animax®* and *Dermalog®*) 7.5 mL, 15 mL, 30 mL (*Derma Vet®*) 7.5 mL, 15 mL, 30 mL (*Dermalone®*) 240 mL (*Quadritop®*) 15 g (*Panolog®*) |

### VETERINARY-LABELED NYSTATIN TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Animax®*** ***Cream*** (Dechra) ***Panolog®*** ***Cream*** (Fort Dodge) ***Cortalone®*** ***Cream*** (Vedco) ***Derma-Vet®*** ***Cream*** (Med-Pharmex) | **Cream:** Nystatin 100,000 units Triamcinolone acetonide 1 mg Neomycin sulfate 2.5 mg Thiostrepton 2500 units | Rx or sold only through licensed veterinarians | Cetearyl alcohol and propylene glycol (*Panolog®* and *Cortalone®*). Cetearyl alcohol and polyethylene glycol (*Derma-Vet® Cream*). Alcohol ether, propylene glycol (*Animax®*). All products listed provide four basic therapeutic effects: anti-inflammatory, antipruritic, antifungal, and antibacterial. *Panolog®*, *Derma-Vet®* and *Animax®* are labeled for dogs and cats. Cortalone® is labeled for dogs only Sizes for all products: 7.5 g, 15 g |

### HUMAN-LABELED NYSTATIN TOPICAL PRODUCTS

In addition to the products listed below, there are vaginal tablets and oral products.

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***Mycostatin®*** (Westwood Squibb) **Nystatin** (various) ***Nystop®*** (Paddock) ***Pedi-Dri®*** (Pedinol) | **Powder:** 100,000 units/g | Rx | Depending on product: 15g, 30g, 60 g |
| ***Mycostatin®*** (Westwood Squibb) **Nystatin** (various) ***Nilstat®*** (Lederle) | **Ointment:** 100,000 units/g | Rx | Depending on product: 15g, 30 g |

**HUMAN-LABELED NYSTATIN TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***Mycostatin®*** (Westwood Squibb) **Nystatin** (various) ***Nilstat®*** (Lederle) | **Cream:** 100,000 units/g | Rx | Depending on product: 15g, 30g, 240 g |
| **Nystatin-Triamcinolone Acetonide** (various) ***Mycogen II®*** (Clay-Park) ***Mycolog-II®*** (Bristol Meyers Squibb) ***Myco-Triacet II®*** (TEVA) | **Ointment:** Nystatin 100,000 units/g Triamcinolone acetonide 0.1% | Rx | Depending on product: 15g, 30g, 60g, 120 g |
| **Nystatin-Triamcinolone Acetonide** (various) ***Myco-Biotic II®*** (Moore) ***Mycogen II®*** (Clay-Park) ***Mycolog-II®*** (Bristol Meyers Squibb) ***Myconel®*** (Marnel) ***Myco-Triacet II®*** (Lemmon) | **Cream:** Nystatin 100,000 units/g Triamcinolone acetonide 0.1% | Rx | Depending on product: 1.5 g pkt, 15g, 30g, 60g, 120 g |

## Selenium Sulfide

### INDICATIONS

Selenium sulfide is useful in seborrheic disorders (mainly for seborrhea oleosa) and for adjunctive treatment of *Malassezia* dermatitis, particularly in dogs exhibiting signs of waxy, greasy, or scaly dermatitis. There may be some residual activity on the skin.

### MECHANISM OF ACTION

Selenium sulfide possesses antifungal (including sporicidal activity), keratolytic, keratoplastic, and degreasing properties. It affects cells of the epidermis and follicular epithelium (alters the epidermal turnover) and interferes with hydrogen bond formation of keratin, thereby reducing corneocyte production. The antifungal mechanism of action of selenium sulfide is not well understood.

### SUGGESTED USES/DOSAGES

When using a medicated shampoo, it is important to allow at least 10 minutes contact time to obtain the desirable effect of active ingredients. Another acceptable regimen is to allow the shampoo to act for 3–5 minutes, rinse it thoroughly, and then repeat the procedure. It is important to completely rinse the shampoo to prevent skin irritation and/or excessive drying. The frequency of shampooing will vary according to the patient's needs.

### PRECAUTIONS/ADVERSE EFFECTS

Selenium sulfide products should not be used on cats. Avoid contact with eyes. Selenium sulfide can discolor jewelry. Clients should wear gloves when using selenium sulfide products. Selenium sulfide can be irritant, and can cause excessive drying and hair coat staining. Mucous membranes and scrotal areas may be particularly sensitive to the irritant effects of the selenium sulfide. A rebound seborrhea may occur, where signs not only recur after discontinuation, but worsen. Vomiting, diarrhea, and nausea may result from ingestion of shampoo containing selenium sulfide, and neurologic signs may occur if large quantities are retained in the gastrointestinal tract long enough for systemic absorption to occur.

### VETERINARY-LABELED SELENIUM SULFIDE TOPICAL PRODUCTS

Currently, there are no labeled veterinary products containing selenium sulfide available in the US. *Seleen*® shampoo (selenium sulfide 1% in a mild detergent base) in 25 mL and 100 mL bottles is available in EU.

### HUMAN-LABELED SELENIUM SULFIDE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***Head & Shoulders Intensive Treatment***® (Procter & Gamble) | **Shampoo/lotion:** 1% | OTC | 400 mL |
| **Selenium Sulfide** (various) | **Shampoo/lotion:** 1% | OTC | 210 mL |
| ***Selsun Blue Medicated Treatment***® (Chattem) | **Shampoo/lotion:** 1% | OTC | Menthol. 325 mL |
| **Selenium Sulfide** (Alpharma) | **Shampoo:** 2.5% | OTC | 4 oz |
| **Selenium Sulfide** (various) | **Lotion:** 2.5% | Rx | 120 mL |
| ***Selsun***® (Abbott) | **Lotion/shampoo:** 2.5% | Rx | 120 mL |

## Terbinafine Hydrochloride

*For **systemic** use, refer to Section 1: Systemic Drugs.*

### INDICATIONS

An allylamine antifungal agent, topical terbinafine may be useful as adjunctive therapy for localized skin lesions associated with *Malassezia*. It may also be used as adjunctive therapy for dermatophytosis in cats and dogs.

### MECHANISM OF ACTION

Terbinafine hydrochloride (HCl) inhibits the biosynthesis of ergosterol by inhibiting the fungal squalene epoxidase enzyme. The resultant depletion of ergosterol within the fungal cell membrane and the intracellular accumulation of squalene are believed to be responsible for the fungicidal effect of terbinafine.

### SUGGESTED USES/DOSAGES

Apply the product to the affected area(s) twice daily until complete resolution of the skin lesions. It is recommended to prevent the animal from licking or chewing at the treated area(s) for at least 30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes, mucous membranes, and open wounds. Clients should wash hands after application or wear gloves when applying the drug. Skin irritation is possible, but unlikely to occur.

### VETERINARY-LABELED TERBINAFINE TOPICAL PRODUCTS

None.

### HUMAN-LABELED TERBINAFINE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***DesenexMax®*** (Novartis) **Generic** | **Cream:** 1% | OTC | Cetyl alcohol, cetyl palmitate, isopropyl myristate, polysorbate 60, sodium hydroxide, sorbitan monostearate, stearyl alcohol, benzoyl alcohol. 12 g |
| ***Lamisil AT®*** (Novartis) | **Cream:** 1% | OTC | Cetyl alcohol, cetyl palmitate, isopropyl myristate, poly sorbate 60, sodium hydroxide, sorbitan monostearate, stearyl alcohol, benzoyl alcohol. 15 g, 30 g |
| ***Lamisil AT®*** (Novartis) | **Spray:** 1% | OTC | Ethanol, propylene glycol. 30 mL |
| ***Lamisil AT®*** (Novartis) | **Gel:** 1% | OTC | Isopropyl myristate, ethanol, benzyl alcohol and others. 12 g, 16 g |

# ANTISEBORRHEIC AGENTS

*Refer also to:*
***Benzoyl Peroxide*** *in the Antibacterial section.*
***Essential fatty acids*** *in the Non-Corticosteroid Anti-inflammatory section.*
***Selenium Sulfide*** *in the Antifungal section.*

## Phytosphingosine Hydrochloride

*For products containing* ***phytosphingosine combined with other active ingredients****, refer to other main active ingredients in Section 2.*

### INDICATIONS

Phytosphingosine hydrochloride (HCl) is a unique topical antiseborrheic compound used for seborrhea sicca or oleosa in dogs.

### MECHANISM OF ACTION

Phytosphingosine hydrochloride is keratoregulating, sebolytic, sebum-regulating, anti-inflammatory (reduces secretion of the inflammatory cytokine, IL-1), antibacterial, and antifungal and it restores the lipid barrier.

### SUGGESTED USES/DOSAGES

Follow label directions for each product.

### PRECAUTIONS/ADVERSE EFFECTS

Phytosphingosine is non-toxic and non-irritant; however, some of the other ingredients in the commercial products can rarely be sensitizing/irritant.

### VETERINARY-LABELED PHYTOSPHINGOSINE HYDROCHLORIDE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Douxo®*** ***Seborrhea Shampoo*** (Sogeval) | **Shampoo:** 0.1% | Sold only through licensed veterinarians | Other active ingredients: cocoylamidopropyl betaine, sodium laureth sulfate, decylglucoside, polyquaternium 7 and 10. It also contains fomblin (stabilizer), cocoglucoside, and coconut alcohol. Labeled for dogs and cats. 6.8 oz, 16.9 oz, 0.8 gal |

**VETERINARY-LABELED PHYTOSPHINGOSINE HYDROCHLORIDE TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Douxo® Seborrhea MicroEmulsion Spray*** (Sogeval) | **Spray:** 0.2% | Sold only through licensed veterinarians | Other active ingredients: hexyl laurate, cetearyl alcohol, PEG40 castor oil, sodium cetearyl sulfate, polyoxyethylene 20, cetylstearyl alcohol, quaternium 82. It also contains *Boswellia serrata* extract and glycerin. Labeled for dogs and cats. 6 oz, 8 oz |
| ***Douxo® Seborrhea Spot-on*** (Sogeval) | **Spot-on solution:** 1% | Sold only through licensed veterinarians | Ethoxydiglycol, povidone. Labeled for dogs and cats. 25 2 mL pipettes/box |

### HUMAN-LABELED PHYTOSPHINGOSINE TOPICAL PRODUCTS

There are several OTC human cosmetic products containing phytosphingosine in the US. These products target mostly lipid barrier restoration and include *Epionce Extreme Barrier Cream®*, *Kronos Phyx Overnight Repair Mask®*, *Skinceuticals Age Interruptor®*, and *Darphin Lipid Replenishing Soothing Balm®*.

## Salicylic Acid

### INDICATIONS

Salicylic acid shampoos, in which salicylic acid is often combined with sulfur, are typically employed to treat patients with seborrheic disorders exhibiting mild to moderate scaling (seborrhea sicca). When salicylic acid and sulfur are combined with benzoyl peroxide, the shampoos can also be used to manage seborrhea oleosa.

### MECHANISM OF ACTION

Salicylic acid has mild antipruritic, antibacterial (bacteriostatic), keratoplastic, and keratolytic actions. Lower concentrations (0.1–2%) are primarily keratoplastic and higher concentrations (3–6%) keratolytic. Salicylic acid lowers skin pH, increases corneocyte hydration, and dissolves the intercellular adhesion between corneocytes. Salicylic acid and sulfur are thought to be synergistic in their keratolytic actions.

### SUGGESTED USES/DOSAGES

When using a medicated shampoo, it is important to allow 10 minutes contact time to obtain the desirable effect of active ingredients. Another acceptable regimen is to allow the shampoo to act for 3–5 minutes, rinse it thoroughly, and then repeat the procedure. It is important to completely rinse the shampoo to prevent skin irritation and/or excessive drying. The frequency of shampooing will vary according to the patient's needs. For veterinary-labeled products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes, mucous membranes, and open wounds. Clients should wash hands after application or wear gloves when applying the shampoo. Skin irritation is possible. Burning, itching, pain, erythema, and swelling can occur from salicylic acid, particularly when it is used in high concentrations (>2%). A rebound seborrheic effect can occur when using shampoo products containing salicylic acid.

### VETERINARY-LABELED SALICYLIC ACID TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Derma-Clens®*** (Pfizer) | **Cream** (% not listed): Salicylic acid Benzoic acid Malic acid | Sold only through licensed veterinarians | Facilitates removal of debris and promotes healing by removing non-living tissue from wounds. Labeled for dogs and cats. 1 oz, 14 oz |
| ***Dermazole® Shampoo*** (Virbac) | **Shampoo:** Salicylic acid 2% Miconazole 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz |
| ***Keratolux® Shampoo*** (Virbac) | **Shampoo:** Salicylic acid 1% Zinc gluconate 0.5% Pyridoxine hydrochloride 0.5% | Sold only through licensed veterinarians | *Spherulite®* microcapsules, glycotechnology (monosaccharides: L-rhamnose, D-mannose, D-galactose; polysaccharide: alkyl polyglucoside), chitosanide. Labeled for dogs and cats. 8 oz, 16 oz |
| ***Vet Solutions Universal Medicated Shampoo®*** (Vet Solutions) | **Shampoo:** Salicylic acid 2% Chloroxylenol 2% Sodium thiosulfate 2% (source of sulfur) | OTC | Labeled for dogs and cats. 16 oz, 1 gal |

## VETERINARY-LABELED SALICYLIC ACID TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| **Medicated Shampoo** (Sogeval) | **Shampoo:** Salicylic acid 2% Chloroxylenol 2% Sodium thiosulfate 2% (source of sulfur) | Sold only through licensed veterinarians | Labeled for dogs and cats. 16 oz |
| ***Micro Pearls Advantage Seba-Hex® Shampoo*** (Vetoquinol) | **Shampoo:** Salicylic acid 2% Chlorhexidine 2% Sulfur 2% | Sold only through licensed veterinarians | *Novasome®* microvesicles. Shake well; wear gloves. Labeled for dogs and cats. 8 oz |
| **Micro Pearls Advantage Seba-Moist Shampoo®** (Vetoquinol) | **Shampoo:** Salicylic acid 2% Sulfur 2% | Sold only through licensed veterinarians | *Novasome®* microvesicles. Shake well; wear gloves. Labeled for dogs and cats. 12 oz, 1 gal |
| ***Nova Pearls Medicated Dandruff Shampoo®*** (Tomlyn) | **Shampoo:** Salicylic acid 2% Sulfur 2% | OTC | *Novasome®* moisturizers. Labeled for dogs and cats. 12 oz, 1 gal |
| ***Oxiderm® Shampoo*** (Sogeval) | **Shampoo:** Salicylic acid 2% Benzoyl peroxide 3% Micronized sulfur 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz |
| ***Oxiderm Shampoo + PS®*** (Sogeval) | **Shampoo:** Salicylic acid 2% Benzoyl peroxide 3% Micronized sulfur 2% Phytosphingosine hydrochloride 0.05% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |

### VETERINARY-LABELED SALICYLIC ACID TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Sebalyt® Shampoo*** (TEVA/DVM) | **Shampoo:** Salicylic acid 2% Sulfur 2% Triclosan 0.5% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 12 oz, 1 gal |
| ***Sebolux® Shampoo*** (Virbac) | **Shampoo:** Salicylic acid 2% Elemental sulfur 2% | Sold only through licensed veterinarians | *Spherulite®* microcapsules, chitosanide, urea, glycerin. Ingredients in free form and in *Spherulites®*. Shake well; wear gloves. Labeled for dogs and cats. 8 oz, 15.5 oz |

### HUMAN-LABELED SALICYLIC ACID TOPICAL PRODUCTS

There are many topical salicylic acid products labeled for human use, including topical creams, ointments, transdermal patches, liquids, and gels that are principally labeled for wart removal. Except for one product (*Salex®*; 6% cream), they are available OTC. There are also many OTC skin cleansers and shampoos containing salicylic acid and usually sulfur (sometimes coal tar or menthol). As there are several similar products formulated and labeled for animal use, human products are not listed here. For more information on these products, refer to a comprehensive human drug reference (e.g., *Facts and Comparisons* or *Micromedex*) or contact a pharmacist.

## Sulfur, Precipitated

### INDICATIONS

Shampoos containing sulfur, often combined with salicylic acid, are typically used to treat patients with seborrheic disorders exhibiting mild to moderate scaling.

### MECHANISM OF ACTION

Sulfur has keratoplastic and keratolytic actions. Lower concentrations of sulfur are primarily keratoplastic by assisting the conversion of cysteine to cystine, which appears to be an important factor in the maturation of corneocytes. As with salicylic acid, the keratolytic effects of sulfur increase with its concentration. Salicylic acid and sulfur are believed to be synergistic in their keratolytic actions. Sulfur can be mildly antipruritic, but it is not a good degreaser. Sulfur also has antibacterial, antifungal, and antiparasitic effects as a result of its conversion to hydrogen sulfide and pentathionic acid by bacteria and keratocytes.

### SUGGESTED USES/DOSAGES

When using a medicated shampoo, it is important to allow 10 minutes contact time to obtain the desirable effect of active ingredients. Another acceptable regimen is to allow the shampoo to act for 3–5 minutes, rinse it thoroughly, and then repeat the procedure. It is important to completely rinse the shampoo to prevent skin irritation and/or excessive drying. The frequency of shampooing will vary according to the patient's needs. For veterinary products, refer to product label for details on individual use.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes, mucous membranes, and open wounds. Clients should wash hands after application or wear gloves when applying. Sulfur can be drying, and can cause pruritus and skin irritation. Residual odor is often bothersome to clients. Sulfur may stain fabrics and hairs. A rebound seborrheic effect can occur when using shampoo products containing sulfur.

### VETERINARY-LABELED SULFUR TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Vet Solutions Universal Medicated Shampoo®*** (Vet Solutions) | **Shampoo:** Sodium thiosulfate 2% (source of sulfur) Salicylic acid 2% Chloroxylenol 2% | OTC | Labeled for dogs and cats. 16 oz, 1 gal |
| **Medicated Shampoo** (Sogeval) | **Shampoo:** Sodium thiosulfate 2% (source of sulfur) Salicylic acid 2% Chloroxylenol 2% | Sold only through licensed veterinarians | Labeled for dogs and cats. 16 oz |
| ***Micro Pearls Advantage Seba-Hex® Shampoo*** (Vetoquinol) | **Shampoo:** Sulfur 2% Chlorhexidine 2% Salicylic acid 2% | Sold only through licensed veterinarians | *Novasome®* microvesicles. Shake well; wear gloves. Labeled for dogs and cats. 8 oz |
| ***Micro Pearls Advantage Seba-Moist® Shampoo*** (Vetoquinol) | **Shampoo:** Sulfur 2% Salicylic Acid 2% | Sold only through licensed veterinarians | *Novasome®* microvesicles. Shake well; wear gloves. Labeled for dogs and cats. 12 oz, 1 gal |
| ***Nova Pearls Medicated Dandruff Shampoo®*** (Tomlyn) | **Shampoo:** Sulfur 2% Salicylic Acid 2% | OTC | *Novasome®* moisturizers. Labeled for dogs and cats. 12 oz, 1 gal |

**VETERINARY-LABELED SULFUR TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Oxiderm® Shampoo*** (Sogeval) | **Shampoo:** Sulfur (micronized) 2% Salicylic acid 2% Benzoyl peroxide 3% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz |
| ***Oxiderm Shampoo + PS®*** (Sogeval) | **Shampoo:** Micronized sulfur 2% Salicylic acid 2% Benzoyl peroxide 3% Phytosphingosine hydrochloride 0.05% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8 oz, 16 oz, 1 gal |
| ***Paraguard® Shampoo*** (First Priority) | **Shampoo:** Sulfur 1% Captan 2% | OTC | Labeled as an anti-ringworm, antifungal, antibacterial shampoo for dogs and cats. 32 oz |
| ***Sebalyt® Shampoo*** (TEVA/DVM) | **Shampoo:** Sulfur 2% Salicylic acid 2% Triclosan 0.5% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8, 12 oz, 1 gal |
| ***Sebolux® Shampoo*** (Virbac) | **Shampoo:** Elemental sulfur 2% Salicylic acid 2% | Sold only through licensed veterinarians | *Spherulite®* microcapsules, chitosanide, urea, glycerin. Ingredients in free form and in *Spherulites®*. Shake well; wear gloves. Labeled for dogs and cats. 8 oz, 16 oz |
| ***SulfOxyDex® Shampoo*** (TEVA/DVM) | **Shampoo:** Sulfur (micronized) 2% Benzoyl peroxide 2.5% | Sold only through licensed veterinarians | Labeled for dogs and cats. 8, 12 oz, 1 gal |

### HUMAN-LABELED SULFUR TOPICAL PRODUCTS

There are several topical products containing sulfur labeled for human use, including topical creams, lotions, shampoos, soaps, and masks that are principally labeled for acne or dandruff. For more information on these products, refer to a comprehensive human drug reference (e.g., *Facts and Comparisons* or *Micromedex*) or contact a pharmacist.

## Tar, Coal

At the time of writing, many veterinary-labeled coal tar products have been withdrawn from the market due to concerns that coal tar may be carcinogenic. This action does not appear to be an FDA mandate, but a voluntary withdrawal from the marketplace.

### INDICATIONS

Use of shampoos containing coal tar in veterinary medicine is somewhat controversial, particularly since all veterinary-labeled products have been withdrawn from the market. However, coal tar shampoos have been used in dogs for treating seborrhea oleosa for many years.

### MECHANISM OF ACTION

Coal tar possesses keratoplastic, keratolytic, vasoconstrictive, antipruritic, anti-inflammatory, and degreasing actions. Its keratoplastic (keratoregulating) action is probably secondary to decreasing mitosis and DNA synthesis of basal epidermal cells.

### SUGGESTED USES/DOSAGES

When using a medicated shampoo, it is important to allow at least 10 minutes contact time to obtain the desirable effect of active ingredients. Another acceptable regimen is to allow the shampoo to act for 3–5 minutes, rinse it thoroughly, and then repeat the procedure. It is important to completely rinse the shampoo to prevent skin irritation and/or excessive drying. The frequency of shampooing will vary according to the patient's needs.

### PRECAUTIONS/ADVERSE EFFECTS

The carcinogenic risks associated with coal tar products are debated. At present, most (including the FDA) believe that coal tar products with concentrations of 5% or less are safe for human use. However, should they be used on animals, clients should wear gloves when applying and wash off any product that contacts their skin. Carcinogenic risk assessment for dogs using coal tar products is not currently available. Coal tar products should not be used on cats because they are especially sensitive to the adverse effects of coal tar. Avoid use in patients who have prior sensitivity reactions to tar products or have dry scaling dermatoses. Be careful in comparing coal tar concentrations on labels. Coal tar solution contains approximately 20% coal tar extract or refined tar. For example, a 10% coal tar solution contains approximately 2% coal tar (refined). Photosensitization, skin drying and skin irritation are possible with tar therapy. Adverse effects are more likely with tar concentrations greater than 3%. Residual odor is often bothersome to clients. Tar may stain fabrics and hair coats, and discolor jewelry.

## VETERINARY-LABELED COAL TAR TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***Nova Pearls Medicated Coal Tar Shampoo®*** (Tomlyn/ Vetoquinol) | **Shampoo:** 5% coal tar solution (equivalent to 1% refined coal tar) | OTC | Slow-release Power Moisturizers encapsulated in Novasome® microcarriers. Labeled for dogs only. **Do not use on cats.** 12 oz, 1 gal |
| ***Perfect Coat Medicated Coal tar Shampoo®*** (Perfect Coat) | **Shampoo:** 5% coal tar solution (equivalent to 1% refined coal tar) | OTC | Sodium laureth sulfate, sodium chloride, cocamidopropyl betaine, disodium oleamido MEA sulfosuccinate, glycerin, cocamide DEA, disodium cocoamphodiacetate, aloe vera gel, propylene glycol, diazolidinyl urea, parabens. Labeled for dogs only. **Do not use on cats.** 16 oz |

## HUMAN-LABELED COAL TAR TOPICAL PRODUCTS: NOT A COMPLETE LIST

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***DHS Tar®*** (Person & Covey) | **Shampoo:** 0.5% (refined) | OTC | Liquid available in 120 mL, 240 mL, 480 mL |
| ***Ionil T Plus®*** (DPT) | **Shampoo:** 1% (refined) | OTC | 236 mL |
| ***MG 217 Medicated Tar®*** (Triton) | **Shampoo:** 3% (refined) | OTC | 120 mL, 240 mL |
| ***Neutrogena T/Gel Original®*** (Neutrogena) | **Shampoo:** 2% (extract) | OTC | 132 mL, 255 mL, 480 mL |
| ***PC-Tar®*** (Geritrex) | **Shampoo:** 1% (refined) | OTC | 180 mL |
| ***Pentrax® Maximum Strength*** (Medicis) | **Shampoo:** 5% (refined) | OTC | 120 mL, 240 mL |

**HUMAN-LABELED COAL TAR TOPICAL PRODUCTS: NOT A COMPLETE LIST** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; size(s) |
|---|---|---|---|
| ***Polytar®*** (GlaxoSmithKline) | **Shampoo:** 1% (refined) | OTC | Lanolin. 177 mL, 355 mL |
| ***Sebex-T®*** (Glay-Park) | **Shampoo:** Coal tar 5% (refined) Sulfur 2% Salicylic acid 2% | OTC | 120 mL, 480 mL |
| ***Sebutone®*** (Westwood-Squibb) | **Shampoo:** Coal tar 1.5% (refined) Sulfur 2% Salicylic acid 2% | OTC | 120 mL, 210 mL, 240 mL |
| ***Tera-Gel®*** (Geritrex) | **Shampoo:** 0.5% (refined) | OTC | 235 mL |
| ***Vaneseb-T®*** (Allergan Herbert) | **Shampoo:** Coal tar 5% (refined) Sulfur 2% Salicylic acid 1% | OTC | 90 mL, 120 mL |
| ***Zetar®*** (Dermik) | **Shampoo:** 1% (refined) | OTC | 180 mL |

# IMMUNOMODULATORY AGENTS

## Imiquimod

### INDICATIONS

An immune response modifier, imiquimod may be useful in the treatment of a variety of skin conditions in animals. In humans, it is labeled for genital or perianal warts, superficial basal cell carcinomas, and actinic keratoses of the face and scalp. Examples of extra-label use of this drug in humans include mycosis fungoides, other types of cutaneous lymphomas, squamous cell carcinoma, Bowen's disease, infant hemangiomas (antiangiogenic effect), molluscum contagiosum, and cutaneous leishmaniasis (in combination with meglumine antimoniate). In dogs and cats, imiquimod may be of benefit in treating actinic keratosis, squamous cell carcinoma, Bowenoid disease, pigmented epidermal plaques and other papillomavirus-associated lesions, feline herpes virus dermatitis, and localized actinic dermatitis or solar-induced carcinoma in situ. Most of these recommendations are anecdotal or based on very few studies.

### MECHANISM OF ACTION

Imiquimod is an imidazoquinolone compound that binds to toll-like receptor 7 and stimulates the patient's own immune system to release a variety of cytokines including interferon-alpha, TNF-alpha, and IL-12. This locally generated cytokine milieu induces a Th1 immune response with the generation of cytotoxic effectors. Imiquimod does not have in-vitro activity against viruses, but stimulates monocytes and macrophages to release cytokines that induce a regression in viral protein production.

### SUGGESTED USES/DOSAGES

Use in animals is still rather limited, and ongoing research on this agent is being performed. Doses and treatment regimens will vary depending on the disease treated and tolerance to the drug. Typically, dosing ranges from applying a thin film once daily to 2–3 times weekly or every other week. Do not let the animal lick or chew at treated area(s) for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work. Treatment duration and frequency may need to be adjusted depending on response and adverse reactions.

### PRECAUTIONS/ADVERSE EFFECTS

Clients should wear gloves when handling or applying the cream. It is advised to avoid getting in eyes or on mucous membranes; however, dogs with oral mucosal papillomas, dogs and horses with corneal squamous cell carcinomas, and horses with periocular sarcoids have been treated without significant ocular problems. While there are low chances for the drug to be absorbed systemically, do not allow the animal to groom/lick the treated site for at least 30 minutes after application, to avoid ingestion and allow the medication to work. Occlusive dressings should not be used over the applied areas. Avoid exposure of the site to sunlight, as there are anecdotal concerns of increased risks of sun damage after use. Local skin reactions are expected with imiquimod therapy, considering its mechanism of action, and these may include one or more of the following: erythema, burning, tenderness, itching, swelling, pain, oozing/exudation, crusting, and erosion. Secondary infections may also occur at the treated site(s). Depigmentation and hair loss may occur as post-treatment sequelae.

### VETERINARY-LABELED IMIQUIMOD TOPICAL PRODUCTS

None.

### HUMAN-LABELED IMIQUIMOD TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Aldara***® (Graceway Pharmaceuticals) **Generics** | **Cream:** 5% | Rx | Cetyl alcohol, stearyl alcohol, white petrolatum, benzyl alcohol, parabens. Single-use 250 mg packets in boxes of 12. Inactive ingredients and number of packets/box may vary with different generic brands |

**HUMAN-LABELED IMIQUIMOD TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Zyclara®*** (Graceway Pharmaceuticals) | **Cream:** 3.75% | Rx | Cetyl alcohol, stearyl alcohol, white petrolatum, benzyl alcohol, parabens. This less concentrated imiquimod cream was recently approved by FDA for the treatment of actinic keratoses of the face and scalp in humans. It is approved for daily use. Single-use 250 mg packets in boxes of 28 |

## Pimecrolimus

### INDICATIONS

A relatively new addition to the human topical armamentarium, pimecrolimus cream may be anecdotally beneficial in veterinary patients in the adjunctive treatment of atopic dermatitis, discoid lupus erythematosus, pemphigus erythematosus, pinnal vascular disease or other cutaneous vasculopathies, alopecia areata, vitiligo, perianal fistulas (maintenance treatment after cyclosporine therapy), and feline proliferative and necrotizing otitis externa. Unlike topical corticosteroids, pimecrolimus does not have atrophogenic or metabolic effects associated with long-term or large-area treatment.

### MECHANISM OF ACTION

Pimecrolimus, similarly to cyclosporine, acts by inhibiting T-lymphocyte activation, primarily by interfering with the phosphatase activity of calcineurin, which ultimately results in the blockage of various cytokine genes transcription, especially interleukin-2. It also inhibits the release of inflammatory cytokines and mediators from mast cells and basophils. Pimecrolimus and tacrolimus may not have identical mechanisms of action, as pimecrolimus, in contrast to tacrolimus, did not impair the primary immune response in mice after a contact sensitizer was applied. Both drugs, however, did impair the secondary immune response. Any clinical significance associated with this difference is not yet clear.

### SUGGESTED USES/DOSAGES

There is limited experience with this drug in veterinary patients. Most dosing recommendations are to use the product twice daily until signs are controlled and then reduce application frequency to the lowest level that maintains the disease under control. Do not let the animal lick or chew at treated area(s) for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Both tacrolimus and pimecrolimus have FDA-mandated "black box" warnings that their use may increase risks for skin cancer and lymphomas in humans; however, most of the data demonstrating carcinogenic risk have come from animal models using greatly excessive doses of pimecrolimus administered orally, and there is no current evidence of a causal relationship between the use of these medications and the occurrence of malignancy in humans. Therefore, topical use of pimecrolimus is probably relatively safe in veterinary patients. However, clients should be informed and instructed to wear gloves or use an applicator (e.g., a Q-tip) when applying the cream, mainly because of the immunosuppressive effects of the drug.

The long-term adverse effects of topical pimecrolimus are currently unknown; therefore, it is prudent to avoid using this medication on a continuous-maintenance basis. When long-term treatment is required, the ultimate goal should be to achieve the lowest possible dose that maintains the disease under control. Topical pimecrolimus is apparently well tolerated in dogs, but localized irritation, erythema, and pruritus have been reported in humans and dogs using the drug. Anecdotal reports state that pimecrolimus may be less irritating than tacrolimus in dogs, but also may not be quite as effective. The cost of the medication may be prohibitive for some clients. One study has shown that tacrolimus applied daily for 4 weeks did not interfere with the intradermal test reactivity in dogs (Marsella *et al*. 2004). No similar studies have been conducted using pimecrolimus, but similar results can be expected.

### VETERINARY-LABELED PIMECROLIMUS TOPICAL PRODUCTS

None.

### HUMAN-LABELED PIMECROLIMUS TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Sizes |
|---|---|---|---|
| ***Elidel*®** (Novartis) **Generics** | **Cream:** 1% | Rx<br>10 g; other sizes may be available with different generic brands | 30 g, 60 g, 100 g |

## Tacrolimus

### INDICATIONS

Tacrolimus ointment may be of benefit in veterinary patients in the adjunctive treatment of atopic dermatitis, discoid lupus erythematosus, pemphigus erythematosus, pinnal vascular disease or other cutaneous vasculopathies, alopecia areata, vitiligo, perianal fistulas (best as maintenance treatment after cyclosporine therapy), and feline proliferative and necrotizing otitis externa. Unlike topical corticosteroids, tacrolimus does not have atrophogenic or metabolic effects associated with long-term or large-area treatment.

### MECHANISM OF ACTION

Tacrolimus is a macrolide antibiotic and, similarly to cyclosporine, it acts by inhibiting T-lymphocyte activation, primarily by interfering with the phosphatase activity of calcineurin, which ultimately results in the blockage of various cytokine genes' transcription, especially interleukin-2. It also inhibits the release of inflammatory cytokines and mediators from mast cells and basophils.

### SUGGESTED USES/DOSAGES

There is limited experience with this drug in veterinary patients. Typically, dosing recommendations are to use the product twice daily until signs are controlled and then reduce application frequency to the lowest level that maintains the disease under control. Do not let the animal lick or chew at treated area(s) for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Tacrolimus has FDA-mandated "black box" warnings that its use may increase risks for skin cancer and lymphomas in humans; however, most of the data demonstrating carcinogenic risk have come from animal models using greatly excessive doses of tacrolimus administered orally, and there is no current evidence of a causal relashionship between the use of tacrolimus and the occurrence of malignancy in humans. Therefore, topical use of tacrolimus is probably relatively safe in veterinary patients. However, clients should be informed and instructed to wear gloves or use an applicator (e.g., a Q-tip) when applying the cream, mainly because of the immunosuppressive effects of the drug.

The long-term adverse effects of topical tacrolimus are currently unknown; therefore, it is prudent to avoid using this medication on a continuous-maintenance basis. When long-term treatment is required, the ultimate goal should be to achieve the lowest possible dose that maintains the disease well controlled. Early reports indicate that topical tacrolimus is usually well tolerated in dogs, but localized irritation, erythema, and pruritus have been reported in humans and dogs treated with the drug. The medication may be cost-prohibitive for some clients. When using tacrolimus 0.1% ointment once daily for 4 weeks, no withdrawal time is recommended prior to intradermal testing for evaluation of immediate reactions; however, a 4-week withdrawal is recommended for evaluation of late-phase reactions. (Marsella *et al*. 2004). Whether tacrolimus needs to be withdrawn prior to IgE serum test is unknown.

### VETERINARY-LABELED TACROLIMUS TOPICAL PRODUCTS

None.

### HUMAN-LABELED TACROLIMUS TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Sizes |
|---|---|---|---|
| **Tacrolimus** (generic) | **Ointment:** 0.03%, 0.1% | Rx | 10 g; other sizes may be available with different generic brands |
| ***Protopic*®** (Astellas Pharma) | **Ointment:** 0.03%, 0.1% | Rx | 30 g, 60 g, 100 g |

# RETINOIDS

## Adapalene (Retinoid Analog)

### INDICATIONS

In humans, adapalene is indicated for the treatment of acne vulgaris. In animals, adapalene may be useful in treating canine or feline chin acne.

### MECHANISM OF ACTION

Adapalene is a naphthoic acid derivative and retinoid analog. The mechanism of action of adapalane in acne vulgaris is unknown, but, similarly to tretinoin and tazarotene, adapalane may modulate follicular epithelial cell differentiation and keratinization, thus preventing the formation of comedones. Moreover, in-vitro studies have shown that adapalene may reduce inflammation.

### SUGGESTED USES/DOSAGES

There is limited experience with adapalene in veterinary medicine; however, similarly to topical tretinoin and tazarotene, it can be used initially at a high concentration (0.3%) and once daily. Treatment should be continued until the condition is controlled and as long as the animal tolerates the treatment. Once the condition is controlled, frequency of administration is reduced to as needed. In animals unable to tolerate therapy, the concentration may be reduced to 0.1% in an attempt to balance efficacy with adverse effects. Do not let the animal lick or chew at treated area(s) for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes, nostrils, or mouth. Clients should wear gloves when applying the product. Adverse effects can include hypersensitivity reactions or local irritation characterized by erythema, dryness, peeling, pruritus. Avoid sun exposure during treatment with adapalene. Avoid use in pregnant or nursing animals.

### VETERINARY-LABELED ADAPALENE TOPICAL PRODUCTS

None.

### HUMAN-LABELED ADAPALENE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Size(s) |
|---|---|---|---|
| **Adapalene** (Fougera) | **Cream:** 0.1% | Rx | 45 g |
| ***Differin*®** (Galderma) | **Cream:** 0.1% | Rx | 15 g, 45 g |
| **Adapalene** (Teva) | **Gel/jelly:** 0.1% | Rx | 45 g |
| ***Differin*®** (Galderma) | **Gel/jelly:** 0.1% | Rx | 15 g, 45 g |
| ***Differin*®** (Galderma) | **Lotion:** 0.1% | Rx | 59 mL, 118 mL |
| ***Differin*®** (Galderma) | **Solution:** 0.1% | Rx | 30 mL, 60 mL |
| ***Differin*®** (Galderma) | **Gel/jelly:** 0.3% | Rx | 45 g |
| ***Epiduo*®** (Galderma) | **Gel/jelly:** Adapalene 0.1% Benzoyl peroxide 2.5% | Rx | 45 g |

## Tazarotene

### INDICATIONS

In humans, tazarotene therapy is primarily indicated for acne vulgaris, plaque psoriasis, and photodamaged skin. It has also been used for the treatment of lamellar ichthyosis and Darier's disease. In animals, topical tazarotene, similar to tretinoin, may be useful in treating localized follicular or hyperkeratotic disorders such as schnauzer comedo syndrome, chin acne, or idiopathic nasal and footpad hyperkeratosis. It is important to note that these recommendations are anecdotal and not based on scientific evidence.

### MECHANISM OF ACTION

Tazarotene is a third-generation retinoid. The exact mechanism of action of retinoids is not well understood, but they may have anti-inflammatory and immunomodulatory effect by stimulating cytotoxic T-cells and natural killer cells, inhibiting polymorphonuclear cells and suppressing lymphocyte proliferation. Retinoids also have an antineoplastic effect by maintaining epithelial cell differentiation and inhibiting tumor cell proliferation. The effect of tazarotene in acne vulgaris is unknown, but studies have shown that it inhibits corneocyte accumulation and the formation of cross-linked envelopes. It is possible that different retinoids have different mechanisms of action, and that they may be effective in different diseases.

### SUGGESTED USES/DOSAGES

There is limited experience with tazarotene in veterinary medicine; however, similarly to topical tretinoin it can be used initially at a high concentration (0.1%) and once daily. Treatment should be continued until the condition is controlled and as long as the animal tolerates the treatment. Once the condition is controlled, the frequency of administration is reduced to as needed. In animals unable to tolerate therapy, the concentration can be reduced to 0.05% in an attempt to balance efficacy with adverse effects. Do not let the animal lick or chew at treated area(s) for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes, nostrils, or mouth. Clients should wear gloves when applying the product. Adverse effects can include hypersensitivity reactions or local irritation characterized by erythema, dryness, peeling, pruritus. Avoid sun exposure during treatment with tazarotene. Avoid use in pregnant or nursing animals.

### VETERINARY-LABELED TAZAROTENE TOPICAL PRODUCTS

None.

### HUMAN-LABELED TAZAROTENE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Size(s) |
|---|---|---|---|
| ***Avage®*** (Allergan) | Cream: 0.1% | Rx | 30 g |
| ***Tazorac®*** (Allergan) | Cream: 0.05%, 0.1% | Rx | 15 g, 30 g, 60g |
| ***Tazorac®*** (Allergan) | Gel/jelly: 0.05%, 0.1% | Rx | 30 g, 100g |

## Tretinoin (All-Trans Retinoic Acid; Vitamin A Acid)

### INDICATIONS

In humans, the primary indication of topical tretinoin therapy is acne vulgaris and photodamaged skin. In animals, topical tretinoin may be useful in treating localized hyperkeratotic disorders such as schnauzer comedo syndrome, idiopathic nasal and footpad hyperkeratosis, or chin acne. It is important to note that these recommendations are anecdotal and not based on scientific evidence.

### MECHANISM OF ACTION

Tretinoin (all-trans retinoic acid) is a retinoid derived from the naturally occurring vitamin-A alcohol. The exact mechanism of action of retinoids is not well understood, but they may have anti-inflammatory and immunomodulatory effect by stimulating cytotoxic T-cells and natural killer cells, inhibiting polymorphonuclear cells and suppressing lymphocyte proliferation. Retinoids also have an antineoplastic effect by maintaining epithelial cell differentiation and inhibiting tumor cell proliferation. Tretinoin appears to prevent new comedone formation and eliminate the formed ones, hence its benefit in the treatment of acne. This effect is mediated by stimulating the mitotic activity and turnover of follicular epithelial cells and decreasing their cohesiveness. It is possible that different retinoids have different mechanisms of action, and that they may be effective in different diseases.

### SUGGESTED USES/DOSAGES

In small animals, topical tretinoin gel is anecdotally used initially at a concentration of 0.05% and is applied once daily. Treatment should be continued until the condition is controlled and as long as the animal tolerates the treatment. Once the condition is controlled, the frequency of administration is reduced to as needed. In animals unable to tolerate therapy, the concentration may be reduced to 0.025%–0.01% in an attempt to balance efficacy with adverse effects. Do not let the animal lick or chew at treated area(s) for at least 20–30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Avoid contact with eyes, nostrils, or mouth. Clients should wear gloves when applying the product. Adverse effects can include hypersensitivity reactions or local irritation characterized by erythema, dryness, peeling, pruritus. Avoid sun exposure during treatment with tretinoin. Avoid use in pregnant or nursing animals.

### VETERINARY-LABELED TRETINOIN TOPICAL PRODUCTS

None.

### HUMAN-LABELED TRETINOIN TOPICAL PRODUCTS

Not a complete list.

**HUMAN-LABELED TRETINOIN TOPICAL PRODUCTS: NOT A COMPLETE LIST**

| Product (company) | Form: concentration | Label status | Size(s) |
|---|---|---|---|
| ***Renova***® (Ortho Dermatologics) | **Cream:** 0.02% | Rx | 40 g, 60 g |
| ***Retin-A***® (Ortho)<br>***Avita***® (Mylan Bertek)<br>***Altinac***® (Upsher-Smith)<br>**Generic** (various) | **Cream:** 0.025% | Rx | 20 g, 45 g |
| ***Retin-A***® (Ortho)<br>***Altinac***® (Upsher-Smith)<br>***Renova***® (Ortho McNeil Neurologics)<br>***Revisa***® (DPT)<br>**Generic** (Spear) | **Cream:** 0.05% | Rx | Depending on product: 20 g, 40 g, 45 g, 60 g |
| ***Retin-A***® (Ortho McNeil)<br>**Generic** (Spear) | **Cream:** 0.1% | Rx | 20 g |
| ***Retin-A***® (Ortho McNeil)<br>**Generic** (Spear) | **Gel:** 0.01% | Rx | 15 g, 45 g |
| ***Retin-A***® (Ortho McNeil)<br>***Avita***® (Mylan Bertek)<br>**Generic** (Spear) | **Gel:** 0.025% | Rx | Depending on product: 15 g, 20 g, 45 g |
| ***Retin-A Micro***® (Ortho Dermatologics | **Gel:** 0.04% (microsphere) | Rx | 20 g, 45 g, 50 g |
| ***Retin-A Micro***® (Ortho Dermatologics) | **Gel:** 0.1% (microsphere) | Rx | 20 g, 45 g, 50 g |

## ANTIPARASITIC AGENTS

*For antiparasitic agents that are administered topically but have a systemic effect, such as* ***ivermectin*** *and* ***selamectin****, and for those administered orally, including* ***lufenuron****,* ***milbemycin****,* ***moxidectin****,* ***nitenpyram****, and* ***spinosad****, refer to Section 1: Systemic Drugs.*

## Amitraz

### INDICATIONS

Amitraz solution is the only FDA-approved treatment for canine demodicosis. It has also been used successfully to manage canine sarcoptic mange and feline surface (caused by *Demodex gatoi*) or follicular demodicosis (caused by *Demodex cati*). Amitraz is used in cats at lower doses than the ones used in dogs, because

cats are more susceptible to its adverse effects. The authors do not typically use amitraz as first-line therapy for demodicosis, since there are more efficacious and more easily administered treatment options currently available, such as ivermectin. The *Preventic*® collar is available for treatment and prevention of flea and tick infestations.

### MECHANISM OF ACTION

The pharmacologic action of amitraz is not well understood. It is a monoamine oxidase (MAO) inhibitor (in mites) and may have effects on the CNS of susceptible organisms. It apparently also has alpha-2-adrenergic activity and inhibits prostaglandin synthesis. Amitraz can cause a significant increase in plasma glucose levels, presumably by inhibiting insulin release via its alpha-2-adrenergic activity. Yohimbine (an alpha-2 blocker) or atipamezole can antagonize this effect.

### SUGGESTED USES/DOSAGES

#### Dogs

**For generalized demodicosis:** Prior to using amitraz any obstacle (e.g., crusting, excessive oil, and/or keratin debris) that could prevent good penetration of the solution into the hair follicle canals should be removed. Therefore, long- and medium-haired dogs should be clipped closely and given a bath with benzoyl peroxide or other appropriate shampoo before the application of amitraz. Make sure, thereafter, to thoroughly dry the skin and hair coat to prevent dilution of the amitraz solution. When dipping with amitraz, DO NOT rinse or towel-dry the skin and coat. Use a freshly prepared dilution for additional dogs or additional treatments. Different treatment protocols have been shown to be efficacious. **The general rule of thumb for therapy duration, independent of the protocol chosen, involves treating for 30 days past two consecutive negative skin scrapings.** Thereafter, it is recommended to follow up the patient for 1 year (and repeat skin scrapings) before declaring the case cured.

**(a)** *Licensed concentration*: Topically treat at a concentration of 250 ppm (one 10.6 mL bottle of *Mitaban*® in 2 gallons of warm water) by applying to the entire animal every 14 days and allowing to air-dry. Follow the rule of thumb above for duration of therapy.

**(b)** Extra-label protocols

- **(i)** For dogs whose owners accept the risk of using the amitraz in an "unlicensed" manner with the goal of increasing efficacy, first try the 250 ppm solution (as above) *once weekly* for 4 weeks. If positive response is seen, continue treatment for an additional 30 days after obtaining two consecutive negative skin scrapings (rule of thumb). If weekly 250 ppm application fails, a 500 ppm solution may be tried (1 bottle in 1 gallon of water) weekly as above. In dogs failing 500 ppm, 1000 ppm may also be attempted, but the likelihood of toxicity increases and the authors have no experience of using this high concentration. If these methods fail, the dog is unlikely to be cured using amitraz.
- **(ii)** Prepare a 0.125% solution by diluting 1 mL of the 12.5% commercially available large animal product (*Taktic*®) in 100 mL of water. Using a sponge, rub the diluted solution (0.125%) *daily onto one-half of the dog's body, and alternate sides on a daily basis*. Air-dry. During the first week of therapy, keep the dog hospitalized and observe for

adverse effects. Follow the rule of thumb above for duration of therapy. Dogs with ***severe pododemodicosis*** should also be treated with daily foot soaks of the 0.125% solution. Dogs with otic demodicosis can be treated with a diluted solution of amitraz (1 mL of *Taktic*® in 8.5 mL of mineral oil) every 3–7 days unless irritation develops. Owners accepting the extra-label therapy must be carefully screened, and must be trained to carefully handle the amitraz solutions.

**For sarcoptic mange (older puppies and adult dogs):** The authors do not use amitraz to treat canine scabies because there are more efficacious and easily administered treatment options currently available, such as ivermectin. If amitraz is selected, the authors advise to use it only when the diagnosis of sarcoptic mange has been confirmed by positive skin scrapings (i.e., do not use amitraz in treatment trials), because of anecdotal reports of treatment failures. *Protocol*: Dilute and treat per label recommendation (see (a) above for demodicosis); apply every 14 days for two or three treatments.

**Cats**

Not labeled to treat feline demodicosis.

**For follicular demodicosis (*Demodex cati*):** Dilute amitraz to 0.0125% (125 ppm) and apply every 7–14 days. Monitor cats very closely for potential side effects. Place an Elizabethan collar until the solution is completely dry.

**For surface demodicosis (*Demodex gatoi*):** Amitraz was reported to be efficacious to treat surface demodicosis when used at 0.0125% solution applied weekly as a dip for 12 weeks (Saari *et al*. 2009). Monitor cats very closely for potential side effects. Place an Elizabethan collar until the solution is completely dry.

## PRECAUTIONS/ADVERSE EFFECTS/DRUG INTERACTIONS

Amitraz liquid concentrates are flammable until diluted with water. Do not stress animals for at least 24 hours after application of *Mitaban*®. When mixing with water, protect exposed skin with rubber gloves. Wash hands and arms well after application to animal. Dispose of unused diluted solution by flushing down the drain. Rinse *Mitaban*® container with water and dispose; do not reuse. Do not reuse collar; wrap in newspaper and throw in trash. Avoid inhalation of vapors. Safety has not been demonstrated in dogs less than 4 months of age, and the manufacturer of *Mitaban*® does not recommend use in these animals. Toy breeds may be more susceptible to CNS effects (transient sedation); therefore, lower dose rates (half of recommended) have been recommended in these breeds. Because of amitraz effects on plasma glucose, use with caution in diabetic patients. Reproductive safety has not been established. Use only when benefits outweigh potential risks of therapy.

The most commonly reported adverse effect after amitraz topical administration is transient sedation that may persist for up to 72 hours (24 hours is usual). If treating around eyes, use an ophthalmic protectant (e.g., petrolatum ophthalmic ointment) before treating. Do not use if dog has deep pyoderma with draining tracts; postpone application until lesions improve after treating with antibiotic and shampoo therapy. Other adverse effects include ataxia, bradycardia, vomiting, diarrhea, hypothermia, and a transient hyperglycemia. Rarely, seizures have been reported. Topical effects can include edema, erythema, and pruritus. Adverse effects are more likely to be seen in debilitated, geriatric, or very small breed dogs.

Amitraz can be toxic to cats and rabbits, and it is probably best to avoid its use in these species; however, amitraz has been used safely in cats in diluted form for the treatment of demodicosis (see above).

Amitraz may be toxic if swallowed (by either animals or humans). Beagles receiving 4 mg/kg PO daily for 90 days demonstrated transient ataxia, CNS depression, hyperglycemia, decreased pulse rates, and lowered body temperature; no animals died. Amitraz toxicity can be significant if amitraz-containing insecticide collars are ingested. Treatment should consist of emesis, retrieval of the collar using endoscopy if possible, and administration of activated charcoal and a cathartic to remove any remaining collar fragments. Because of the risk of an increased chance of gastric dilatation, gastrotomy may not be a viable option. Yohimbine at a dose of 0.11– 0.2 mg/kg IV (start with low dosage) may be of benefit for overdose effects. Because yohimbine has a short half-life it may need to be repeated, particularly if the animal has ingested an amitraz-containing collar that has not been retrieved from the gastrointestinal tract. Atipamezole has also been used to treat amitraz toxicity. Contact a poison center for more information, if necessary.

Because of their immunosuppressive effects, **corticosteroids** and **other immunosuppressant drugs** (e.g., **azathioprine**, **cyclophosphamide**, **cyclosporine**) should not be used in animals with demodicosis.

Amitraz may interact with other MAO inhibitors (including **selegiline**) or tricyclic antidepressants (e.g., **amitriptyline**, **clomipramine**). Concomitant use is not recommended. Sun exposure should be avoided until amitraz solution has dried completed.

### VETERINARY-LABELED AMITRAZ TOPICAL PRODUCTS

Not a complete list.

### HUMAN-LABELED AMITRAZ TOPICAL PRODUCTS

None.

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Mitaban®*** (Pfizer) | **Solution for dilution:** 19.9% | Sold only through licensed veterinarians | FDA labeled and approved for dogs. **Not labeled for cats. Note:** Liquid is flammable until diluted. 10.6 mL btl |
| ***Taktic® EC*** (Intervet/ Schering-Plough) | **Solution (emulsifiable concentrate) for dilution:** 12.5% | OTC | EPA labeled for use on swine, dairy or beef cattle. **Label states not to use on dogs or horses. Note:** Liquid is flammable until diluted. 760 mL can |
| ***Preventic®*** (Virbac) | **Collar:** 9% | Sold only through licensed veterinarians | EPA labeled for dogs ≥12 weeks old. **Not labeled for cats.** Effective for 3 months. 18 inches for dogs 60 lb and 25 inches for dogs >60 lb |

## Deltamethrin

### INDICATIONS

In the US, deltamethrin-impregnated collars are recommended for killing fleas and ticks on dogs. In countries where leishmaniasis is a problem, deltamethrin-impregnated collars are also indicated for repelling and killing the phlebotomine sandfly vectors.

### MECHANISM OF ACTION

Deltamethrin is a synthetic pyrethroid and acts by disrupting the sodium channel current in arthropod nerve cell membranes, resulting in paralysis and death.

### SUGGESTED USES/DOSAGES

The manufacturer recommends applying a new collar every 6 months, and claims that maximum effect may not occur before 2–3 weeks after collar placement. Follow label for specific use instructions.

### PRECAUTIONS/ADVERSE EFFECTS

Deltamethrin should not be used on dogs younger than 12 weeks of age. It can be harmful if swallowed or absorbed through the skin. Avoid contact with eyes, skin, or clothing. Exercise caution when applying the product on debilitated, pregnant, nursing, old, or medicated animals. Skin reaction at the application site may occur. Mammalian exposure to deltamethrin is classified as safe; however, it should be used very carefully around water because it is highly toxic to aquatic animals, especially fish.

### VETERINARY-LABELED DELTAMETHRIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Size |
|---|---|---|---|
| ***Scalibor® Protector Band for Dogs*** (Intervet/ Schering-Plough) | **Collar:** 4.0% | Rx | Effective for 6 months. One size fits all. 0.9 oz |

### HUMAN-LABELED DELTAMETHRIN TOPICAL PRODUCTS

None.

**Note:** There are various deltamethrin-containing products available in various formulations for use in the environment. Information on these products is readly available online.

## Dinotefuran + Pyriproxyfen, ± Permethrin

### INDICATIONS

The product containing dinotefuran and pyriproxyfen (*Vectra®*), labeled for dogs and cats, is used for control of adult and all immature flea stages including eggs, larvae, and pupae. The exclusive dog product which contains permethrin in

addition to dinotefuran and pyriproxyfen (*Vectra 3D®*) kills and repels adult and immature fleas, ticks, and mosquitoes.

### MECHANISM OF ACTION

Dinotefuran is a nitroguanidine, neonicotinoid insecticide with a structure similar to acetylcholine. It permanently binds to the same insect receptor sites as acetylcholine and activates the nerve impulse at the synapse, causing stimulation that results in tremors, incoordination, and insect death. Dinotefuran does not bind to mammalian acetylcholine receptor sites.

Pyriproxyfen is a second-generation insect growth regulator. It acts by interrupting the development of flea eggs, larvae, and early pupae. It mimics the action of an insect growth hormone known as juvenile hormone, which regulates the molting of insects from one stage to the other. High concentrations of juvenile hormone prevent molting to the next flea stage. Normally, this hormone is broken down by an esterase, resulting in low concentrations and insect molting. Because pyriproxyfen is not broken down by juvenile hormone esterase, any flea stages exposed to high concentrations of pyriproxyfen are unable to molt to the next stage, and die.

Permethrin is a synthetic pyrethroid with rapid knockdown and repellent effects against fleas, ticks, and mosquitoes. It is a neurotoxin that binds to the voltage-gated sodium channel, preventing it from closing normally and thereby causing repetitive activity in the sensory and motor pathways. This results in tremors, incoordination, and insect death.

### SUGGESTED USES/DOSAGES

Refer to the package information for specific instructions on application and dosages of dinotefuran-containing products. Monthly applications are recommended for dogs and cats. It is labeled for cats and kittens 8 weeks of age or older (*Vectra®*) and dogs or puppies 7 weeks of age or older (*Vectra®* and *Vectra 3D®*). According to the manufacturer, bathing or swimming does not interfere with efficacy; however, the authors do not recommend bathing the pet within 48 hours before or after application.

### PRECAUTIONS/ADVERSE EFFECTS

The dog product containing permethrin (*Vectra 3D®*) **cannot be used on cats, or on dogs that cohabit with a cat**. The manufacturer recommends not using *Vectra®* or *Vectra 3D®* on debilitated, aged, medicated, pregnant, or nursing animals and animals known to be sensitive to pesticide products. Mild transitory skin erythema may occur at the application site. Avoid eye and oral contact, since dinotefuran can cause substantial (but temporary) eye irritation.

### VETERINARY-LABELED DINOTEFURAN COMBINATION TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Vectra® for Cats & Kittens*** (VetPharm) | **Solution:** Dinotefuran 22 % Pyriproxyfen 3 % | OTC | EPA approved. For cats and kittens <9 lb and ≥8 weeks: dose size = 0.8 mL |
| ***Vectra® for Cats*** (VetPharm) | **Solution:** Dinotefuran 22 % Pyriproxyfen 3 % | OTC | EPA approved. For cats ≥9 lb: dose size = 1.2 mL |
| ***Vectra® for Dogs & Puppies*** (VetPharm) | **Solution:** Dinotefuran 4.95 % Pyriproxyfen 0.44 % | OTC | EPA approved. For dogs and puppies ≥8 weeks<br>Dogs and puppies 2.5–10 lb: 1.3 mL<br>Dogs and puppies 11–20 lb: 2.0 mL<br>Dogs 21–55 lb: 4.0 mL<br>Dogs 56–100 lb: 6.0 mL |
| ***Vectra 3D®*** (VetPharm) | **Solution:** Dinotefuran 4.95 % Pyriproxyfen 0.44 % Permethrin 36.08 % | OTC | EPA approved. **Must not be used on cats, or on dogs that cohabit with cats**<br>Dogs and puppies 2.5–20 lb, ≥7 weeks: 1.6 mL<br>Dogs and puppies 21–55 lb, ≥7 weeks: 3.6 mL<br>Dogs 56–95 lb: 4.7 mL<br>Dogs >95 lb: 8.0 mL |

### HUMAN-LABELED DINOTEFURAN TOPICAL PRODUCTS

None.

## Fipronil ± (S)-Methoprene

### INDICATIONS

In the US, fipronil is approved for the treatment and prevention of fleas, ticks, and chewing lice in dogs and cats. It has also been used successfully for *Trombicula autumnalis* (chigger) infestation, sarcoptic mange, cheyletiellosis, and otoacariosis.

### MECHANISM OF ACTION

Fipronil is a phenylpyrazole antiparasitic agent that in invertebrates inhibits the passage of chloride ions in GABA (gama-aminobutiric acid)- and glutamate-regulated chloride channels, resulting in nervous system hyperactivity and ultimate parasite death. The manufacturer states that fipronil accumulates in the

oils of the skin sebaceous glands and continues to be released over a period of time, resulting in long residual activity. Topically applied, the drug apparently spreads over the body in approximately 24 hours via translocation. When fipronil is combined with the insect growth regulator (S)-methoprene (e.g., *Frontline® Plus*), flea eggs and flea larvae are also killed. (S)-Methoprene mimics flea juvenile growth hormone, halting larval development during metamorphosis. It also concentrates in female flea ovaries, causing non-viable eggs to be produced.

## SUGGESTED USES/DOSAGES

**For fleas, ticks, or chewing lice:** Fipronil *spot-on* monthly treatments are usually recommended.

**For *Trombicula autumnalis* infestation:** Fipronil *spray* (0.25%) is recommended. The following protocol has been published (Nuttall *et al*. 1998): Monthly applications throughout the trombiculid season at the dose of 3–6 mL/kg. It is important to thoroughly wet the coat, with special emphasis on the areas typically affected (feet, ears, face, perineum, and tail). In some cases the interval between applications needs to be shortened to every 14 days.

**For sarcoptic mange:** Fipronil *spray* (0.25%) is recommended. The authors do not use fipronil spray to treat sarcoptic mange because of the availability of other efficacious products that are easier to administer. If fipronil spray is selected, we do not recommend its use in treatment trials (i.e., mites are not found on skin scrapings), because of anecdotal reports of treatment failures with this product. Two protocols have been published: (a) apply once weekly for 4 weeks (Koutinas *et al*. 2001); (b) apply every 2–3 weeks for three treatments (Curtis 1996). The goal is to thoroughly wet the coat, paying special attention to the areas typically affected by the disease (ears, face, ventrum, and extremities). It is recommended to use a towel soaked with fipronil to treat the face. Dosages ranging from 3 mL/kg to 39 mL/kg were used in these reports. Decrease in pruritus may be noticed as early as 7 days after the first application.

**For cheyletiellosis:** Fipronil *spray* (0.25%) is recommended. The authors do not use fipronil spray to treat cheyletiellosis because of the availability of other efficacious products that are easier to administer. If fipronil spray is selected, we do not recommend its use in treatment trials (i.e., mites are not found on skin scrapings), because of anecdotal reports of treatment failures with this product. The following protocol has been published (Chadwick 1997): two treatments at 30-day interval. It is important to thoroughly wet the coat, paying special attention to the affected areas. A dose of 3 mL/kg was used in the published report.

**For otoacariosis:** The following protocol is recommended: Apply 0.05 mL of fipronil solution inside each ear canal and 0.4 mL between the shoulder blades. Resolution of clinical signs can be seen as early as 7 days post-treatment. Additional applications may be needed. Fipronil needs to be applied in the ear canals to be effective.

## PRECAUTIONS/ADVERSE EFFECTS

Do not use on puppies or kittens less than 8 weeks of age. Animals that have demonstrated sensitivity reactions to fipronil or any of the ingredients in the product should probably not be re-treated. Temporary irritation may occur at the

site of administration. The manufacturer recommends consulting a veterinarian before using on debilitated, aged, or medicated patients. This product is contraindicated in rabbits, as deaths have occurred with the spray. Do not apply or spray in the eyes. Do not contaminate food or water, and dispose of container properly. Avoid human contact with skin, eyes, or clothing, and wear gloves when applying/spraying. Avoid contact with the animal until dry. Wash well with soap and water if contact occurs. If using spray, do so in a well ventilated area. Product is labeled as remaining effective after bathing, water immersion, or exposure to sunlight; however, the authors do not recommend bathing the pet within 48 hours before or after application. Spotted areas may appear wet or oily for up to 24 hours after application. Rarely, hypersensitivity has been reported.

### VETERINARY-LABELED FIPRONIL ± (S)-METHOPRENE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Comments, size(s) |
|---|---|---|---|
| ***Frontline® Spray Treatment for Cats and Dogs*** (Merial) | **Spray:** Fipronil 0.29% | OTC | EPA approved. Labeled for dogs, cats, puppies and kittens ≥8 weeks. 8.5 oz, 17 oz |
| ***Frontline® Top Spot for Cats and Kittens*** (Merial) | **Solution:** Fipronil 9.7% | OTC | EPA approved. Labeled for cats or kittens ≥8 weeks. Single-dose applicators in packages of 3's and 6's |
| ***Frontline® Top Spot for Dogs and Puppies*** (Merial) | **Solution:** Fipronil 9.7% | OTC | EPA approved. Labeled for dogs or puppies ≥8 weeks. Single-dose applicators in packages of 3's and 6's |
| ***Frontline® Plus for Cats and Kittens*** (Merial) | **Solution:** Fipronil 9.8% (S)-Methoprene 11.8% | OTC | EPA approved. Labeled for cats or kittens ≥8 weeks. Single-dose applicators in packages of 3's and 6's |
| ***Frontline® Plus for Dogs and Puppies*** (Merial) | **Solution:** Fipronil 9.8% (S)-Methoprene 8.8% | OTC | EPA approved. Labeled for dogs or puppies ≥8 weeks. Single-dose applicators in packages of 3's and 6's<br>Dogs 11–22 lb: 0.67 mL<br>Dogs 23–44 lb: 1.34 mL<br>Dogs 45–88 lb: 2.68 mL<br>Dogs 89–132 lb: 4.02 mL |

### VETERINARY-LABELED FIPRONIL ± (S)-METHOPRENE TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Comments, size(s) |
|---|---|---|---|
| ***Parastar® for Dogs and Puppies*** (Novartis) | **Solution:** Fipronil 9.7% | Sold only through licensed veterinarians | EPA approved. Labeled for dogs or puppies ≥8 weeks. Single-dose applicators in packages of 3's and 6's<br>Dogs ≤ 22 lb: 0.67 mL<br>Dogs 23–44 lb: 1.34 mL<br>Dogs 45–88 lb: 2.68 mL<br>Dogs 89–132 lb: 4.02 mL |
| ***EasySpot® for Cats and Kittens*** (Novartis) | **Solution:** Fipronil 9.7% | Sold only through licensed veterinarians | EPA approved. Labeled for cats or kittens ≥8 weeks. Single dose applicators in packages of 3's |

### HUMAN-LABELED FIPRONIL ±(S)-METHOPRENE TOPICAL PRODUCTS

None.

## Imidacloprid Combinations

### INDICATIONS

The imidacloprid and pyriproxyfen topical solution (*Advantage II®*) is indicated for the prevention and treatment of all flea stages in dogs and cats and chewing lice in dogs. The imidacloprid, permethrin, and pyriproxyfen product (*K9 Advantix II®* – for dogs only) is indicated for repelling and killing fleas (all stages), ticks, and mosquitoes. Moreover, it repels biting flies and kills chewing lice. The imidacloprid and moxidectin product (*Advantage Multi® for Dogs* in the US and *Advocate®* in EU) is labeled for the prevention of heartworm disease, adult fleas, adult and immature hookworms, adult and immature roundworms (*Toxocara canis*), and adult whipworms. It has been also used successfully for the treatment of sarcoptic mange, cheyletiellosis, and mild cases of demodicosis. The feline combination product (*Advantage Multi® for Cats*) is indicated for the prevention of heartworm disease, adult fleas, ear mites, in addition to adult and immature hookworms and roundworms.

### MECHANISM OF ACTION

Imidacloprid acts on nicotinic acetylcholine receptors on the postsynaptic membrane, causing CNS impairment and death. Insects have more nicotinic acetylcholine receptors than mammals and are therefore more sensitive to these agents. This is a different mechanism of action than other insecticidal agents

such as organophosphates, pyrethrins, carbamates, insect growth regulators (IGRs), and insect development inhibitors (IDIs). The manufacturer states that when applied topically the compound is not absorbed into the bloodstream or internal organs.

Moxidectin, present in *Advantage Multi®*, is a macrocyclic lactone, and as such it binds to the glutamate-gated ion channels specific to parasites and increases the influx of chloride ions, resulting in hyperpolarization of neuronal cells and paralysis and death of the parasite.

Permethrin, present in *K9 Advantix II®*, is a pyrethroid (synthetic pyrethrin) that kills and repels ticks and mosquitoes. Permethrin acts by disrupting the sodium channel current in arthropod nerve cell membranes, resulting in paralysis and death.

Pyriproxyfen, present in *Advantage II®* and *K9 Advantix II®*, is a second-generation IGR and acts by interrupting the development of flea eggs, larvae, and early pupae. It mimics the action of an IGH known as juvenile hormone, which regulates the molting of insects from one stage to the other.

### SUGGESTED USES/DOSAGES

Refer to the package information for specific instructions on application of imidacloprid products. They are generally administered once monthly. While swimming, bathing, and rain do not apparently significantly affect the duration of action, repeated shampooing may require additional treatment(s) before the monthly dosing interval is completed. Do not reapply more often than once weekly for these animals. Recommended treatment protocols for the extra-label use of imidacloprid combined with moxidectin (*Advantage Multi®*) are as follows:

**For sarcoptic mange:** Two applications at a 4-week interval, or three applications at 3-week intervals, at the dose recommended by the manufacturer per body weight.

**For cheyletiellosis:** Two applications at a 4-week interval, at the dose recommended by the manufacturer per body weight.

**For generalized demodicosis:** Weekly to every-other-week applications, using the manufacture's recommended dose per body weight for 30 days past two consecutive negative skin scrapings. The authors only recommend using this medication for mild cases, because of its limited efficacy. Better results can be obtained with weekly applications compared to bi-weekly (Paterson *et al*. 2009).

### PRECAUTIONS/ADVERSE EFFECTS/OVERDOSES

The manufacturer lists the following contraindications for imidacloprid (alone): do not use in puppies younger than 7 weeks old or kittens younger than 8 weeks old. The manufacturer recommends consulting a veterinarian before using on debilitated, aged, pregnant, or nursing animals, or those on medication. Erythema and pruritus at the application site may occur with any of the imidacloprid topical formulations. The imidacloprid combination product with permethrin and pyriproxyfen **(*K9 Advantix II®*) must not be used on cats**. Avoid this combination product in households with both dogs and cats, particularly if cats are in close contact or will groom dogs in the household. The manufacturer states that imidacloprid is non-teratogenic, non-hypersensitizing, non-mutagenic, non-allergenic, non-carcinogenic, and non-photosensitizing.

When the product is used as directed, adverse effects are unlikely. Because the drug is bitter-tasting, oral contact may cause excessive salivation. Hypersalivation, tremors, vomiting, and reduced appetite may occur in cats after oral exposure to *Advantage Multi®*. Uncommon to rare adverse reactions reported in dogs treated with *Advantage Multi®* in a field study included pruritus, lethargy, reduced appetite, and hyperactivity. Do not get product in eyes. If eye contact occurs (human or animal), flush well with ophthalmic irrigation solution or water. While gloving is not mandated, it should be encouraged, as contact with skin should be avoided. Wash hands with soap and water after handling. Keep out of reach of children and do not contaminate feed or food. Dispose of product carefully (in the trash); the permethrin-containing product is extremely toxic to fish. There were 188 exposures to imidacloprid reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. Of these cases 95 were dogs, with 11 showing clinical signs, and 92 were cats, in which 20 showed clinical signs. Common findings in dogs, in decreasing frequency, included vomiting, diarrhea, and hypersalivation. Common findings in cats, in decreasing frequency, included hypersalivation, vomiting, and anorexia.

## VETERINARY-LABELED IMIDACLOPRID TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Advantage II® for Dogs*** (Bayer) | **Solution:** Imidacloprid 9.1% Pyriproxyfen 0.46% | Sold only through licensed veterinarians | EPA approved. Kills all flea stages and lice. For dogs and puppies ≥7 weeks. In cards of 4 or 6 tubes Dogs < 10 lb = 0.4 mL (green) Dogs 11–20 lb = 1 mL (teal) Dogs 21–55 lb = 2.5 mL (red) Dogs > 55 lb = 4 mL (blue) |
| ***Advantage II® for Cats*** (Bayer) | **Solution:** Imidacloprid 9.1% Pyriproxyfen 0.46% | Sold only through licensed veterinarians | EPA approved. Kills all flea stages and lice. For cats and kittens ≥8 weeks. In cards of 4 or 6 tubes Cats 5–9 lb = 0.4 mL (orange) Cats > 9 lb = 0.8 mL (purple) |
| ***Advantage Multi® for Dogs*** (Bayer) | **Solution:** Imidacloprid 10% Moxidectin 2.5% | Sold only through licensed veterinarians | EPA approved. Approved for dogs ≥7 weeks and > 3 lb |

## VETERINARY-LABELED IMIDACLOPRID TOPICAL PRODUCTS
(continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Advantage Multi® for Dogs*** (Bayer) | | | Dogs 3–9 lb = 0.4 mL, Advantage Multi 9<br>Dogs 9.1–20 lb = 1 mL, Advantage Multi 20<br>Dogs 20.1–55 lb = 2.5 mL, Advantage Multi 55<br>Dogs 55.1–88 lb = 4 mL, Advantage Multi 88<br>Dogs 88.1–110 lb = 5 mL, Advantage Multi 110<br>Dogs > 110 lb = use appropriate combination |
| ***Advantage Multi® for Cats*** (Bayer) | **Solution:**<br>Imidacloprid 10%<br>Moxidectin 1% | Sold only through licensed veterinarians | EPA approved. Approved for cats ≥9 weeks and >2 lb<br>Cats 2–5 lb = 0.23 mL, Advantage Multi 5<br>Cats 5.1–9 lb = 0.4 mL, Advantage Multi 9<br>Cats 9.1–18 lb = 0.8 mL, Advantage Multi 18<br>Cats > 18 lb = use appropriate combination |
| ***K9 Advantix II®*** (Bayer) | **Solution:**<br>Imidacloprid 8.8%<br>Permethrin 44%<br>Pyriproxyfen 0.44% | Sold only through licensed veterinarians | EPA approved. Repels and kills all flea stages, ticks, chewing lice and mosquitoes. Repels biting flies. Approved for dogs and puppies ≥7 weeks. **Do not use on cats.** In cards of 4 or 6 tubes<br>Dogs < 10 lb = 0.4 mL (green)<br>Dogs 11–20 lb = 1 mL (teal)<br>Dogs 21–55 lb = 2.5 mL (red)<br>Dogs > 55 lb = 4 mL (blue) |

## HUMAN-LABELED IMIDACLOPRID TOPICAL PRODUCTS
None.

## (S)-Methoprene Combinations

*For products containing **fipronil**, refer to the Fipronil ± (S)-Methoprene listing.*

### INDICATIONS

Methoprene is usually added to premise sprays and topical products labeled for dogs and cats to eliminate insects (usually fleas), via its ability to prevent maturation of eggs or larva.

### MECHANISM OF ACTION

(S)-Methoprene mimics insect juvenile growth hormone, halting larval development during metamorphosis and interrupting the flea life cycle. It also concentrates in female flea ovaries, causing non-viable eggs to be produced. When it is combined with an adulticide (e.g., permethrin, fipronil, phenothrin), all stages of the parasite are killed and re-infestation is less likely.

### SUGGESTED USES/DOSAGES

For specific use and dosage recommendations, refer to the product's label.

### PRECAUTIONS/ADVERSE EFFECTS

Methoprene may be found in products also containing **permethrin or phenothrin, which can be toxic to cats**, particularly small kittens. **Only use on cats those products containing permethrin or other pyrethroids labeled specifically for use on cats.** Hypersensitivity can occur to these compounds. Do not use in eyes or on mucous membranes. Methoprene (used alone) has low toxicity in mammals. Potentially, skin irritation or hypersensitivity reactions could occur. As methoprene is broken down by UV light, protect unused product from light.

## VETERINARY-LABELED (S)-METHOPRENE TOPICAL: NOT A COMPLETE LIST

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Adams Spot On® Flea & Tick Control*** (Farnam) | **Solution:**<br>(S)-Methoprene 3%<br>Permethrin 45% | OTC | EPA approved. Kills and repels adult fleas, ticks and mosquitoes. It also prevents flea eggs from developing into adult fleas. For dogs ≥ 6 months. **Do not use on cats**.<br>Packaged and labeled by the dog's weight in tubes of 3's<br>Dogs ≤ 30 lb = 0.034 oz<br>Dogs 31–60 lb = 0.068 oz<br>Dogs > 60 lb = 0.101 oz |
| ***Bio Spot On® Flea & Tick Control For Dogs*** (Farnam) | **Solution:**<br>(S)-Methoprene 3%<br>Permethrin 45% | OTC | EPA approved. Kills and repels adult fleas, ticks and mosquitoes. It also prevents flea eggs from developing into adult fleas. For dogs ≥ 6 months. **Do not use on cats.**<br>Packaged and labeled by the dog's weight in tubes of 3's<br>Dogs ≤ 30 lb = 0.034 oz<br>Dogs 31–60 lb = 0.068 oz<br>Dogs > 60 lb = 0.101 oz |
| ***Hartz UltraGuard Plus® Flea & Tick Drops for Dogs and Puppies*** (Hartz Mountain)<br>***Hartz UltraGuard Pro® Flea & Tick Drops for Dogs and Puppies* – with easy-to-use *Pro-Glide*® applicator** (Hartz Mountain) | **Solution/drops:**<br>(S)-Methoprene 2.3%<br>Phenothrin 85.7% | OTC | EPA approved. Phenothrin is a pyrethroid similar to permethrin; refer to the permethrin monograph for more information. For dogs ≥ 12 weeks or ≥4 lb. **Do not use on cats or kittens.** Kills fleas, ticks, mosquitoes and flea eggs for 30 days; repels fleas and ticks. Packaged and labeled by the dog's weight in tubes of 3's<br>Dogs 4–15 lb = 1.1 mL<br>Dogs 16–30 lb = 1.3 mL<br>Dogs 30–60 lb = 4.1 mL<br>Dogs > 60 lb = 5.9 mL |

(continued)

**VETERINARY-LABELED (S)-METHOPRENE TOPICAL: NOT A COMPLETE LIST** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| **Hartz UltraGuard *OneSpot*® *Treatment for Cats and Kittens*** (Hartz Mountain) | **Solution:**<br>(S)-Methoprene 2.9% | OTC | EPA approved. For kittens ≥12 weeks<br>Kills and prevents flea eggs and larvae for up to 30 days.<br>1 mL applicators |
| ***Hartz UltraGuard Plus*® *Drops for Cats*** (Hartz Mountain)<br>***Hartz UltraGuard Pro*® *Flea & Tick Drops for Cats* – with *Pro-cision Flo*® applicator** (Hartz Mountain) | **Solution/drops:**<br>(S)-Methoprene 3.6%<br>Etofenprox 40% | OTC | EPA approved. For cats ≥12 weeks<br>Kills fleas, flea eggs and deer ticks; kills and repels mosquitoes<br>Cats < 5 lb: 1 mL<br>Cats ≥ 5 lb: 1.8 mL |
| ***Bio-Spot*® *Flea & Tick Spray for Dogs and Puppies*** (Farnam) | **Spray:**<br>(S)-Methoprene 0.27%<br>Pyrethrins 0.2%<br>Piperonyl butoxide: 0.37% | OTC | EPA approved. Kills and repels fleas, ticks and mosquitoes. Prevents flea eggs from hatching. For dogs ≥ 12 weeks.<br>24 oz |
| ***Bio-Spot*® *Flea & Tick Repellent for Puppies*** (Farnam) | **Spray:**<br>(S)-Methoprene 0.1%<br>Pyrethrin 0.2%<br>Piperonyl butoxide 0.37% | OTC | EPA approved. Kills fleas and ticks and prevents flea eggs from hatching. For puppies ≥12 weeks. 16 oz |
| ***Hartz UltraGuard Plus*® *Flea & Tick Spray for Dogs*** (Hartz Mountain) | **Spray:**<br>(S)-Methoprene 0.07%<br>Tetrachlorvinphos 1.08% | OTC | EPA approved. Tetrachlorvinphos is an organophosphate insecticide. Not for use on puppies <12 weeks. Kills fleas and ticks for up to 7 days; prevents flea eggs from hatching for up to 30 days. 10 oz, 16 oz |

**VETERINARY-LABELED (S)-METHOPRENE TOPICAL: NOT A COMPLETE LIST** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Hartz UltraGuard Plus® Flea & Tick Spray for Cats*** (Hartz Mountain) | **Spray**<br>(S)-Methoprene 0.07%<br>Tetrachlorvinphos 1.08% | OTC | EPA approved. Tetrachlorvinphos is an organophosphate insecticide. Not for use on kittens <12 weeks. Kills fleas and ticks for up to 7 days; prevents flea eggs from hatching for up to 30 days. 8oz |
| ***Vet-Kem Ovitrol Plus® Flea, Tick & Bot Spray*** (Wellmark) | **Spray:**<br>(S)-Methoprene 0.27%<br>Pyrethrins 0.20%<br>Piperonyl Butoxide 0.37% | OTC | EPA approved. Kills and repels fleas, ticks, lice, flies, mosquitoes and gnats for up to 2 months. Prevents flea eggs from hatching Labeled for dogs, cats, puppies and kittens. Not for puppies or kittens <12 weeks. N-octyl bicycloheptene dicarboximide: 0.62%. 16oz, 1 gal |
| ***Bio Spot® Shampoo*** (Farnam) | **Shampoo:**<br>(S)-Methoprene 0.10%<br>Pyrethrins 0.15%<br>Piperonyl butoxide 1.50% | OTC | EPA approved. Kills fleas, ticks and lice. For dogs and cats ≥12 weeks. 12oz |
| ***Hartz UltraGuard Plus® Flea and Tick Dog Shampoo*** (Hartz Mountain) | **Shampoo:**<br>(S)-Methoprene 0.101%<br>d-trans allethrin 0.109%<br>N-octyl bicycloheptene dicarboximide 0.154% | OTC | EPA approved. Contains aloe. Kills adult flea and flea eggs and ticks for up to 30 days. Do not use on puppies <12 weeks. 18oz |

**VETERINARY-LABELED (S)-METHOPRENE TOPICAL: NOT A COMPLETE LIST** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Hartz UltraGuard Plus® Foaming Flea and Tick Shampoo for Cats*** (Hartz Mountain) | **Shampoo:**<br>(S)-Methoprene 0.101%<br>d-trans allethrin 0.109%<br>N-octyl bicycloheptene dicarboximide 0.154% | OTC | EPA approved. Kills adult flea and flea eggs and ticks for up to 30 days. Do not use on kittens <12 weeks. 5.25 oz |
| ***Vet-Kem Ovitrol Plus Flea & Tick Shampoo® for Dogs and Cats*** (Wellmark) | **Shampoo:**<br>(S)-Methoprene 1.1%<br>Pyrethrins 0.15%<br>Piperonyl butoxide 1.05% | OTC | EPA approved. Kills adult fleas, lice and ticks and prevents flea eggs from hatching Not for puppies or kittens <12 weeks. 12 oz |
| ***Hartz UltraGuard Plus® Flea & Tick Collar for Dogs*** (Hartz Mountain)<br>***Hartz UltraGuard Plus® Flea & Tick Collar for Puppies*** (Hartz Mountain) | **Collar:**<br>(S)-Methoprene 1.02%<br>Tetrachlorvinphos 14.55% | OTC | EPA approved. Kills and repels fleas and ticks and prevents flea eggs from hatching for up to 7 months. Not for use on puppies <6 weeks<br>Tetrachlorvinphos is an organophosphate insecticide and inappropriate use of this product may cause cholinesterase inhibition such as salivation, miosis, incoordination, muscle fasciculation and/or weakness, vomiting and diarrhea<br>Dogs: Fits up to 23 inch necks. Net contents: 33g<br>Puppies: Fits up to 15 inch necks. Net contents: 22g |

**VETERINARY-LABELED (S)-METHOPRENE TOPICAL: NOT A COMPLETE LIST** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Hartz UltraGuard Plus® Flea & Tick Collar for Dogs and Puppies* – with *Reflect-X Shield*** (Hartz Mountain) | **Collar:**<br>(S)-Methoprene 1.02%<br>Tetrachlorvinphos 14.55 % | OTC | EPA approved. Kills and repels fleas and ticks and prevents flea eggs from hatching for up to 7 months. Not for use on puppies <6 weeks<br>Tetrachlorvinphos is an organophosphate insecticide and inappropriate use of this product may cause cholinesterase inhibition such as salivation, miosis, incoordination, muscle fasciculation and/or weakness, vomiting and diarrhea. Fits up to 22-inch necks. Net contents: 26 g Reflect-X Shield (night-time safety feature). |
| ***Hartz UltraGuard Plus® Flea & Tick Collar for Cats and Kittens*** (Hartz Mountain) | **Collar:**<br>(S)-Methoprene 1.02%<br>Tetrachlorvinphos 14.55 % | OTC | EPA approved. Kills fleas and ticks and prevents flea eggs from hatching for up to 7 months. Not for use on kittens <12 weeks. Tetrachlorvinphos is an organophosphate insecticide and inappropriate use of this product may cause cholinesterase inhibition such as salivation, miosis, incoordination, muscle fasciculation and/or weakness, vomiting and diarrhea. Net contents: 17 g. Also available with Reflect-X Shield (night-time safety feature) |
| ***Sergeant's Double Duty® Flea & Tick Collar for Cats*** (Sergeant's) | **Collar:**<br>(S)-Methoprene 2.1%<br>Propoxur 10 % | OTC | EPA approved. Kills fleas, ticks and flea eggs for up to 8 months Not for use on kittens < 12 weeks. Propoxur is a carbamate insecticide. Do not use this product on cats/kittens simultaneously or within 30 days before or after treatment with or exposure to cholinesterase inhibiting drugs or pesticides (e.g., carbaryl or tetrachlorvinphos, etc.). Fits neck to 26 inches |

**VETERINARY-LABELED (S)-METHOPRENE TOPICAL: NOT A COMPLETE LIST** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Sergeant's Double Duty® Flea & Tick Collar for Dogs & Puppies*** (Sergeant's) | **Collar:**<br>(S)-Methoprene 2.1%<br>Propoxur 10% | OTC | EPA approved. Kills adult fleas, larvae and flea eggs and ticks for up to 5 months. Do not use on puppies < 12 weeks. Propoxur is a carbamate insecticide. Do not use this product on dogs/puppies simultaneously or within 30 days before or after treatment with or exposure to cholinesterase inhibiting drugs or pesticides (e.g., carbaryl or tetrachlorvinphos, etc.). Fits neck to 26 inches |
| ***Vet-Kem PowerBand® Flea & Tick Collar for Dogs*** (Wellmark)<br>***Vet-Kem Breakaway® Plus Flea & Tick Collar for Cats*** (Wellmark) | **Collar:**<br>(S)-Methoprene 2.1%<br>Propoxur 10% | OTC | EPA approved. Kills immature fleas, adult fleas and flea eggs for up to 8 months; kills ticks up to 6 months. Do not use on puppies or kittens < 12 weeks. Propoxur is a carbamate insecticide. Do not use this product on cats/kittens simultaneously or within 30 days before or after treatment with or exposure to cholinesterase inhibiting drugs or pesticides (e.g., carbaryl or tetrachlorvinphos, etc.)<br>Dogs (all sizes): 34g Cats (all sizes): 10.5g |

### HUMAN-LABELED (S)-METHOPRENE TOPICAL PRODUCTS

None.

## Permethrin and Permethrin Combinations

*For **additional permethrin products**, refer to the Dinotefuran, Imidacloprid, (S)-Methoprene, and Pyriproxyfen listings.*

### INDICATIONS

Permethrin is a synthetic pyrethroid that acts as an adulticide insecticide/miticide. It has knockdown activity against fleas, lice, ticks, and certain mites (e.g., *Cheyletiella*, *Sarcoptes scabiei*)) and also has repellent activity. In small animal medicine, it is used primarily for control of flea and tick infestations on dogs.

### MECHANISM OF ACTION

Permethrin acts by disrupting the sodium channel current in arthropod nerve cell membranes, resulting in paralysis and death.

### SUGGESTED USES/DOSAGES

For specific use and dosage recommendations, refer to the product's label.

### PRECAUTIONS/ADVERSE EFFECTS

**Permethrin (and other synthetic pyrethroids) can be very toxic to cats, particularly small kittens; therefore, only use products containing pyrethroids labeled for use on cats.** Moreover, permethrin-containing products should not be used in households with both dogs and cats where the specific product is prohibited for use on cats. Hypersensitivity to these compounds can occur. Do not use in eyes or on mucous membranes. Pruritus or mild skin irritations are uncommon but can occur at the application site. Clients should wear gloves when applying and wash off any product that contacts their skin.

### VETERINARY-LABELED PERMETHRIN TOPICAL PRODUCTS

Not a complete list.

## VETERINARY–LABELED PERMETHRIN TOPICAL: NOT A COMPLETE LIST

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Bansect® Squeeze-On Flea & Tick Control for Dogs®*** (Sergeant's) | **Solution:** Permethrin 45% | OTC | EPA approved. Kills and repels fleas and ticks. For dogs > 6 months. **It cannot be used on cats, or on dogs that cohabit with a cat.** 3 tubes per package Dogs < 33 lb = 1.5 mL Dogs > 33 lb = 3 mL |
| ***Freedom® 45 Spot-On for Dogs*** (Star Horse) | **Solution:** Permethrin 45% | OTC | EPA approved. Kills fleas, ticks, mosquitoes, lice and mites. For dogs ≥12 weeks. **It cannot be used on cats, or on dogs that cohabit with a cat** 2 or 3 tubes per package Dogs ≤ 33 lb = 1.5 mL Dogs 33–66 lb = 3 mL Dogs > 66 lb = 6 mL |
| ***Adams Spot On® Flea & Tick Control*** (Farnam) | **Solution:** Permethrin 45% (S)-Methoprene 3% | OTC | EPA approved. Kills and repels adult fleas, ticks and mosquitoes. It also prevents flea eggs from developing into adult fleas. For dogs ≥6 months. **It cannot be used on cats, or on dogs that cohabit with a cat.** 3 tubes per package Dogs ≤ 30 lb = 0.034 oz Dogs 31–60 lb = 0.068 oz Dogs > 60 lb = 0.101 oz |
| ***Bio Spot On® Flea & Tick Control For Dogs*** (Farnam) | **Solution:** Permethrin 45% (S)-Methoprene 3% | OTC | EPA approved. Kills and repels adult fleas, ticks and mosquitoes. It also prevents flea eggs from developing into adult fleas. For dogs ≥6 months. **It cannot be used on cats, or on dogs that cohabit with a cat.** 3 tubes per package Dogs ≤ 30 lb = 0.034 oz Dogs 31–60 lb = 0.068 oz Dogs > 60 lb = 0.101 oz |

**VETERINARY–LABELED PERMETHRIN TOPICAL: NOT A COMPLETE LIST** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***K9 Advantix II®*** (Bayer) | **Solution:**<br>Permethrin 44%<br>Imidacloprid 8.8%<br>Pyriproxyfen 0.44% | Sold only through licensed veterinarians | EPA approved. Repels and kills all flea stages, ticks, chewing lice and mosquitoes. Repels biting flies. Approved for dogs and puppies ≥7 weeks. **Do not use on cats.** In cards of 4 or 6 tubes<br>Dogs < 10 lb = 0.4 mL (green)<br>Dogs 11–20 lb = 1 mL (teal)<br>Dogs 21–55 lb = 2.5 mL (red)<br>Dogs > 55 lb = 4 mL (blue) |
| ***Liberty 50 Plus® IGR Spot-On*** (Star Hors) | **Solution:**<br>Permethrin 50%<br>Pyriproxyfen 1.2% | OTC | EPA approved. Kills and repels fleas, ticks, mosquitoes, lice and mites. Kills flea larvae and prevents eggs from hatching. For dogs >12 weeks. **It cannot be used on cats, or on dogs that cohabit with a cat.** Available for extra small, small, large and extra large dogs. |
| ***ProTICall® Insecticide for Dogs*** (Intervet-Schering-Plough) | **Spot-on liquid:**<br>Permethrin 65% | OTC | EPA approved. Kills and repels fleas, ticks and mosquitoes. Dosing amounts vary with dog weight; refer to directions. Labeled for use on puppies >4 weeks. **It cannot be used on cats, or on dogs that cohabit with a cat.** 6 × 1 mL applicators |
| **Flea Halt® Flea and Tick Spray for Dogs** (Farnam) | **Spray:**<br>Permethrin 0.1%<br>Pyrethrins 0.05%<br>Piperonyl butoxide 0.5% | OTC | EPA approved. Kills and repels fleas, ticks, flies, mosquitoes, gnats, chiggers and lice. For dogs >3 months. **It cannot be used on cats, or on dogs that cohabit with a cat.** 32 oz btl |
| ***Scratchex® Flea & Tick Spray For Dogs and Cats*** (Farnam) | **Spray:**<br>Permethrin 0.050%<br>Pyrethrins 0.056%<br>Related compounds 0.004% | OTC | Kills fleas and ticks. For dogs and cats ≥ 12 weeks. 7 oz btl |

### HUMAN-LABELED PERMETHRIN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; size(s); comments |
|---|---|---|---|
| ***Elimite***® (Allergan) **Generics** (various) | **Cream:** Permethrin 5% | Rx | Used for treating scabies in humans. 60 g |
| ***Acticin***® (Mylan Pharmaceuticals) **Generic** | **Cream:** Permethrin 5% | Rx | Used for treating scabies in humans. 30 g (generic), 60 g (brand name) |
| **Generic** (various) | **Lotion/cream rinse:** Permethrin 1% | OTC | Used for treating head lice in humans. 60 mL |

## Picaridin

### INDICATIONS

Picaridin is a human-labeled insect and acarid repellent of mosquitos, flies, fleas, ticks, and chiggers that may be used on dogs and cats. Picaridin is considered as effective as but safer than products based on DEET (N,N-diethyl-meta-toluamide), which may not be safe for use on dogs and cats.

### MECHANISM OF ACTION

Picaridin, also known as icaridin, pikaridin, propidine, and hydroxyethyl isobutyl piperidine carboxylate (INCI), is a piperidine derivative. The exact mechanism of action is unknown. Picaridin both repels and deters insects, so that insects move away from the chemical and do not feed if they encounter skin or clothing that has been treated. Insects appear to detect the chemical through olfactory sensing. Picaridin was shown to stimulate sensory hairs on the mosquito's antennae, and this appears to prevent the insect from recognizing its host's cues. Picaridin has no adverse affect on plastic, synthetics, plastic coatings, and sealants. It is almost colorless and odorless.

### SUGGESTED USES/DOSAGES

The use of picaridin on dogs and cats is completely anecdotal. Labeled for topical use only. For specific use recommendations, refer to the product's label for human use.

### PRECAUTIONS/ADVERSE EFFECTS

There is very limited information on the adverse effects of picaridin in dogs. No dermal or systemic toxicity were observed when picaridin was used at 50, 100, and 200 mg/kg in dogs in laboratory studies. There are no informative reports on potential adverse effects of picaridin in cats.

### VETERINARY-LABELED PICARIDIN TOPICAL PRODUCTS

None.

### HUMAN-LABELED PICARIDIN TOPICAL PRODUCTS

Other human-labeled products besides the ones listed below may be available.

| Product (company) | Form: concentration | Label status | comments/other ingredients/size(s) |
|---|---|---|---|
| ***Skin So Soft Bug Guard Plus Picaridin® Aerosol Spray*** (Avon)<br>***Skin So Soft Bug Guard Plus Picaridin® Pump Spray*** (Avon) | **Spray:** Picaridin 10% Vitamin E | OTC | EPA approved for use in humans (body and clothing). Extra-label use on dogs and cats. Repels mosquitoes for up to 8 hours. Provides effective protection against gnats, no-seeums, sand flies, and biting midges. Avoid ingestion. DEET-free. 4 oz |
| ***Natrapel® 8 Hour Pump*** (Adventure Medical Kits)<br>***Natrapel® 8 Hour Continuous Spray*** (Adventure Medical Kits)<br>***Natrapel® 8 Hour Wipes*** (Adventure Medical Kits) | **Spray/wipes:** 20% | OTC | EPA approved for use in humans (body and clothing). Extra-label use on dogs and cats. Repels mosquitoes for up to 8 hours. Avoid ingestion. DEET-free<br>1 oz, 3.5 oz pump btl (*Natrapel® Pump*)<br>5 oz spray btl (*Natrapel® Spray*)<br>12 wipes (*Natrapel® Wipes*) |
| ***Cutter® Advanced Sport Insect Repellent*** (Spectrum Group)<br>*Cutter®* ***Advanced Wipes*** (Spectrum Group) | **Spray/wipes:** 15% | OTC | EPA approved for use in humans (body and clothing). Extra-label use on dogs and cats. Repels mosquitoes for up to 4 hours. Avoid ingestion. DEET-free<br>6 oz pump aerosol spray btl (*Cutter® Advanced Sport Insect Repellent*)<br>12 wipes (*Cutter® Advanced Wipes*) |
| ***Cutter® Advanced Insect Repellent*** (Spectrum Group) | **Spray:** 5.75% | OTC | EPA approved for use in humans (body and clothing). Extra-label use on dogs and cats. Repels mosquitoes for up to 4 hours. Avoid ingestion. DEET-free. 6 oz pump spray btl |

## Pyrethrin Combinations

*For **otic** use, refer to the Otic section*

### INDICATIONS

Pyrethrins are naturally derived insecticides that act as an adulticide insecticides/miticides. They have knockdown activity against fleas, lice, ticks, and *Cheyletiella*. In small animal medicine, pyrethrins are used primarily for fleas and ticks on dogs and cats.

### MECHANISM OF ACTION

Pyrethrins act by disrupting the sodium channel current in arthropod nerve cell membranes, resulting in paralysis and death. Pyrethrins are often found in combination with the insect growth regulators, methoprene or pyriproxyfen and with the synergist piperonyl butoxide. Piperonyl butoxide inhibits insect metabolic enzymes (cytochrome P450 system), allowing a lower dose of primary insecticide to be used.

### SUGGESTED USES/DOSAGES

For specific use and dosage recommendations, refer to the product's label.

### PRECAUTIONS/ADVERSE EFFECTS

Pyrethrins are among the safest insecticidal products available, but **cats should not be allowed to groom wet product after using dips or sprays**. Hypersensitivity to these compounds can occur. Do not use in eyes or on mucous membranes. Avoid hypothermia when using liquid products (sprays, dips, etc.), particularly in small animals and when ambient temperatures are low. Pruritus or mild skin irritation can occur at application site, but uncommonly. Clients should wear gloves when applying and wash off any product that contacts their skin.

### VETERINARY-LABELED PYRETHRIN TOPICAL PRODUCTS

Not a complete list.

## VETERINARY-LABELED PYRETHRIN TOPICAL PRODUCTS: NOT A COMPLETE LIST

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Adams Flea & Tick Dust II®*** (VPL) | **Dust:**<br>Pyrethrins 0.1%<br>Carbaryl 12.5%<br>Piperonyl butoxide 1% | OTC | EPA approved. Silica gel 10%. Kills fleas, ticks and lice. Odorless. Labeled for dogs, cats, puppies, and kittens >12 weeks old. 3 oz |
| ***Adams® Plus Flea & Tick Mist* with Insect Growth Regulator** (IGR) (Farnam) | **Spray:**<br>Pyrethrins 0.18%<br>Pyriproxyfen 0.125% | OTC | EPA approved. N-octyl bicycloheptane dicarboxamide 1% (insecticide synergist). Kills and repels fleas, ticks, and mosquitoes. Also kills flea eggs and larvae. Labeled for dogs and cats. 16 oz, 32 oz |
| ***Adams® Flea & Tick Mist for Cats*** (Farnam) | **Spray:**<br>Pyrethrins 0.18%<br>Pyriproxyfen 0.125% | OTC | EPA approved. N-octyl bicycloheptane dicarboxamide 1% (insecticide synergist). Kills and repels fleas, ticks and mosquitoes. Also kills flea eggs and larvae. Labeled for cats. 16 oz |
| ***Bio-Spot® Flea & Tick Spray for Dogs and Puppies*** (Farnam) | **Spray:**<br>Pyrethrins 0.2%<br>Piperonyl butoxide 0.37%<br>(S)-Methoprene 0.27% | OTC | EPA approved. Kills and repels fleas, ticks and mosquitoes. Prevents flea eggs from hatching. Labeled for dogs ≥12 weeks. 24 oz |
| ***Bio-Spot® Flea & Tick Repellent for Puppies*** (Farnam) | **Spray:**<br>Pyrethrins 0.2%<br>Piperonyl butoxide 0.37%<br>(S)-Methoprene 0.1% | OTC | EPA approved. Kills fleas and ticks and prevents flea eggs from hatching Labeled for puppies ≥12 weeks. 16 oz |

(continued)

## VETERINARY-LABELED PYRETHRIN TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Flea Halt® Flea and Tick Spray for Dogs*** (Farnam) | **Spray:**<br>Pyrethrins 0.05%<br>Permethrin 0.1%<br>Piperonyl butoxide 0.5% | OTC | EPA approved. Kills and repels fleas, ticks, flies, mosquitoes, gnats, chiggers and lice. Labeled for dogs >3 months. **Do not use on cats.** 32 oz |
| ***Scratchex® Flea & Tick Spray for Dogs and Cats*** (Farnam) | **Spray**<br>Pyrethrins 0.056%<br>Permethrin 0.05%<br>Related compounds 0.004% | OTC | EPA approved. Kills fleas and ticks. Labeled for dogs and cats ≥12 weeks. 7 oz |
| ***Vet-Kem Ovitrol Plus® Flea, Tick & Bot Spray*** (Wellmark) | **Spray:**<br>Pyrethrins 0.2%<br>(S)-Methoprene 0.27%<br>Piperonyl butoxide 0.37% | OTC | EPA approved. N-octyl bicycloheptene dicarboximide: 0.62%. Kills and repels fleas, ticks, lice, flies, mosquitoes, and gnats for up to 2 months. Prevents flea eggs from hatching. Labeled for dogs, cats, puppies, and kittens. Not for puppies or kittens <12 weeks. 16 oz, 1 gal |
| ***Adams® Plus Flea & Tick Shampoo*** **with Insect Growth Regulator** (IGR) (Farnam) | **Shampoo:**<br>Pyrethrins 0.075%<br>Pyriproxyfen 0.086%<br>Piperonyl butoxide 0.75% | OTC | EPA approved. Kills fleas, ticks, and lice. Prevents flea eggs from hatching. Labeled for dogs and cats. 12 oz |
| ***Bio Spot® Shampoo*** (Farnam) | **Shampoo:**<br>Pyrethrins 0.15%<br>Piperonyl butoxide 1.5%<br>(S)-Methoprene 0.1% | OTC | EPA approved. Kills fleas, ticks, and lice. Prevents flea eggs from hatching. Labeled for dogs and cats ≥12 weeks. 12oz |

## VETERINARY-LABELED PYRETHRIN TOPICAL PRODUCTS (continued)

| Product (company) | Form: concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Bio Spot® Shampoo*** (Farnam) | **Shampoo:**<br>Pyrethrins 0.1%<br>Pyriproxyfen 0.01%<br>Piperonyl butoxide 0.5% | OTC | EPA approved. Kills adult fleas, flea larvae, and ticks. Labeled for dogs only. 12 oz |
| ***Ecto-Soothe® 3X Shampoo*** (Virbac) | **Shampoo:**<br>Pyrethrins 0.15%<br>Piperonyl butoxide 1.5% | OTC | EPA approved. Spherulite® microcapsules, N-octyl bicycloheptane dicarboxamide (MGK 264) 0.5%. Kills ticks, fleas, and lice. For dogs and cats ≥12 weeks. 8 oz, 16 oz, 1 gal |
| ***Vet-Kem Ovitrol Plus® Flea & Tick Shampoo*** (Wellmark) | **Shampoo:**<br>Pyrethrins 0.15%<br>Piperonyl butoxide 1.05%<br>(S)-Methoprene 1.1% | OTC | EPA approved. Kills adult fleas, ticks, and lice and prevents flea larvae from hatching. Not for puppies or kittens <12 weeks. 12 oz |
| ***Adams Pyrethrin Dip®*** (Farnam) | **Dip:**<br>Pyrethrins 0.97%<br>Piperonyl butoxide 3.74% | OTC | EPA approved. N-octyl bicycloheptene dicarboxamide 5.7%, di-n-propyl isocinchomeronate 1.94%. Kills and repels fleas, ticks, lice, gnats, mosquitoes, and flies. Not for puppies or kittens <12 weeks. Must be diluted before use. 4 oz |
| ***Bio Spot Pyrethrin Dip®*** (Farnam) | **Dip:**<br>Pyrethrin 0.97%<br>Piperonyl butoxide 3.74% | OTC | EPA approved. N-octyl bicycloheptene dicarboxamide 5.70%, di-n-propyl isocinchomeronate 1.94%. Kills and repels fleas, ticks, lice, gnats, mosquitoes, and flies. Labeled for dogs and cats >12 weeks. 4 oz |
| ***Pyrethrins Dip and Spray®*** (Davis) | **Dip and spray:**<br>Pyrethrin 3%<br>Piperonyl butoxide 30% | OTC | EPA approved. Petroleum distillate 12%. Kills fleas, ticks, and lice. Labeled for puppies or kittens >6 weeks. Must be diluted before use. Keep away from open flame. 16 oz, 1 gal |

### HUMAN-LABELED PYRETHRIN TOPICAL PRODUCTS

None.

## Pyriproxyfen Combinations

*For products containing **dinotefuran**, refer to the Dinotefuran + Pyriproxyfen, ± Permethrin listing*

### INDICATIONS

Like methoprene, pyriproxyfen is an insect growth regulator. It is added to premise sprays and topical products labeled for dogs and cats to eliminate insects (usually fleas) via its ability to prevent maturation of eggs or larva.

### MECHANISM OF ACTION

Pyriproxyfen is a second-generation insect growth regulator and acts by interrupting the development of flea eggs, larvae, and early pupae. It mimics the action of an insect growth hormone known as juvenile hormone, which regulates the molting of insects from one stage to the other. High concentrations of juvenile hormone prevent insect molting to the next stage. Normally, this hormone is broken down by an esterase, resulting in low concentrations and insect molting. Because pyriproxyfen is not broken down by juvenile hormone esterase, any flea stages exposed to high concentrations of pyriproxyfen are unable to molt to the next stage, and die.

### SUGGESTED USES/DOSAGES

For specific use and dosage recommendations, refer to the product's label.

### PRECAUTIONS/ADVERSE EFFECTS

Pyriproxyfen may be found in products also containing **permethrin, which can be toxic to cats**, particularly small kittens. **Only use on cats those products containing permethrin or other pyrethroids labeled specifically for cats.** Pyriproxyfen (used alone) has low toxicity in mammals. Potentially, skin irritation or hypersensitivity reactions could occur. Clients should wear gloves when applying products containing permethrin or other insecticides, and wash off any product that contacts their skin.

### VETERINARY-LABELED PYRIPROXYFEN TOPICAL PRODUCTS

Not a complete list; there are premise sprays and other topical products containing pyriproxyfen.

## VETERINARY-LABELED PYRIPROXYFEN TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Adams® Plus Flea & Tick Mist* with Insect Growth Regulator** (IGR) (Farnam) | **Spray:**<br>Pyriproxyfen 0.125%<br>Pyrethrins 0.18% | OTC | EPA approved. Kills and repels fleas, ticks, and mosquitoes. Also kills flea eggs and larvae. Labeled for dogs and cats. N-octyl bicycloheptane dicarboxamide 1% (insecticide synergist). 16 oz, 32 oz |
| ***Adams® Flea & Tick Mist for Cats*** (Farnam) | **Spray:**<br>Pyriproxyfen 0.125%<br>Pyrethrins 0.18% | OTC | EPA approved. N-octyl bicycloheptane dicarboxamide 1% (insecticide synergist). Kills and repels fleas, ticks, and mosquitoes. Also kills flea eggs and larvae. Labeled for cats only. 16 oz |
| ***Knock-out® Spray* Area Treatment** (Virbac) | **Spray:**<br>Pyriproxyfen (Nylar®) 0.015%<br>Tetramethrin 0.4%<br>Phenothrin 0.3% | Rx | **For environmental/indoor use only. Do not use on animals.** One treatment gives continuous flea protection for 120 days. 14 oz aerosol can. Covers approximately 2000 square feet. Caution: flammable |
| ***Knock-out ES® Spray* Area Treatment** (Virbac) | **Spray:**<br>Pyriproxyfen (Nylar®) 0.1%<br>Pyrethrins 0.05%<br>Permethrin 0.435%<br>N-octyl bicycloheptene dicarboximide 0.4% | Rx | **For environmental/indoor use only. Do not use on animals.** Kills adult fleas and ticks and controls larvae. Prevents flea reinfestation for 7 months. 16 oz aerosol inverted can. Covers approximately 2100 square feet. Caution: flammable |
| ***Knock-out Room and Area Fogger® Spray*** (Virbac) | **Fogger:**<br>Pyriproxyfen (Nylar®)0.1%<br>Pyrethrins 0.05%<br>Permethrin 0.4%<br>N-octyl bicycloheptene dicarboximide 0.4%<br>Related compounds 0.035% | Rx | **For environmental/indoor use only. Do not use on animals.** Kills fleas for 7 months. Also kills ticks, cockroaches, spiders, and ants. 16 oz aerosol inverted can. Use one fogger for each 6000 cubic feet (approximately 27 feet × 8 feet ceiling). Caution: flammable |

(continued)

**VETERINARY-LABELED PYRIPROXYFEN TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Adams® Plus Flea & Tick Shampoo* with Insect Growth Regulator** (IGR) (Farnam) | **Shampoo:**<br>Pyriproxyfen 0.086%<br>Pyrethrins 0.075%<br>Piperonyl butoxide 0.750% | OTC | EPA approved. Kills fleas, ticks, and lice. Prevent flea eggs from hatching. Labeled for dogs and cats. 12 oz |
| ***Bio Spot® Shampoo*** (Farnam) | **Shampoo:**<br>Pyriproxyfen 0.01%<br>Pyrethrins 0.1%<br>Piperonyl butoxide 0.5% | OTC | EPA approved. Kills adult fleas and larvae and ticks. Labeled for dogs only. 12 oz |
| ***Liberty® 50 Plus IGR Spot-On*** (Star Hors) | **Solution:**<br>Pyriproxyfen 1.2%<br>Permethrin 50% | OTC | EPA approved. Kills and repels fleas, ticks, mosquitoes, lice, and mites. Kills flea larvae and prevents eggs from hatching. Labeled for dogs >12 weeks. **It cannot be used on cats, or on dogs that cohabit with a cat.** Available in three dosage sizes: <33 lb, 33–66 lb, >66 lb |
| ***TriForce® Canine Squeeze-On*** (Tradewinds) | **Solution:**<br>Pyriproxyfen 2%<br>Cyphenothrin 40% | OTC | EPA approved. Kills and repels fleas, ticks, and mosquitoes. Kills flea larvae and prevents eggs from hatching. For use on dogs ≥12 weeks. **It cannot be used on cats, or on dogs that cohabit with a cat.** Available in four dosage sizes: 9–20 lb, 21–39 lb, 40–60 lb and ≥61 lb |

**VETERINARY-LABELED PYRIPROXYFEN TOPICAL PRODUCTS** (continued)

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Advantage II® for Dogs*** (Bayer) | **Solution:**<br>Pyriproxyfen 0.46%<br>Imidacloprid 9.1% | Sold only through licensed veterinarians | EPA approved. Kills all flea stages and lice. For dogs and puppies ≥ 7 weeks. In cards of 4 or 6 tubes<br>Dogs < 10 lb = 0.4 mL (green)<br>Dogs 11–20 lb = 1 mL (teal)<br>Dogs 21–55 lb = 2.5 mL (red)<br>Dogs > 55 lb = 4 mL (blue) |
| **Advantage II® for Cats** (Bayer) | **Solution:**<br>Pyriproxyfen 0.46%<br>Imidacloprid 9.1% | Sold only through licensed veterinarians | EPA approved. Kills all flea stages and lice. For cats and kittens ≥ 8 weeks. In cards of 4 or 6 tubes<br>Cats 5–9 lb = 0.4 mL (orange)<br>Cats > 9 lb = 0.8. mL (purple) |
| **K9 Advantix II®** (Bayer) | **Solution:**<br>Pyriproxyfen 0.44%<br>Permethrin 44%<br>Imidacloprid 8.8% | Sold only through licensed veterinarians | EPA approved. Repels and kills all flea stages, ticks, chewing lice, and mosquitoes. Repels biting flies. Approved for dogs and puppies ≥7 weeks. Do not use on cats. In cards of 4 or 6 tubes<br>Dogs < 10 lb = 0.4 mL (green)<br>Dogs 11–20 lb = 1 mL (teal)<br>Dogs 21–55 lb = 2.5 mL (red)<br>Dogs > 55 lb = 4 mL (blue) |

### HUMAN-LABELED PYRIPROXYFEN TOPICAL PRODUCTS

None.

## Rotenone

### INDICATIONS

Dermatologists will occasionally prescribe rotenone to treat the localized form of canine demodicosis when clients request an intervention, despite the high likelihood for spontaneous resolution of this disease.

### MECHANISM OF ACTION

Rotenone works by interfering with the electron transport chain in the mitochondria, preventing the conversion of nicotinamide adenine dinucleotide (NADH) to adenosine triphosphate (ATP), a usable form of cellular energy. Rotenone occurs naturally in the roots and stems of various tropical and subtropical plants, especially the ones from the genus *Lonchocarpus* or *Derris*. It is characterized as a broad-spectrum pesticide, insecticide, and piscicide.

### SUGGESTED USES/DOSAGES

Apply to the affected area(s) once daily until two consecutive negative skin scrapings are obtained. Prevent the animal from licking at the treated area(s) for at least 30 minutes after application, to avoid ingestion and allow the medication to work.

### PRECAUTIONS/ADVERSE EFFECTS

Rotenone is mildly toxic to mammals; however, it is very toxic to fish and insects.

### VETERINARY-LABELED ROTENONE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Other ingredients; size |
|---|---|---|---|
| ***Goodwinol® Ointment*** (Goodwinol Products Corp) | Rotenone 0.45% Benzocaine 2.05% | Rx | Lanolin. Labeled for dogs. 1 oz |

### HUMAN-LABELED ROTENONE TOPICAL PRODUCTS

None.

## Spinetoram

### INDICATIONS

Spinetoram (*Assurity®*) is recommended by the manufacturer for the prevention and treatment of flea infestations in cats and kittens 8 weeks of age or older.

### MECHANISM OF ACTION

Spinetoram activates the nicotinic acetylcholine receptors (nAChRs) causing the death of fleas. The manufacturer claims that *Assurity®* starts working within 30 minutes and kills 98–100% of fleas within 12 hours.

### SUGGESTED USES/DOSAGES

One low-volume dose treats cats of all sizes/body weights. The manufacturer recommends applying the tube contents topically to the skin at the base of the cat's neck once monthly. Refer to package insert for more details.

### PRECAUTIONS/ADVERSE EFFECTS

For external use on cats and kittens only. Do not use on kittens less than 8 weeks of age. The manufacturer recommends veterinarian consultation prior to using the product on debilitated, aged, pregnant, or nursing animals, or animals known to be sensitive to pesticides. Sensitivities, such as hair sparseness, hair loss, skin irritation or discoloration, or salivation, may occur. Spinetoram can be hazardous to humans if swallowed. It causes moderate eye irritation. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Avoid contact with eyes or clothing.

### VETERINARY-LABELED SPINETORAM TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Comments/size(s) |
|---|---|---|---|
| ***Assurity®*** (Elanco) | **Solution:** 39.6% | Rx | EPA approved. Labeled for cats ≥8 weeks. One applicator contains 0.019 oz (0.57 mL). 6 doses per package |

### HUMAN-LABELED SPINETORAM TOPICAL PRODUCTS

None.

## MISCELLANEOUS

## All Natural

*For completeness, refer to other topical products containing solely natural ingredients in other monograph sections*.

| Product (company) | Form: concentration | Label status | Other ingredients/comments/size(s) |
|---|---|---|---|
| ***Biobalm***® (Aventix Animal Dermo-Care) | **Ointment:**<br>Palm and soy seed oils<br>Cajputi essential oil | Sold only through licensed veterinarians | Labeled for dogs and cats. Recommended for idiopathic hyperkeratosis of the footpads and nose, other footpad disorders (e.g., fissures, split paw-pad disease), hydration of elbow callus, and skin protection against heat or cold injuries. Palm and soy seed oils provide omega 6 and 3 essential fatty acids to hydrate the skin. Cajputi essential oil provides soothing and antiseptic effects. 50 mL |
| ***Bug Band Pump Spray***® (BugBand) | **Spray:**<br>Geraniol | OTC | Insect repellent that can be used in dogs and cats. Inactive ingredients include beeswax, soy bean oil, xanthan gum, glycerin, chamomile butter extract, shea butter, potassium sorbate, sodium coco sulfate, sorbitan tristearate, d-alpha-tocopherol, and deionized water. Frequent applications (every few hours) may be needed. Avoid ingestion, mainly with cats. 4 oz, 6 oz |
| ***Elimiderm***® (Van Beek Natural Science) | **Cream:**<br>Essential oils from oregano, cinnamon, and clove leaf oil: carvacrol, thymol eugenol, cinnameldahyde 900 mg<br>Vitamin E 8.5 IU<br>Aloe vera 53 mg<br>Sersquitepenoid 51 mg<br>Salicin 7.8 mg | Sold only through licensed veterinarians | Labeled for dogs and cats. Indicated for skin conditions associated with bacteria and fungal/yeast infections. Also recommended for minor cuts and acute moist dermatitis. May also aid in limiting inflammation. 0.75 oz |

**ALL NATURAL** (continued)

| Product (company) | Form: concentration | Label status | Other ingredients/comments/size(s) |
|---|---|---|---|
| ***LickGuard® Topical Ointment*** (Van Beek Natural Science) | **Ointment:** Carvacrol, menthol, limonene, carvone, thymol, eugenol, allicin, cinnamic aldehyde | Sold only through licensed veterinarians | Labeled for dogs and cats. Other ingredients: beeswax, deionized water, lanolin, petrolatum, potassium chloride, sesquiterpenoid, sodium chloride, spearmint oil. This product contains all-natural unpleasant-tasting ingredients. The manufacturer recommends using it in conditions where licking by the animal is discouraged, such as acral lick dermatitis, suture lines, minor cuts, bandages. 0.75 oz |
| ***Skin So Soft Original Bath Oil®*** (Avon)<br>***Skin So Soft Original Bath Oil Spray®*** (Avon) | **Spray:** *Daucus carota sativa* (carrot) seed oil<br>Mineral oil | OTC | Human cosmetic line. Extra-label insect repellent that can be used topically on dogs and cats. Contains fragrance. Frequent applications (every few hours) may be needed. Moisturizer. Avoid ingestion, mainly with cats. 5 oz, 16.9 oz, 24 oz |

## Capsaicin

### INDICATIONS

Capsaicin has been anecdotally recommended for the treatment of acral lick dermatitis in dogs. The authors have no experience using this compound to treat canine acral lick dermatitis.

### MECHANISM OF ACTION

Capsaicin (8-methyl N-vanillyl-6-noneamide) is a compound obtained from red peppers. The rationale for using topical capsaicin is related to its effect on substance P, an endogenous undecapeptide widely distributed in afferent sensory fibers. Substance P is a neurotransmitter and transmits the pain and itch sensations from the periphery to the central nervous system. It is also a potent vasodilator, and it may be the vasoactive substance responsible for the axon-reflex vasodilation or flare. Repeated local applications of capsaicin have been demonstrated to deplete substance P from peripheral sensory neurons, and then block further synthesis and transport of substance P within the neuron, preventing its re-accumulation. Capsaicin appears to act principally on unmyelinated type C sensory neurons, which are associated with cutaneous pain and pathological itch sensations. The alkaloid does not appear to act directly on central cells in the spinal cord and brain.

### SUGGESTED USES/DOSAGES

As the duration of action of capsaicin is short, the recommendation is to apply a thin layer of the product 3–5 times daily for at least 4 weeks before any benefit can be noted. **Capsaicin should *not* be applied on eroded or ulcerated skin surfaces.** Therefore, it is important to make sure any eroded or ulcerated area, typically present in acral lick dermatitis, is resolved before starting capsaicin therapy.

### PRECAUTIONS/ADVERSE EFFECTS

The following adverse reactions have been reported in people. Application-site adverse effects such as erythema, pain, edema, pruritus, local discomfort (burning, stinging) are common. Local discomfort and pain occur more frequently if the product is applied less than three times daily. Coughing, sneezing, and shortness of breath have been reported with inhalation of airborne capsaicin. Vomiting, diarrhea, and irritation of mucosal lining may occur with ingestion of capsaicin. Avoid contact with mucosal surfaces and eroded or ulcerated skin.

### VETERINARY-LABELED CAPSAICIN TOPICAL PRODUCTS

None.

### HUMAN-LABELED CAPSAICIN TOPICAL PRODUCTS

Not a complete list.

### HUMAN-LABELED CAPSAICIN TOPICAL PRODUCTS: NOT A COMPLETE LIST

| Product (company) | Form: concentration | Label status | Size(s) |
|---|---|---|---|
| ***Capsicum Oleoresin®*** (Glades Pharmaceuticals), ***Trixaicin®*** (Qualitest), ***Zostrix®*** (Medicis), **Generic** | **Cream:** 0.025% | OTC | Depending on product: 21 g, 45 g, 60 g, 90 g |
| ***Capsicum Oleoresin®*** (Glades Pharmaceuticals), ***Capzasin-HP®*** (Thompson Medical), ***Zostrix® High Potency*** (Medicis), **Generic** | **Cream:** 0.075% | OTC | Depending on product: 30 g, 56.6 g, 60 g, 90 g |
| ***Capsicum Oleoresin®*** (Glades Pharmaceuticals), ***Dolorac®*** (Medicis), **Generic** | **Cream:** 0.25% | OTC | Depending on product: 30 g, 90 g |
| ***Capzasin-P®*** (Thompson Medical) | **Lotion:** 0.025% | OTC | 60 mL |
| ***Capzasin-HP®*** (Thompson Medical)<br>***Pharmacist's Capsaicin®*** (Reese) | **Lotion:** 0.075% | OTC | 58 mL<br>59.1 mL |
| ***Zostrix® Balm*** (Medicis)<br>***Zostrix® Stick HP*** (Medicis) | **Ointment:** 0.025% | OTC | 21 g<br>0.7 oz |

## Dimethyl Sulfoxide

### INDICATIONS

In small animal veterinary dermatology, dimethyl sulfoxide (DMSO) is used primarily as an adjunctive therapy for acral lick dermatitis, hyperplastic otitis externa, and calcinosis cutis. It is combined with a glucocorticoid ± a non-steroidal anti-inflammatory drug for the treatment of acral lick dermatitis and hyperplastic otitis externa, or used as sole therapy for calcinosis cutis.

### MECHANISM OF ACTION

DMSO is an organosulfur compound with various pharmacologic effects. It scavenges free-radical hydroxide, and the metabolite dimethyl disulfide scavenges free-radical oxygen. These actions help to explain some of the anti-inflammatory, anti-ischemic, cryopreservative, and radioprotective effects of DMSO. It also has antibacterial (weak) and antifungal properties. The anti-inflammatory effect of DMSO is greater when it is used for acute rather than chronic inflammation. DMSO has an unique property of penetrating the skin and mucosa easily, and has been used as a drug delivery system.

### SUGGESTED USES/DOSAGES

For acral lick dermatitis, the combination of DMSO and fluocinolone acetonide (*Synotic*®) with or without the addition of flunixin meglumine (*Banamine*®) is typically applied 2–3 times daily with the goal of reducing the associated fibrosis and inflammation. For hyperplastic otitis externa, *Synotic*® is commonly used 2–3 times daily or as indicated to reduce the hyperplasia. It is important to note that DMSO is only part of the treatment regimen for these conditions. The use of DMSO to treat calcinosis cutis is anecdotal and empirical at this time. The recommendation is to apply the medical-grade product to one-third of the affected area daily until resolution of clinical signs. To the authors' knowledge, there are no reports demonstrating that the topical use of DMSO in conjunction with the adequate treatment of hyperadrenocorticism (most common cause of calcinosis cutis in dogs) accelerates the resolution of lesions.

### PRECAUTIONS/ADVERSE EFFECTS

DMSO is a very safe drug when used as labeled. Local skin reactions are possible, however, including a "burning" sensation, erythema, vesiculation, and dryness. It can also be irritating to the mucosal membranes. Reversible ocular lens changes have been noted in laboratory animals when DMSO is used long-term and at high doses. Garlic or oyster-like breath odor is very common when administering DMSO. It is recommended to wear gloves when applying DMSO-containing products. Monitor serum $Ca^{++}$ concentration once a month during treatment of calcinosis cutis, as hypercalcemia may occur.

### VETERINARY-LABELED DIMETHYL SULFOXIDE TOPICAL PRODUCTS

| Product (company) | Form: concentration | Label status | Comments; size(s) |
|---|---|---|---|
| ***Domoso® Gel*** (Fort Dodge) | **Gel:** 90% (medical grade) | Sold only through licensed veterinarians | 60 g, 120 g |
| ***Domoso® Solution*** (Fort Dodge) | **Solution:** 90% (medical grade) | Sold only through licensed veterinarians | 16 oz, 1 gal |
| ***Synotic® Otic Solution*** (Fort Dodge) | **Solution (otic):** DMSO 60% Fluocinolone acetonide 0.01% | Sold only through licensed veterinarians | 60 mL. May be compounded if unavailable |
| ***Synotic® Otic Solution*** (Fort Dodge) + ***Banamine®*** (Schering Plough); Compounded | **Solution:** DMSO 60% Fluocinolone acetonide 0.01% Flunixin meglumine 0.01% | Sold only through licensed veterinarians | Mix 3 mL of *Banamine*® in 8 mL of *Synotic*® |

### HUMAN-LABELED DIMETHYL SULFOXIDE TOPICAL PRODUCTS

Not an all-inclusive list, as several OTC products are available.

| Product (company) | Form: concentration | Label status | Size |
|---|---|---|---|
| ***Rimso-50® Topical Solution*** (Research Medical), ***Rimso–50® Irrigation Solution*** (Ben Venue Laboratories), **generic** | **Many forms available:** 50% | OTC | 50 mL |
| **DMSO Cream Rose Scented** (Nature's Gift) | **Cream:** 70% | OTC | 4 oz |
| **DMSO Gel with Aloe Vera** (Nature's Gift) | **Gel:** 70% | OTC | 30% aloe vera. 4 oz |

## Sunscreen

### INDICATIONS

Sunscreens are used to protect depigmented or lightly pigmented, thin-haired or alopecic skin surfaces against principally UVB damage.

### MECHANISM OF ACTION

UVB radiation (wavelength: 290–320 nm) causes sunburns, malignancies, and tanning, whereas UVA radiation (wavelength: 320–400 nm) causes tanning and may act with UVB radiation to promote malignancies. Sunscreens act mostly by two processes: "scattering" and "absorption" of UV radiation.

**Physical sunscreen** formulations form an opaque coating on the skin surface (e.g., zinc oxide paste), scattering or reflecting the UV energy away from its original path and thereby preventing or minimizing sunburns, photo-aging, and tanning. Non-opaque products that include particulate sunscreens such as titanium oxide and zinc oxide will also have the same effect.

**Chemical sunscreens** absorb UV energy by incorporating the energy into the electron structure of the sunscreen molecule. This often results in re-radiation of the energy as infrared radiation (heat), which has a less damaging wavelength. The physical sunscreens can also absorb UV energy.

Most commercially available products will combine two or more active sunscreen ingredients. Products with a sun protection factor (SPF) > 30 typically have better protection, because many of their ingredients have some UVA radiation absorption. Concentrations of active ingredients correlate directly with the spectrum of action of the product. SPF value is not allowed on labels of pet products.

### SUGGESTED USES/DOSAGE

Apply to the desired area(s) before sun exposure and reapply every 1–2 hours as needed. Do not allow the animal to lick at the applied site(s) for at least 20–30 minutes after application, to avoid ingestion and allow the product to work.

### PRECAUTIONS/ADVERSE EFFECTS

For external use only; therefore avoid eye contact and ingestion.

## VETERINARY-LABELED SUNSCREEN PRODUCTS

| Product (company) | Form: active ingredients/ concentration | Label status | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Dermoscent® SunFree*** (Aventix Animal Dermo-Care) | **Spray:** Titanium dioxide | Sold only through licensed veterinarians | Aqua alumina, stearic acid, sorbitan oleate, caprylic/ capric triglyceride, glycerin, candelilla cera, magnesium stearate, tocopheryl acetate. Candelilla cera provides filmogen action to hydrate the skin. Labeled for dogs and cats. Manufacturer claims SPF value of 30. UVA and UVB protection. All ingredients are natural and formulation is water-resistant. 30 mL |
| ***Epi-Pet® Sun Protector Spray*** (Epi-Pet Skin Treatment) | **Spray:** Ethylhexl methoxycinnamate 7.5% Octyl salicylates 5% Homosalate 7.5% Benzophenone–3 6.00% | OTC | Other ingredients: alcohol denaturated, aqua, ethylhexyl salicylates, C-12-15 alkyl benzoate, acrylates/octylacrylamide copolymer, tocopheryl acetate, perfume. FDA approved for dogs. Manufacturer claims SPF value of 30–45. UVA and UVB protection. 4 oz |
| ***Vet's + Best® Sun Relief Spray*** (Vet's Best) | **Spray:** Titanium dioxide | OTC | Other ingredients: aloe vera, willowherb extract, *Boswellia* extract, witch hazel. Labeled for dogs. All ingredients are natural. 4 oz |
| ***Doggles® Pet Sunscreen*** (Doggles) | **Spray:** DMDM hydantion Glyceryl trioctanoate Propolene glycol Dicaprylate dicaprate | OTC | Distilled water. Labeled for dogs. **Manufacturer claims SPF value of 15. UVA and UVB protection.** 2 oz |

### HUMAN-LABELED SUNSCREEN PRODUCTS

There are various human sunscreen products available OTC. Children's sunscreen may be used on dogs and cats in the absence of veterinary products. As there are products formulated and labeled for animal use, human products are not listed here. For more information on these products, refer to a comprehensive human drug reference (e.g., *Micromedex*) or contact a pharmacist.

## OTIC PREPARATIONS

While not a complete list, the following examples are representative of the topical otic preparations available to the veterinarian. Products listed may be available over the counter (OTC), may require prescription, or may be sold only through licensed veterinarians. Refer to the product label before using any product.

## General information

It is important to demonstrate to clients the ear-cleaning technique and the administration of topical otic medications when treating ear diseases. Advise clients to discontinue the product application and contact a veterinarian if the ears become redder or more inflamed at any time during the course of cleaning or treatment, as local cutaneous adverse reactions may occur.

When treating infectious otitis, antibiotic and/or antifungal topical medications should be administered at least twice daily in order to be effective. It is very important to recheck the patient before discontinuing treatment of otitis, as the medication(s) should be administered until 1–2 weeks after a negative cytology and/or ear culture, depending on the infectious microorganism(s) present and the patient's history. When using topical steroids to reduce otic hyperplasia and stenosis, 1–4 times daily applications may be used. The frequency and duration of ear cleaning varies according to the needs of the individual patient.

Adverse effects associated with ear cleaning and ear medications can include maceration, contact reactions, otitis media, ear canal avulsion, Horner's syndrome, facial nerve paralysis, and variable signs of ototoxicity including deafness and vestibular symptoms (e.g., ataxia, nystagmus, head tilt).

## Ototoxicity

Ototoxicity is defined as a harmful effect of a medication on the eighth cranial nerve or the organs of hearing and balance. The absence or rupture/perforation of the tympanic membrane can allow potentially ototoxic topical medications to reach the inner ear and cause toxicity. The incidence of ototoxicity in dogs and cats is unknown.

It is documented that more than 50% of dogs with chronic ear disease have absent or ruptured tympanic membrane (Cole *et al*. 1998), and considering that most cases of ear disease in dogs and cats are treated topically, veterinarians should be familiar with the ototopical drugs that are considered safe or potentially ototoxic.

In dogs and cats, ototoxic signs are often subtle and not detected until severe damage to the sensorineural cells of the cochlea and vestibular apparatus has already occurred, resulting in deafness and vestibular signs (nystagmus, ataxia, head tilt, etc.).

Most of the information available to veterinarians regarding ototoxicity presumably associated with ear cleaners and medications is anecdotal or based on humans or laboratory animal studies. Therefore, care should be taken when extrapolating to dogs and cats information based on personal experience or studies conducted in other species. In addition, the type of otic damage (e.g., vestibular and/or auditory dysfunction such as hearing loss) and its correlation with potentially ototoxic topical products is mostly speculative at this time.

Disease duration may influence the absorption of otic products in the inner ear. In the early stages of otitis media the permeability of the round (cochlear) window membrane increases; in contrast, as the disease becomes chronic, thickening of the membrane is noted, preventing the penetration of ototoxic substances into the inner ear. Interestingly, some ototoxic medications are pro-inflammatory (see Table 2, below), causing thickening of the middle ear mucosa and the membrane of the round window, which limits their absorption into the inner ear (Gotthelf 2005).

Duration of therapy and age can influence the severity of nervous tissue damage and the reversibility of ototoxic signs. It was previously shown in guinea pigs that the degree of cochlear damage and hearing loss worsens as the duration of neomycin application to the middle ear increases (Brummett *et al*. 1976). Young animals seem to be more sensitive to the ototoxicity of antibiotics (Gotthelf 2005). Neomycin was shown to be particularly ototoxic when used in the ears of 2- or 3-week-old kittens (Leake and Hradek 1988).

## EAR CLEANERS, ANTISEPTICS

There are many ear cleaners available, and for most of them there is no information regarding safety for the ears of dogs and cats. One study carried out in dogs and guinea pigs showed that among the ingredients tested (squalene, dyoctil sodium succinate, carbamide peroxide, and triethanolamine), only squalene caused no morphologic or neurologic abnormality after 4 weeks of treatment based on brain auditory evoked response (BAER) test and neurologic examination (Mansfield *et al*. 1997).

Package inserts of chlorhexidine otic preparations advise against their use when the possibility of tympanic membrane rupture exists. The ototoxicity potential of chlorhexidine appears to differ according to its concentration. Studies evaluating chlorhexidine ototoxicity in cats have shown pronounced degeneration of cochlear and vestibular hair cells with 2% chlorhexidine gluconate, and minor but repeatable intracellular abnormalities at 0.05%. However, even with the most diluted chlorhexidine solution (0.05%) there were still vestibular signs (Igarashi and Suzuki 1985, Igarashi and Oka 1988). A study performed in dogs with myringotomies showed that 0.2% chlorhexidine applied twice daily in the ears for 21 days appears to be safe as an irrigating solution for the middle ear (Merchant *et al*. 1995). However, a more recent study showed that chlorhexidine gluconate 0.5% solution and ethyl alcohol 70% in water, but not povidone iodine 10% (equal to 1% iodine in aqueous solution), administered topically in the middle ear of sand rats once daily for 5 consecutive days, had a profound effect on both vestibular and cochlear functions (Perez *et al*. 2000). The authors recommend caution when using chlorhexidine solution at any concentration in the ears of dogs and cats, particularly in those with unknown status or rupture of tympanic membranes.

Agents that are believed to be safe in dogs and cats for ear flushing in the presence of ruptured tympanic membrane include sterile water, sterile saline, tris-EDTA, and possibly chlorhexidine at a concentration of less than 0.05% (Paterson 2008). Administration of ceruminolytic agents, except for squalene-containing products, should be avoided in the middle ear and in cases with unknown status or rupture of the tympanic membrane.

### VEHICLES

Inactive or vehicle ingredients added to ear cleaners and medications can also cause ototoxicity. Propylene glycol, a solvent often present in topical otic medications and known to cause inflammation in the external canal, can also cause inflammation in the mucoperiosteum leading to excessive granulation tissue and bony changes within the bulla. Propylene glycol has also been implicated as one of the causal agents of cholesteatoma formation in the middle ears of chinchillas (Vassalli *et al*. 1988). Alcohol-based disinfectants may also cause damage to the middle ear canal. Aqueous povidone iodine seems to be safe in the middle ear, but not tincture of iodine, which contains alcohol (Gotthelf 2005). Therefore, propylene glycol- and alcohol-containing products should be avoided if the status of the tympanic membrane cannot be determined or if it is ruptured.

### ANTIMICROBIAL AGENTS

Aminoglycosides are believed to be ototoxic in humans by causing damage initially to the hair cells of the cochlea, which later results in degeneration of other cochlear structures (Huizing and de Groot 1987). There have been many anecdotal reports of acute deafness in dogs associated with administration of gentamicin-containing otic products. However, in a controlled study where a low-dose aqueous gentamicin solution (3 mg/mL) was applied directly into the middle ear of 10 normal dogs twice daily for 21 days, there was no abnormal effect on cochlear or vestibular functions (Strain *et al*. 1995). Additionally, a study performed in guinea pigs showed that polymixin caused more cochlear damage (66% loss of cochlear hair cells) than gentamicin (6.5% loss) (Barlow *et al*. 1995). Gentamicin, neomycin, streptomycin, and kanamycin may be slowly eliminated from the inner ear and cause delayed ototoxicity (Gotthelf 2005).

Cochlear damage, manifested as dramatic reduction in BAER testing, has been reported with topical application of tobramycin and amikacin in the ears of dogs (Paterson 2008). Cats appear to be more susceptible to aminoglycoside ototoxicity than dogs.

Results of a retrospective study including 60 ears of dogs with ruptured tympanic membranes, treated for 6–8 weeks with various medications, showed that compared to baseline the mean BAER test scores increased with gentamicin (8 mL of injectable gentamicin [40 mg/mL] mixed in 118 mL of tris-EDTA), silver sulfadiazine cream (diluted 50:50 with sterile water), and marbofloxacin (5 mL of the diluted 200 mg injectable solution mixed in 118 mL of tris-EDTA) (Nuttall and Paterson 2008). On the other hand, there was reduction in the mean BAER scores for ears treated with ticarcillin (3.2 g of clavulanate-potentiated ticarcillin injectable solution mixed with 6 mL of sterile water) and tobramycin (2 mL of injectable tobramycin [40 mg/mL] mixed with 8 mL of tris-EDTA). In this study, *Otomax*® ointment (gentamicin, clotrimazole, and betamethasone) was

associated with a dramatic reduction in hearing. However, administration of clotrimazole (15 g tube [2% cream] mixed 50:50 with sterile water) did not change the BAER score. No vestibular signs were reported before or after therapy with any of the treatments.

Topical chloramphenicol has been shown to cause cochlear damage and deafness in humans and laboratory animals (Morizono and Johnstone 1975, Brown *et al*. 1981, Rybak and Krishna 2004). However, the ototoxicity potential of chloramphenicol in dogs and cats is currently unknown.

Based on these studies, topical administration of aminoglycosides (including gentamicin, amikacin, and tobramycin), polymyxin, and ticarcillin should be avoided, or they should be used with caution, with ruptured or unknown-status tympanic membrane until more information is obtained from further studies.

Antimicrobial medications that appear to be safe for the middle ear include fluoroquinolones (ciprofloxacin, enrofloxacin, marbofloxacin, ofloxacin), aqueous semisynthetic penicillins and some cephalosporins (ceftazidime, cefmenoxime), and antifungals including clotrimazole, miconazole, nystatin, and tonalftate (Paterson 2008).

### ANTI-INFLAMMATORY AGENTS

Glucocorticoids such as dexamethasone and fluocinolone are believed to be safe for use in the middle ear (Paterson 2008). However, a combination of fluocinolone and dimethyl sulfoxide (DMSO) (*Synotic*®), often used to treat hyperplastic and inflamed ears, may not be safe for administration in the ear if the tympanic membrane is ruptured due to the potential ototoxicity of DMSO (Weidong Qi *et al*, 2008).

### ANTIPARASITIC AGENTS

To the authors' knowledge there are no studies in animals reporting the potential for ototoxicity of antiparasitic ototopical medications commonly used in dogs and cats. Therefore, caution should be taken when administering these drugs to ears with tympanic membranes that are ruptured or of unknown status.

The following tables, slightly modified from Gotthelf (2005), show a list of ototopical agents believed to be safe (Table 1) and potentially ototoxic (Table 2) for the middle ear. Please note that most of the reported drugs in these tables have been extrapolated from studies conducted in humans or laboratory animals; therefore, the true safety or ototoxicity potential for most of these drugs is not yet proven in dogs and cats.

Until more is known about the ototoxicity potential of various topical agents used in dogs and cats, veterinarians should (1) read the entire label of ear medications and cleaners prior to use; (2) determine the status of the tympanic membranes; and (3) use caution when selecting ototopical medications and ear cleaners to be used directly in the middle ear. Patients should be closely monitored during treatment with ototopical medications for early identification of toxic effects, which can avoid irreversible damage.

**TABLE 1. SAFE OTOTOPICAL AGENTS**

| | |
|---|---|
| **Antibiotics** | Carbenicillin<br>Ceftazidime<br>Cefmenoxime<br>Ciprofloxacin<br>Enrofloxacin<br>Fosfomycin<br>Ofloxacin<br>Penicillin G |
| **Potentiating antibacterial agents** | Tris-EDTA |
| **Anti-inflammatory agents** | Dexamethasone<br>Triamcinolone<br>Fluocinolone |
| **Antifungal agents** | Clotrimazole<br>Nystatin<br>Tolnaftate |
| **Ceruminolytic agents and solvents** | Isopropyl myristate<br>Squalene |

From Gotthelf (2005), *Small Animal Ear Diseases: An Illustrated Guide*, 2nd edn. Reproduced with permission from Elsevier.

**TABLE 2. POTENTIALLY OTOTOXIC TOPICAL AGENTS**

| | |
|---|---|
| **Antibiotics** | Aminoglycosides (all)<br>Bacitracin *<br>Chloramphenicol *<br>Chlortetracycline *<br>Colistin *<br>Erythromycin<br>Gramicidin *<br>Hygromycin B<br>Iodochlorhydroxyquinolone<br>Minocycline<br>Oxytetracycline *<br>Pharmacetin<br>Polymixin B<br>Tetracycline *<br>Ticarcillin *<br>Vancomycin<br>Viomycin |
| **Antiseptics** | Acetic acid<br>Benzalkonium chloride *<br>Benzethonium chloride<br>Cetrimide<br>Chlorhexidine *<br>m-Cresyl acetate |

**TABLE 2. POTENTIALLY OTOTOXIC TOPICAL AGENTS** (continued)

| | |
|---|---|
| | Ethanol<br>Iodine and iodophors<br>Merthiolate |
| **Antifungal agents** | Amphotericin B *<br>Griseofulvin * |
| **Ceruminolytic agents and solvents** | Carbamide peroxide *<br>Dimethyl formamide<br>Dioctyl sodium sulfosuccinate *<br>Ethanol<br>Propylene glycol *<br>Polyethylene glycol 400<br>Triethanolamine<br>Toluene |
| **Miscellaneous agents** | Cyclosphosphamide<br>Dapsone<br>Detergents<br>Dimethyl sulfoxide (DMSO)<br>Diphenylhydrazine<br>Mercury<br>Potassium bromide<br>Triethyl tin bromide<br>Trimethyl tin chloride |

*Compounds with reported inflammatory effect in the middle ear.
From Gotthelf (2005), *Small Animal Ear Diseases: An Illustrated Guide*, 2nd edn. Reproduced with permission from Elsevier.

## Ceruminolytic Agents

Ceruminolytic products emulsify and remove ceruminous and purulent exudate by providing a surfactant, detergent, and bubbling activity. They may be indicated for removal of ceruminoliths prior to considering ear flushing under anesthesia. They work best if applied 10–15 minutes prior to cleaning. If they are needed during in-hospital ear-flushing procedures, their use should be followed by multiple flushes with warm sterile isotonic saline. Dioctyl sodium sulfosuccinate (DSS), calcium sulfosuccinate, urea, or carbamide peroxide are considered potent ceruminolytic agents. Squalene, triethanolamine polypeptide elite condensate, and hexamethyltetracosane are less potent agents. Propylene glycol, glycerin, and oil are considered very mild ceruminolytic agents. Urea peroxide-containing products will release oxygen when activated and produce a foaming action that helps break down cerumen. These products, however, can be irritating to already inflamed ears. It is important to demonstrate the cleaning technique in the examination room and advise the client to discontinue application and contact the veterinarian if the ears become redder or more inflamed at any time during the course of cleaning. The frequency of cleaning varies according to the needs of the individual patient.

## CERUMINOLYTIC AGENTS

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***ADL Foaming Ear Cleanser®*** (ADL) | Cocamidopropyl betaine, isosteramidopropyl morpholine lactate, salicylic acid, eucalyptol | Labeled for dogs. 4 oz, 8 oz |
| ***Cerumene®*** (Vetoquinol) | 25% squalene in isopropyl myristate liquid, petrolatum base | Labeled for dogs and cats. 4 oz |
| ***ClearX Ear Cleaning Solution®*** (TEVA/DVM) | Dioctyl sodium sulfosuccinate (DSS) 6.5%, urea (carbamide) peroxide 6% | Labeled for dogs and cats. 4 oz |
| ***Cerulytic®*** (Virbac) | Benzyl alcohol, propylene glycol dicaprylate, butylated hydroxytoluene (BHT), fragrance | Labeled for dogs and cats. 4 oz |
| ***Corium-20®*** (Virbac) | Purified water, specially denatured (SD) alcohol 40B 23%, glycerol, polysorbate 80, fragrance | Labeled for dogs and cats. 8 oz |
| ***KlearOtic® Ear Cleanser*** (Dechra) | Squalene 22% | Labeled for dogs and cats. 4 oz |
| ***Douxo® Micellar Solution*** (Sogeval) | Phytosphingosine, polysorbate, propylene glycol, poloxamer 184, imidazolidin urea, polidocanol, polysaccarides, alcohol, light fragrance | Labeled for dogs and cats. 4.2 oz, 8.4 oz |
| ***Vet Solutions Ear Cleansing Solution®*** (Vetoquinol) | Deionized water, aloe vera gel, specially denatured (SD) alcohol 40-2, propylene glycol, lactic acid, glycerin, dioctyl sodium sulfosuccinate, salicylic acid, fragrance, benzoic acid, benzyl acid | Labeled for dogs and cats. 4 oz, 8 oz, 16 oz |
| ***Earoxide Ear Cleanser®*** (Tomlyn/ Vetoquinol) | Carbamide peroxide 6.5% in a glycerin base | Labeled for dogs and cats. 2 oz, 4 oz |
| ***CleaRx Ear Cleansing Solution®*** (TEVA/DVM) | Dioctyl sodium sulfosuccinate 6.5%, urea peroxide 6% | Labeled for dogs and cats. 4 oz |

**CERUMINOLYTIC AGENTS** (continued)

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***OtiFoam®*** (TEVA/DVM) | Water, cocamidopropyl betaine, PEG-60, almond glycerides, mackalene 426, salicylic acid, oil of eucalyptus. | Labeled for dogs and cats. 8 oz |
| ***OtiRinse Ear Cleansing/ Drying Solution®*** (TEVA/DVM) | Salicylic acid, benzoic acid, lactic acid, propylene glycol, benzyl alcohol, specially denatured (SD) alcohol 40, dioctyl sodium sulfosuccinate, aloe vera, fragrance | Labeled for dogs and cats. 8 oz |
| ***Auroclens®*** (Arnolds) | Vegetable oil emulsion (water and coconut oil) | Not available in US; available in UK. Labeled for dogs and cats. 30 mL, 100 mL |
| ***Specicare® Dog Ear Cleaner*** (Leo) ***Specicare® Cat Ear Cleaner*** (Leo) | Boric acid, isopropanolol, propylene glycol, sodium borate Glycerol, propylene glycol, polysorbate 80, glycerin, chlorothymol, sodium stearate, sodium lauryl sulfate, citric acid | Not available in US; available in UK. Labeled for dogs and cats. 50 mL |
| ***Cerusolve®*** (Genitrix) | Polyethylene glycol, glycerin, thymol, menthol, xylene | Not available in US; available in UK. Labeled for dogs and cats. 100 mL |
| ***Logic® Ear Cleaner*** (Sanofi) | Xylene 2% | Not available in US; available in UK. Labeled for dogs and cats. 60 mL |

## Cleaning/Drying Agents

Cleaning and drying agents are typically used after debris or exudate has been removed from the ear canals with a ceruminolytic agent. Their ingredients are usually an acid or isopropyl alcohol. Cleaning and drying ear solutions can be used on a maintenance regimen to help prevent ear infections and after bathing or swimming to keep the external ear canals water-free. When recommending ear flushing as part of the treatment regimen, it is important to demonstrate the cleaning technique in the examination room and advise the client to discontinue application and contact the veterinarian if the ears become redder or more inflamed at any time during the course of cleaning. The frequency of cleaning varies according to the needs of the individual patient.

## CLEANING/DRYING AGENTS

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***ADL Ear Flushing Drying Lotion®*** (ADL) | Isopropyl alcohol, salicylic acid, eucalyptol, acetamine monoethanolamine (MEA), propylene glycol, acetic acid, aluminum acetate, hydrolyzed oat protein, wheat amino acids | Labeled for dogs. 8 oz, 32 oz |
| ***Bur-Otic HC®*** (Virbac) | Hydrocortisone 1%, Burow's solution, propylene glycol, water, benzalkonium chloride, acetic acid | Labeled for dogs and cats. 1 oz |
| ***Alocetic Ear Rinse®*** (TEVA/DVM) | Water, acetic acid, nonoxynol-12, fragrance, methylparaben, 1,3-dimethylol-5,5-dimethyl (DMDM), hydantoin, aloe vera gel | Labeled for dogs and cats. 4 oz, 12 oz |
| ***CleaRx Ear Drying Solution®*** (TEVA/DVM) | Acetic acid, colloidal sulfur, hydrocortisone | Labeled for dogs and cats. 1 oz |
| ***Corium-20®*** (Virbac) | Purified water, specially denatured (SD) alcohol 40-B 23%, glycerol, polysorbate 80, fragrance | Labeled for dogs and cats. 8 oz |
| ***Domeboro® Otic*** (Miles) | Acetic acid 2%, aluminum acetate | Human product. 2 oz |
| ***Vet Solutions Ear Cleansing Solution®*** (Vetoquinol) | Deionized water, aloe vera gel, specially denatured (SD) alcohol 40-2, propylene glycol, lactic acid, glycerin, dioctyl sodium sulfosuccinate, salicylic acid, fragrance, benzoic acid, benzyl acid | Labeled for dogs and cats. 4 oz, 8 oz, 16 oz |
| ***Epi-Otic® Cleanser with Spherulites*** (Virbac) | Lactic acid 2.5%, salicylic acid 0.1%, *Spherulite®* microcapsules, encapsulated chitosanide, docusate sodium, propylene glycol, parachloromethaxylenol (PCMX) | Labeled for dogs and cats. 4 oz, 8 oz, 16 oz |
| ***Epi-Otic Advanced®*** (Virbac) | Salicylic acid 0.2%, disodium EDTA, docusate sodium, PCMX, a monosaccharide complex (l-rhamnose, d-galactose, d-mannose), odor neutralizer | Labeled for dogs and cats. 4 oz, 8 oz |
| ***Gent-L-Clens®*** (Intervet/Schering-Plough) | Lactic acid, salicylic acid in propylene glycol | Labeled for dogs and cats. 4 oz |

## CLEANING/DRYING AGENTS (continued)

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***MalAcetic Otic®*** (Dechra) ***MalAcetic Otic® AP*** (contains apple fragrance) (Dechra) | Acetic acid 2%, boric acid 2% | Labeled for dogs and cats. 4 oz, 8 oz, 16 oz (*MalAcetic Otic®*) 4 oz and 16 oz (*MalAcetic Otic® AP*) |
| ***Oti-Calm®*** (TEVA/DVM) | Benzoic acid, malic acid, salicylic acids; oil of eucalyptus | Labeled for dogs and cats. 4 oz, 12 oz |
| ***Oti-Clens®*** (Pfizer) | Propylene glycol, malic acid, benzoic acid, salicylic acid | Labeled for dogs and cats. 4 oz |
| ***Oti-Soothe®*** (Sogeval) ***Oti-Soothe®*** *with Cucumber Melon Scent* (Sogeval) | Aloe vera gel, lactic acid, salicylic acid, benzoic acid, deionized water, propylene glycol, specially denatured (SD) alcohol 40, benzyl alcohol, glycerin, dioctyl sodium, sulfosuccinate | Labeled for dogs and cats. 4, 8, 16 oz, 1 gal |
| ***Oti-Soothe®*** + ***PS*** (Sogeval) ***Oti-Soothe®*** + ***PS*** *with Cucumber Melon Scent* (Sogeval) | Aloe vera gel, lactic acid, salicylic acid, benzoic acid, deionized water, propylene glycol, specially denatured (SD) alcohol 40, benzyl alcohol, glycerin, dioctyl sodium, sulfosuccinate, phytosphingosine hydrochloride 0.01% | Labeled for dogs and cats. 4, 8, 16 oz, 1 gal |
| ***OtiRinse® Solution*** (TEVA/DVM) | Salicylic acid, benzoic acid, dioctyl sodium sulfosuccinate, aloe vera, fragrance | Labeled for dogs and cats. 8 oz |
| ***Otocetic® Solution*** (Vedco) | Acetic acid 2%, boric acid 2% | Also surfactant. Labeled for dogs. 4 oz, 16 oz |
| ***Aloeclens® Otic Cleanser*** (Butler Schein) | Deionized water, propylene glycol, aloe vera gel, specially denatured (SD) alcohol 40-2, lactic acid, glycerin, dioctyl sodium sulfosuccinate, salicylic acid, fragrance, benzoic acid, benzyl alcohol | Also ceruminolytic and surfactant. Labeled for dogs and cats. 8 oz. |
| ***Euclens® Otic Cleanser*** (Butler Schein) | Propylene glycol, malic acid, benzoic acid, salicylic acid, eucalyptus oil | Also ceruminolytic. Labeled for dogs and cats. 4 oz, 16 oz. |

**CLEANING/DRYING AGENTS** (continued)

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***Swimmer's Ears Astringent®*** (Vedco) | Specially denatured (SD) alcohol 40, deionized water, butylene glycol, carbomer, chloroxylenol, aminomethyl propanol (AMP), fragrance | Labeled for dogs. 4 oz |
| ***CleanAural® for Dogs*** (Dechra) ***CleanAural® for Cats*** (Dechra) | Isopropyl alcohol, sodium borate, menthol, chlorothymol, sodium lauryl sulfate | Not available in US; available in EU and CA. Labeled for dogs and cats. 50 mL, 100 mL |
| ***Sancerum®*** (Intervet/ Schering-Plough) | Lactic acid 2.5%, salicylic acid 0.1%, chloroxylenol, propylene glycol, docusate sodium | Also surfactant, drying and antimicrobial. Not available in US; available in UK. Labeled for dogs and cats. 125 mL |
| ***Dermisol®*** (Pfizer) | Benzoic acid 0.15%, malic acid 2.25%, propylene glycol 40%, salicylic acid 0.0375% | Also surfactant and antimicrobial. Also labeled for skin care such as wound cleaning. Not available in US; available in UK. Labeled for dogs and cats. 100 mL |

## Antiseptic Agents

Topical antiseptic ear flushes include products containing acetic acid, chlorhexidine, ketoconazole, and hypochlorous acid. These products are typically used as adjunctive therapy for ear infections (e.g., bacterial and/or yeast) but can also be used as sole treatment in mild, first-time infections. Acetic acid works as an acidifying and antimicrobial agent.

Chlorhexidine has activity against Gram-positive and Gram-negative bacteria and fungi. Products containing chlorhexidine should be used cautiously in ear canals with ruptured tympanic membranes because of the potential for ototoxicity. Chloroxylenol is mostly active against bacteria. Ketoconazole is a fungistatic antifungal that interferes with the synthesis of ergosterol, an essential component of the fungal cell membrane, by inhibiting the cytochrome P450 CYP51

(lanesterol C14-demethylase). Hypochlorous acid is a broad-spectrum antimicrobial with rapid activity against Gram-positive and Gram-negative bacteria and fungal/yeast organisms. Its mode of action against microorganisms mimics that of neutrophils in the body. The main route of attack against microorganisms is disruption of the cellular membrane.

When recommending ear flushing as part of the treatment regimen, it is important to demonstrate the cleaning technique in the examination room and advise the client to discontinue application and contact the veterinarian if the ears become redder or more inflamed at any time during the course of cleaning. The frequency of cleaning varies according to the needs of the individual patient.

## ANTISEPTIC AGENTS

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***Acetic Acid 2% in Aqueous Aluminum Acetate Otic Solution®*** (Bausch & Lomb) | Acetic acid, boric acid, aluminum acetate | Human product. 60 mL |
| ***MalAcetic Otic®*** (Dechra) ***MalAcetic Otic® AP*** (apple fragrance) (Dechra) | Acetic acid 2%, boric acid 2% | Labeled for dogs and cats 4 oz, 8 oz, 16 oz (*MalAcetic Otic®*) 4 oz and 16 oz (*MalAcetic Otic® AP*) |
| ***MalAcetic® Ultra Otic*** (Dechra) | Acetic acid 1%, boric acid 1%, ketoconazole 0.15%, hydrocortisone 1% | Labeled for dogs and cats. 2 oz, 8 oz |
| ***Mal-A-Ket Plus TrizEDTA Flush®*** (Dechra) | Ketoconazole 0.15%, chlorhexidine 0.15%, tris-EDTA, pH 8 | Labeled for dogs and cats. 4 oz, 12 oz |
| ***Otocetic Solution®*** (Vedco) | Acetic acid 2%, boric acid 2%, surfactants | Labeled for dogs. 4 oz, 16 oz |
| ***Keto-Tris Flush®*** (Sogeval) | Ketoconazole 0.1%, tris-EDTA, pH 8 | Labeled for dogs and cats. 4 oz, 16 oz |
| ***Vetericyn Feline Ear Rinse®*** (Innovacyn) | Hypochlorous acid 0.003%, sodium chloride 0.023%, sodium hypochlorite 0.004%, electrolyzed water 99.97% (with Microcyn® technology) | Neutral pH, gentle. Labeled for cats. 4 oz |

**ANTISEPTIC AGENTS** (continued)

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***Vetericyn Canine Ear Rinse®*** (Innovacyn) | Hypochlorous acid 0.003%, sodium chloride 0.023%, sodium hypochlorite 0.004%, electrolyzed water 99.97% (with Microcyn® technology) | Neutral pH, gentle. Labeled for dogs. 4 oz |
| ***Pharmaseb Flush®*** (Animal Pharmaceuticals) | Chloroxylenol 0.3% Ketoconazole 0.3% | Water-based. Propylene glycol, benzyl alcohol. Can be used as a cleanse agent for skin and ears. Labeled for dogs and cats. 4 oz, 8 oz |

## Antibiotic Potentiating Agents

Tris-ethylene diamine tetra-acetic acid (tris-EDTA) has an antimicrobial and antibiotic potentiating activity. It is alkalinizing (pH 8), blocks the *Pseudomonas* efflux pump, potentiates antibiotics such as enrofloxacin and aminoglycosides, disrupts the bacterial cell wall by chelating metal ions and making it more porous (most efficient for Gram-negative bacteria such as *Pseudomonas*), inhibits the effects of ulcerating bacterial enzymes, and is non-ototoxic (safe in the middle ear). Products containing tris-EDTA work best when applied 15–30 minutes before the topical antibiotic. These products are available as sole ingredient or combined with chlorhexidine or ketoconazole.

When recommending ear flushing as part of the treatment regimen, it is important to demonstrate the cleaning technique in the examination room and advise the client to discontinue application and contact the veterinarian if the ears become redder or more inflamed at any time during the course of cleaning. The frequency of cleaning varies according to the needs of the individual patient.

**ANTIBIOTIC POTENTIATING AGENTS**

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***Keto-Tris Flush®*** (Sogeval) | Tris-EDTA, ketoconazole 0.1%, | Labeled for dogs and cats. 4, 16 oz |
| ***Keto-Tris Flush®*** + ***PS*** (Sogeval) | Tris-EDTA, ketoconazole 0.1%, phytosphingosine hydrochloride 0.01% | Labeled for dogs and cats. 4, 16 oz |

**ANTIBIOTIC POTENTIATING AGENTS** (continued)

| Trade name (manufacturer) | Ingredients | Comments; sizes |
|---|---|---|
| ***Mal-A-Ket Plus TrizEDTA Flush®*** (Dechra) | Tris-EDTA, ketoconazole 0.15%, chlorhexidine 0.15% | Labeled for dogs and cats. 4 oz, 12 oz |
| ***TrizEDTA® Aqueous Flush*** (Dechra) | Tris-EDTA | Labeled for dogs and cats. 4 oz, 16 oz |
| ***TrizULTRA + Keto®*** (Dechra) | Tris-EDTA, ketoconazole 0.15% | Labeled for dogs and cats. 4 oz, 12 oz |
| ***TrizCHLOR® Flush*** (Dechra) | Tris-EDTA, chlorhexidine 0.15% | Labeled for dogs and cats. 4 oz |

## Corticosteroid Preparations

*Refer also to Corticosteroid + Antimicrobial Preparations*

Corticosteroid-containing ear medications are used in cases of acute or chronic otitis with the goal of reducing inflammation, edema, tissue hyperplasia, stenosis of the ear canal, pain and pruritus. In addition, they are efficacious in decreasing secretion from sebaceous, and ceruminous glands reducing the build up of debris in the ear canals. Ear cleaning solutions that contain glucocorticoids without an antibiotic can be used as maintenance therapy in cases of allergic otitis. However, use the lowest potent glucocorticoid at the lowest possible frequency to prevent undesirable side effects. When using topical corticosteroids to reduce otic hyperplasia and stenosis, 1–4 times daily applications may be used according to each individual's need.

**CORTICOSTEROID PREPARATIONS**

| Trade name (manufacturer) | Active ingredients | Other ingredients; comments; sizes |
|---|---|---|
| ***Bur-Otic HC®*** (Virbac) | Hydrocortisone 1%, Burow's solution | Propylene glycol, water, benzalkonium chloride, acetic acid. Ear cleaner but may be used as drops as well. Labeled for dogs and cats. 1 oz |
| ***Cort/Astrin Solution®*** (Vedco) | Hydrocortisone 1%, Burow's solution | Labeled for dogs and cats. 1 oz, 16 oz |
| ***MalAcetic® Ultra Otic*** (Dechra) | Hydrocortisone 1%, boric acid 2%, acetic acid 1%, ketoconazole 0.15% | Labeled for dogs and cats. 2 oz, 8 oz |

**CORTICOSTEROID PREPARATIONS** (continued)

| Trade name (manufacturer) | Active ingredients | Other ingredients; comments; sizes |
|---|---|---|
| ***Synotic Otic Solution®*** (Fort Dodge) | Fluocinolone acetonide 0.01%; dimethyl sulfoxide (DMSO) 60% | Propylene glycol and citric acid. May be compounded if unavailable. Labeled for dogs. 60 mL |
| ***Derm-Otic Oil®*** (Hill Dermaceuticals) | Fluocinolone acetonide 0.01% | Human product. Blend of oils, isopropyl alcohol, isopropyl myristate, light mineral oil, oleth–2, refined peanut oil, fragrance. 20 mL |

## Antibacterial Preparations

*Refer also to Corticosteroid + Antimicrobial Preparations and Compounded Antibiotic Formulations*

Antibacterial ear preparations are commonly used to treat infections caused by bacteria such as *Staphylococcus* or *Pseudomonas*. Very few otic products containing solely an antibiotic are commercially available to treat bacterial otitis; therefore, the clinician often has to use ophthalmic products or injectable antibiotics directly into the ear canals to treat these infections when other active ingredients are not desired or bacteria are resistant to the commercially available products. When using acidifying ear cleansers and treating an infection with an aminoglycoside- or fluoroquinolone-containing agent, it is recommended to use these products about 1 hour apart, since low pH can decrease the activity of aminoglycosides and fluoroquinolones. Bacterial culture and susceptibility should be performed to select the ideal antibiotic, particularly to treat any case of *Pseudomonas* ear infection. The product has to be applied 2–3 times daily in adequate amounts to coat the entire ear canal. Advise the client to discontinue the medication and contact the veterinarian if the ears become redder or more inflamed at any time during treatment. It is important to recheck the patient before discontinuing treatment of otitis.

**ANTIBACTERIAL PREPARATIONS**

| Trade name (manufacturer) | Active ingredients | Other ingredients/sizes |
|---|---|---|
| ***Baytril Otic®*** (Bayer) | Enrofloxacin 0.5%<br>Silver sulfadiazine 1% | Benzyl alcohol (as a preservative) and cetylstearyl alcohol (as a stabilizer) in a neutral oil and purified water emulsion. Labeled for dogs. 15 mL, 30 mL |

**ANTIBACTERIAL PREPARATIONS** (continued)

| Trade name (manufacturer) | Active ingredients | Other ingredients/sizes |
|---|---|---|
| ***Gentocin®* *Ophthalmic Solution* or *Ointment*** (Intervet/ Schering-Plough) | Gentamicin sulfate 0.3% | Extra-label use in the ears. Labeled for dogs and cats. Many human ophthalmic products also available. Disodium phosphate 2.9 mg, monosodium phosphate 0.1 mg, sodium chloride 7.4 mg, benzalkonium chloride 0.05 mg as preservative, purified water. 5 mL (solution), 3.5 g (ointment) |
| ***Tobrex®* *Ophthalmic Solution* or *Ointment*** (Alcon Laboratories) **Generic** | Tobramycin 0.3% | Human product. Extra-label use in the ears of dogs and cats. Benzalkonium chloride 0.01% (preservative), boric acid, sodium sulfate, sodium chloride, tyloxapol, sodium hydroxide and/or sulfuric acid (to adjust pH), purified water. 5 mL |
| ***Ciloxan®* *Ophthalmic Solution* or *Ointment*** (Alcon Laboratories) **Generic** | Ciprofloxacin hydrochloride 0.3% | Human product. Extra-label use in the ears of dogs and cats. Solution: benzalkonium chloride 0.006% (preservative), sodium acetate, acetic acid, mannitol, edetate disodium, hydrochloric acid and/or sodium hydroxide, purified water. 5 mL, 10 mL Ointment: mineral oil, white petrolatum. 3.5 g |

## Antifungal Preparations

*Refer also to Corticosteroid + Antimicrobial Preparations and Antibiotic Potentiating Agents*

Antifungal ear preparations are used to treat *Malassezia* otitis and rarely otic candidiasis. Most of the commercially available products also contain an antibiotic and/or a glucocorticoid. Listed here are exclusively the products without an antibiotic agent. The medication has to be applied 2–3 times daily in adequate amounts to coat the entire ear canal. Advise the client to discontinue the medication and contact the veterinarian if the ears become redder or more inflamed at any time during treatment. It is important to recheck the patient before discontinuing treatment of otitis.

### ANTIFUNGAL PREPARATIONS

| Trade name (manufacturer) | Active ingredients | Other ingredients; comments; sizes |
|---|---|---|
| ***ClotrimaTop® Solution*** (Butler) **Clotrimazole® Solution** (VET Solutions) | Clotrimazole 1% | Labeled for dogs and cats. Propylene glycol, specially denatured (SD) alcohol 40, chloroxylenol, cocamidopropyl, PG-dimonium chloride phosphate, benzyl alcohol. 30 mL |
| ***Lotrimin® Solution*** (Intervet/Schering-Plough) **Clotrimazole Topical Solution** (Taro) **Generic** | Clotrimazole 1% | Labeled for dogs and cats. Polyethylene glycol 400 10 mL, 30 mL (Clotrimazole) 10 mL (*Lotrimin®*) |
| ***MicaVed® Lotion*** (Vedco) ***Micazole® Lotion*** (Buttler) ***Miconosol® Lotion*** (Med Pharmex) ***Priconazole® Lotion 1%*** (Priority Care) | Miconazole 1% | Labeled for dogs and cats. Polyethylene glycol 400, ethyl alcohol 55%. 60 mL, 120 mL (MicaVed®) 60 mL (*Micazole®*, *Miconosol®*, *Priconazole®*) |

## Corticosteroid + Antimicrobial Preparations

Most otic antimicrobial preparations commercially available combine an antifungal, an antibiotic, and a glucocorticoid agent. The medication has to be applied 2–3 times daily in adequate amounts to coat the entire ear canal. Advise the client to discontinue the medication and contact the veterinarian if the ears become redder or more inflamed at any time during treatment. It is important to recheck the patient before discontinuing treatment of otitis.

### CORTICOSTEROID + ANTIMICROBIAL PREPARATIONS

| Trade name (manufacturer) | Active ingredients | Other ingredients; comments; size(s) |
|---|---|---|
| ***Cortomycin®*** (Major Pharmaceutical) ***Oti-Sone® Otic Suspension*** (Ocumed) ***Pediotic® Otic Suspension*** (GlaxoSmithKline) **Generics** | Hydrocortisone 10 mg/mL Neomycin sulfate 3.5 mg/mL Polymyxin B 10,000 U/mL | Human products. Extra-label use in ears of dogs and cats 7.5 mL (*Cortomycin®*, *Pediotic®*) 10 mL (*Cortisporin®*, *Oti-Sone®*) |

## CORTICOSTEROID + ANTIMICROBIAL PREPARATIONS (continued)

| Trade name (manufacturer) | Active ingredients | Other ingredients; comments; size(s) |
|---|---|---|
| ***Betagen® Otic Solution*** (Med-Pharmex) ***GenOne® Otic Solution*** (VetOne) **Gentaotic®** (Butler) ***GentaVed® Otic Solution*** (Vedco) | Betamethasone valerate 1 mg/mL Gentamicin sulfate 3 mg/mL | Labeled for dogs and cats 15 mL (*Betagen®*) 7.5 mL and 15 mL (*GenOne®*) 7.5 mL, 15 mL, 240 mL (*Gentaotic®*, *GentaVed®*) |
| ***Animax® Ointment*** (Dechra) ***Derma-Vet® Ointment*** (Med-Pharmex) ***Dermalog® Ointment*** (RXV) ***Dermalone® Ointment*** (Vedco) ***Quadritop® Ointment*** (Butler) ***Panolog® Ointment*** (Fort Dodge) ***Entederm® Ointment*** (VetOne) | Triamcinolone acetonide 0.1% Neomycin sulfate 0.25% Nystatin 100,000 U/mL Thiostrepton 2500 units | Labeled for dogs and cats 7.5 mL, 15 mL, 30 mL, 240 mL (*Animax®*, *Dermalog® Entederm*) 7.5 mL, 15 mL, 30 mL (*Derma-Vet®*) 7.5 mL, 15 mL, 30 mL (*Dermalone®*) 240 mL (*Quadritop®*) 15 g (*Panolog®*) |
| ***Mometamax® Otic Suspension*** (Intervet/Schering-Plough) | Mometasone furoate 1 mg/g Gentamicin 3 mg/g Clotrimazole 10 mg/g | Labeled for dogs only. The manufacturer recommends once daily treatment. 15 g, 30 g |
| ***DVMax® Ointment*** (TEVA/DVM) ***Gentizol® Ointment*** (VetOne) ***MalOtic® Ointment*** (Vedco) ***Otibiotic® Ointment*** (Butler) ***Otomax® Ointment*** (Intervet/Schering-Plough) ***Tri-Otic®*** (Med-Pharmex) ***Vetromax®*** (Dechra) | Betamethasone valerate 0.1% Gentamicin sulfate 0.3% Clotrimazole 1% | Labeled for dogs only 10 g, 20 g, 215 g (*DVMax®*) 7.5 g (*Gentizol®*) 7.5 g, 10 g, 15 g, 25 g (*MalOtic®*) 25 g (*MalOtic®* gel) 15 g, 215 g (*Otibiotic®*) 15 g, 30 g, 215 g (*Otomax®*) 7.5 g, 25 g, 215 g (*Tri-Otic®*) 7.5 g and 15 g (*Vetromax®*) |

## CORTICOSTEROID + ANTIMICROBIAL PREPARATIONS (continued)

| Trade name (manufacturer) | Active ingredients | Other ingredients; comments; size(s) |
|---|---|---|
| ***Posatex® Otic Suspension*** (Intervet/ Schering-Plough) | Mometasone furoate 0.1% Posaconazole 0.1% Orbifloxacin 1% | Labeled for dogs only. The manufacturer recommends once daily treatment. 7.5 g, 15 g and 30 g |
| ***Surolan® Otic Suspension*** (Vetoquinol) | Prednisolone acetate 5 mg/mL Miconazole nitrate 23 mg/mL Polymyxin B sulfate 0.5293 mg/mL | Labeled for dogs only. 15 mL, 30 mL |
| ***Tresaderm®*** (Merial) | Dexamethasone 0.1% Neomycin 0.25%, Thiabendazole 4% | Glycerin, propylene glycol, ethyl and benzyl alcohol, hypophosphorous acid, calcium hypophosphite. Labeled for bacterial and fungal otitis and otoacariosis in dogs and cats for a maximum of 1 week duration. 7.5 mL, 15 mL |
| ***Tritop® Ointment*** (Pfizer) | Neomycin sulfate 0.5% Isoflupredone acetate 0.1%, Tetracaine hydrochloride 0.5% | Labeled for dogs and cats. 10 g |
| ***TobraDex® Ophthalmic Solution*** (Alcon) **Generics** | Tobramycin 0.3% Dexamethasone 0.1% | Human product. Extra-label use in ears of dogs and cats. 2.5 mL, 5 mL |
| ***Zymox® Otic*** (Three Point Enzyme System) | Hydrocortisone 1% Lysozyme, Lactoferin, Lactoperoxidase | Labeled for dogs and cats. 36.96 mL |
| ***Easotic®*** (Virbac) | Hydrocortisone aceponate 1.11 mg/mL Gentamicin sulfate 1505 IU/mL Miconazole nitrate 15.1 mg/mL | Oily suspension. Paraffin. Not available in US, available in EU. Labeled for dogs. The manufacturer recommends once-daily treatment. 10 mL |

**CORTICOSTEROID + ANTIMICROBIAL PREPARATIONS** (continued)

| Trade name (manufacturer) | Active ingredients | Other ingredients; comments; size(s) |
|---|---|---|
| ***Aurizon®*** (Vetoquinol) | Dexamethasone acetate 0.9 mg<br>Marbofloxacin 3 mg<br>Clotrimazole 3 mg | Oily suspension. Propyl gallate. Not available in US, available in CA and EU. Labeled for dogs. The manufacturer recommends once-daily treatment.<br>10 mL, 20 mL |

## Antiparasitic Preparations

*For completeness, refer also to Selamectin in Section 1, and Fipronil ± (S)-Methoprene in Section 2.*

Included here are only preparations labeled to be applied directly in the ear canals for the treatment of otoacariosis. However, parasiticides that have systemic or more generalized effect such as selamectin or fipronil may be preferred, because *Otodectes cynotis* mites are known to also live outside the ear canals and re-infest the ears.

**ANTIPARASITIC PREPARATIONS**

| Trade name (manufacturer) | Active ingredients | Dose (manufacturer) | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Acarexx® Otic Suspension*** (Idexx) | Ivermectin 0.01% | Clean ear and apply 0.5 mL in each ear; repeat one time if necessary | For ear-mite infestation on cats or kittens ≥4 weeks. 12 foil pouches with 2 0.5 mL ampoules per foil pouch |
| ***Adams Pene-Mite®*** (Farnam) | Pyrethrins 0.05%<br>Piperonyl butoxide 0.5% | Clean ear and apply every-other-day for 12 days | Recommended for dogs and cats ≥12 weeks. 0.5 oz |
| ***Cerumite® 3X*** (Vetoquinol) | Pyrethrins 0.15%<br>Piperonyl butoxide 1.5% | Clean ear and apply a sufficient amount to coat the ear canals not more frequent than twice a week | N-octyl bicycloheptene dicarboximide. For ear-mite infestation on dogs and cats. 0.5 oz |

**ANTIPARASITIC PREPARATIONS** (continued)

| Trade name (manufacturer) | Active ingredients | Dose (manufacturer) | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***EarMed Mite® Lotion*** (Davis) ***Cooper's Best Ear Mite® Lotion*** (Aspen Veterinary Resources) | Oil of pennyroyal Oil of lemongrass Oil of lavender | Clean ear and apply daily for 7–10 days. Repeat the procedure in 2 weeks if needed | Aloe. For ear-mite infestation on dogs and cats 2 oz (EarMed Mite®) 6 oz (Cooper's Best Ear Mite®) |
| ***Ear Miticide®*** (Phoenix Pharmaceuticals) **Ear Mite® Solution** (Durvet) | Rotenone 0.12% | Clean ear and apply twice, allowing 1-day interval | Associated resins 0.16%. For ear-mite infestation on dogs and cats ≥12 weeks 2 oz (Ear Miticide®) 4 oz (Ear Mite®) |
| ***Eradimite®*** (Fort Dodge) | Pyrethrins 0.15%, Piperonyl butoxide 1.5% | Clean ear and apply once daily every 2 days until resolution of infestation. | For ear-mite and spinose ear-tick infestation on dogs and cats. 1 oz |
| ***Happy Jack Mitex®*** (Happy Jack) | Pyrethrins 0.05% Piperonyl butoxide 0.5% | Clean ear and apply once daily for 7–10 days. Repeat in 2 weeks if needed. | For ear-mite infestation on dogs and cats. 0.5 oz, 1 oz |
| ***Hartz Advanced Care® Ear Mite Treatment*** (Hartz) | Pyrethrins 0.05% Piperonyl butoxide 0.5% | Clean ear and apply once daily for 7–10 days. Repeat in 2 weeks if needed | Aloe. For ear-mite infestation on cats ≥12 weeks. 0.06 oz |
| ***MilbeMite® Otic*** (Novartis) | Milbemycin oxime 0.1% | Clean ear and apply entire contents of tube in external ear canal; one tube per ear. Repeat in 30 days if recommended by the veterinarian. | For ear-mite infestation on cats or kittens ≥4 weeks. Box of 10 pouches of 2 tubes of 0.25 mL each |

**ANTIPARASITIC PREPARATIONS** (continued)

| Trade name (manufacturer) | Active ingredients | Dose (manufacturer) | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Mita-Clear®*** ***Lotion*** (Pfizer) | Pyrethrins 0.15%, Piperonyl butoxide 1.5% | Clean ear; instill enough to wet ear canal and massage. Retreat in 7 days | N-octyl bicycloheptene dicarboximide 0.5%, di-n-propyl isocinchomeronate 1%. For ear-mite infestation on dogs and cats. 22 mL |
| ***Otomite Plus®*** (Virbac) | Pyrethrins 0.15%, Piperonyl butoxide 1.5% | Clean ear and instill enough to wet ear canal and massage. Retreat in 7 days | N-octyl bicycloheptene dicarboximide 0.5%, di-n-propyl isocinchomeronate 1%. For ear-mite infestation on dogs and cats. 0.5 oz |
| ***Performer®*** ***Ear Mite Killer*** (Agrilabs) | Pyrethrins 0.15% Piperonyl butoxide 1% | Clean ear and apply for 7–10 days | N-Octyl bicycloheptene dicarboximide 0.50%, di-n-propyl isocinchomeronate 1.0%. For ear-mite infestation on dogs and cats ≥ 12 weeks. 6 oz |
| ***QuadraClear®*** ***Ear Drops*** (Van Beek) | Pyrethrin 0.61 mg/mL Sesquiterpenoid 25 mg/mL Salicin 0.61 mg/mL Property blend of carvacrol 58 mg/mL | Clean ear and apply twice daily for 7–10 days | 1–8 cineol, thymol, menthol, cinnamic aldehyde. For ear-mite infestation on dogs and cats. Other manufacturer's recommendations include: bacterial and yeast ear infections. 1 oz |
| ***Sentry HC*** ***EARMITEfree®*** ***Ear Miticide*** ***for Dogs*** (Sergeant Pet Care Products) | Pyrethrins 0.06% Pyperonyl butoxide 0.6% | Clean ear and apply twice daily until the infestation is resolved | For mite and tick ear infestation on dogs ≥12 weeks. 1 oz |

**ANTIPARASITIC PREPARATIONS** (continued)

| Trade name (manufacturer) | Active ingredients | Dose (manufacturer) | Other ingredients; comments; size(s) |
|---|---|---|---|
| ***Sentry HC EARMITEfree® Ear Miticide for Cats*** (Sergeant Pet Care Products) | Pyrethrins 0.06% Pyperonyl butoxide 0.6% | Clean ear and apply twice daily until the infestation is resolved | For mite and tick ear infestation on cats ≥12 weeks. 1oz |
| ***Sergeant's Vetscription® Ear Mite and Tick Treatment*** (Sergeant Pet Care Products) | Pyrethrins 0.06% Pyperonyl butoxide 0.6% | Clean ear and apply twice daily until the infestation is resolved | For use on cats ≥ 12 weeks. 3 oz |
| ***Tresaderm®*** (Merial) | Thiabendazole 4% Neomycin sulfate 0.25% Dexamethasone 0.1% | Clean ear and apply twice daily until the infestation is resolved | Glycerin, propylene glycol, ethyl and benzyl alcohol, hypophosphorous acid, calcium hypophosphite. Labeled for otoacariosis, bacterial and fungal otitis in dogs and cats for a maximum of 1 week duration. 7.5 mL, 15 mL |

## Compounded Antibiotic Preparations

The use of these compounded preparations for the treatment of ear infections is extra-label and based on anecdotal reports. Several different formulations may be reported for a certain drug, and currently there is no accurate information on how they compare in terms of efficacy and safety. Despite lack of scientific evidence on their use for otic diseases, these preparations are included here because they are becoming commonly used by dermatologists with the increase in antibiotic resistance and limited availability of commercial ototopical preparations. These medications may be particularly useful for the treatment of resistant bacterial otic infections such as those caused by *Pseudomonas* and methicillin-resistant *Staphylococcus*.

The authors recommend that the injectable antibiotics be used based on culture and sensitivity results. However, it is important to remember that antibiotic sensitivity of samples collected from the ear canals is based on antibiotic serum concentration and not concentration in the ear tissue. Also, topical medications in the ear canals may be effective despite reported resistance, as the antibiotic concentration in the ear is reported to be 1000 times higher than in the serum. Adverse cutaneous reactions and ototoxicity may occur. Use of injectable antibiotics in the ears may be very expensive.

## COMPOUNDED ANTIBIOTIC PREPARATIONS

| Active ingredient(s); concentration; supply | Trade name(s) | Formulation(s) |
|---|---|---|
| Amikacin sulfate 50 mg/mL or 250 mg/mL vials (injectable) | *AmTech AmiMax® C, CaniGlide®, Amiglyde-V®, AmiJect D®, Amikacin C®, Amikacin K-9 Injection®, Amikin®, Amikacin Sulfate®* | 5 mL of 50 mg/mL or 1 mL of 250 mg/mL can be used alone or added to a 2 oz squirt bottle mixed with Burow's solution and hydrocortisone (HB101) filled to the 2 oz mark |
| Enrofloxacin 22.7 mg/mL (small animal) or 100 mg/mL (large animal) vials (injectable) | *Baytril®* | 1 part of 22.7 mg/mL diluted enrofloxacin mixed with 4 parts Synotic®, 1% hydrocortisone or Burrow's solution and hydrocortisone (HB101)<br>22.7 mg/mL enrofloxacin mixed with dexamethasone<br>6–12 mL of 100 mg/mL diluted enrofloxacin mixed in a 4 oz bottle of tris-EDTA or Burow's solution and hydrocortisone (HB101)<br>12 mL of 100 mg/mL diluted enrofloxacin mixed in 12 mL of tris-EDTA, 4–8 mg of dexamethasone, and 1–2 mL of DMSO<br>13 mL of the 100 mg/mL enrofloxacin mixed with 120 mL of tris-EDTA |
| Marbofloxacin 2% (injectable) | *Marbocyl SA®* | 5 mL of diluted 200 mg/mL marbofloxacin mixed with 118 mL of sterile water or tris-EDTA |

## COMPOUNDED ANTIBIOTIC PREPARATIONS (continued)

| Active ingredient(s); concentration; supply | Trade name(s) | Formulation(s) |
|---|---|---|
| Ticarcillin disodium and clavulanate potassium 13.1 g vial (injectable) | *Timentin*® | 13.1 g ticarcillin vial mixed with 13 mL of sterile water. **Note:** solution should be refrigerated<br>13.1 g ticarcillin solution mixed with 100 mL saline – aliquot to single doses of 0.5–2 mL and store in the freezer thawing out one aliquot each day. **Note:** Once thawed the solution should be used within 8 hours |
| Tobramycin 40 mg/mL (injectable) | *Nebcin*® | 2 mL of 40 mg/mL of tobramycin mixed with 8 mL of tris-EDTA or sterile water |
| Chloramphenicol (topical) | Chloramphenicol (previously commercially available as brand name *Liquichlor*® by Evsco) | 4.2 mg/mL chloramphenicol, 4.2 mg/mL tetracaine, 1.7 mg/mL prednisolone, 0.21 mg/mL squalene (mineral oil base) |
| Mupirocin (topical) 30 g tube | *Muricin*® 2% Ointment, generic | 1/2 22 mg tube added to a 2 oz bottle and mixed with Burow's solution and hydrocortisone (HB101) such as Hydro-Plus®, filled to the 2 oz mark<br>1 22 mg tube mixed in 60 mL of sterile water/saline |
| Silver Sulfadiazine 1% Cream (topical) 20, 50, 400 g jar | *Silvadene*® cream, generic | 1 part of silver sulfadiazine cream mixed with 9 parts of sterile water<br>1 part of silver sulfadiazine cream mixed with 1 part of sterile water |

**Note:** For specific and accurate information on proper use, packaging, storage, stability, and beyond-use date (the date after which a compounded preparation is not to be used, which is determined from the date the preparation is compounded) of each compounded preparation listed, the veterinarian should consult a pharmacist and refer to Chapter 795 (Pharmaceutical compounding-non-steroidal preparations) of the *US Pharmacopeia* (USP).

# Section 3 Allergen-Specific Immunotherapy

## Definition

According to the World Health Organization (WHO), allergen-specific immunotherapy (ASIT), also known as hyposensitization, desensitization, or allergy shots, "is the practice of administering gradually increasing quantities of an allergen extract to an allergic subject to ameliorate the symptoms of subsequent exposure to the causative allergen" (Bousquet *et al*. 1998). In veterinary medicine, ASIT is the only specific therapy for atopic dermatitis (AD) and is established based on relevant allergens that have been identified according to the results of intradermal testing and/or in-vitro allergy serum testing.

## Indications

ASIT is indicated for dogs and cats with seasonal or year-round AD after identification of relevant allergens based on intradermal and/or allergy serum testing; for cases where allergen exposure is unavoidable; and when all symptomatic therapeutic trials have been ineffective or have been associated with unacceptable side effects. Moreover, prior to starting the treatment, the owner should be willing to administer injections and accept the time commitment, mainly during the initial phase. Due to its mode of action, ASIT is the only therapeutic intervention that has the potential to prevent the development of clinical signs and alter the long-term course of AD. Therefore, ideally, allergy testing and ASIT should be recommended early during the course of AD, but after a 1-year history of allergy symptoms, to try to avoid the need for long-term administration of glucocorticoids or cyclosporine, which is often associated with undesirable side effects. In addition, compared to many therapies commonly used for AD, ASIT is typically more cost-effective over time, mainly for large breed dogs.

## Mechanism of Action

The mechanism of action of ASIT is very complex and not well understood.

In humans treated with ASIT, numerous changes in cellular and humoral responses have been reported, which may contribute to its efficacy. These include alterations in T-helper cell response such as increased ratio of allergen-induced Th1 cytokines to Th2 cytokines and increased production of

*Canine and Feline Dermatology Drug Handbook*, First Edition.
Sandra N. Koch, Sheila M.F. Torres and Donald C. Plumb.

Published 2012 by Blackwell Publishing Ltd.

T-regulatory-1-like cells; increase in the production of regulatory cytokines such as interleukin (IL)-10 and transforming growth factor (TGF)-beta; increase in IgG1 and IgG4 production; decrease in allergen-specific IgE production and suppression of mast cells, basophils, and eosinophils. None of the in-vitro assay results in humans has correlated completely with a patient's favorable clinical response to ASIT.

There are few studies in dogs and cats reporting changes in cellular and humoral responses associated with ASIT. There seems to be a shift to a Th1 response by enhancing interferon-gamma expression (Shida *et al*. 2004) and a significant increase in both T-regulatory cell numbers and IL-10 concentrations after successful ASIT (Keppel *et al*. 2008). In a study of experimental feline asthma, cats receiving rush immunotherapy (RIT) showed a decrease of IL-4 and IL-5 in the broncheoalveolar lavage fluid and an increase in interferon-gamma and IL-10 transcription (Reinero *et al*. 2006).

ASIT has been reported in different studies to increase total IgG serum antibody concentrations, more specifically serum IgG1, in dogs with AD (Hites *et al*. 1989, Foster *et al*. 2002, Fraser *et al*. 2004); however, these findings are controversial regarding correlation between serum IgG increase and the degree of clinical response. In cats with experimental allergic asthma, RIT induced an increase in specific IgG antibodies to Bermuda grass allergens and a significant decrease in eosinophil-associated airway inflammation (Reinero *et al*. 2006). More studies need to be performed to better explain the exact mechanism of action of ASIT that leads to clinical improvement of AD in dogs and cats.

## Precautions and Contraindications

ASIT should not be used in patients with a previous history of severe adverse reactions to ASIT. Avoidance or caution should be taken if administering ASIT to patients that developed an allergic or anaphylactic reaction to allergens administered during an intradermal test.

## Clinical Efficacy

ASIT has been used by many veterinarians and dermatologists for many years, and it is considered by most to be the mainstay treatment of AD. Different ASIT reviews and recent therapeutic guidelines for AD suggest a probable beneficial effect of ASIT for the management of canine and feline AD (Griffin and Hillier 2001, Loewenstein and Muller 2009, Olivry *et al*. 2010a, 2010b). In addition, based on open uncontrolled studies, the reported success rates for ASIT in dogs and cats with AD range from 50% to 100% and 50% to 75%, respectively (Loewenstein and Muller 2009), with efficacy being described as at least 50% improvement in clinical signs and/or a decrease in the dosage or frequency of concurrent anti-inflammatory or antipruritic medications. This wide range of response seems to be influenced by variation among the different studies regarding allergy testing methodology, allergen selection, dose and concentration of allergens, protocol and response criteria, among other factors. Finally, because of insufficient numbers of randomized, controlled clinical studies, the true efficacy of ASIT in dogs and cats is currently unknown.

Anecdotal and open-label studies have shown that some predictive factors such as age of the dog at disease onset, age of the dog at ASIT initiation, duration of allergy symptoms, dog breed and sex, and seasonality of clinical signs can influence the clinical outcome of ASIT (Griffin and Hillier 2001, Loewenstein and Muller 2009). However, results from these studies have been conflicting, and currently there is more evidence showing that these factors most likely do not significantly interfere with the success rate of ASIT. Another predictive factor reported to possibly influence the outcome of ASIT is the number of allergens the patient is allergic to and included in the ASIT, with controversial results among different reports (Scott 1981, Walton Angorano and MacDonald 1991). However, more recent reports indicated no correlation between number of allergens used and efficacy of ASIT (Nuttall 1998, Schnabl *et al*. 2006).

There are conflicting results regarding the response to specific types of allergens selected for ASIT in veterinary medicine, with some studies reporting better response to pollens than to other allergens and others showing no difference among different allergens used, such as pollens and house-dust mites (Loewenstein and Muller 2009). Therefore, further studies are needed to investigate the correlation between different types of allergens and ASIT clinical outcome in dogs and cats.

Based on anecdotal reports and the authors' experiences, some animals suddenly stop responding to ASIT after having their allergies well controlled, and a subset of those animals may respond to a new ASIT reformulation based on repeated allergy testing, suggesting that hypersensitivity to new allergens may occur in dogs and cats.

## Time to Efficacy and Duration of Therapy

Currently, the time to obtain maximal clinical efficacy and the ideal duration of ASIT in dogs and cats are unknown. Anecdotal reports indicate that ASIT may take up to 12 months to achieve maximal benefit, with initial improvement usually seen after 2–9 months of therapy in dogs, and 1–4 months in cats (Loewenstein and Muller 2009). Therefore, because of a possible delayed response, ASIT should be continued for at least 1 year before critically evaluating clinical efficacy.

Typically, most dermatologists recommend life-long treatment with ASIT when there is clinical response. However, open controlled studies with unspecified or variable follow-up periods showed sustained clinical improvement after discontinuation of ASIT in 4–35% of the dogs (Loewenstein and Muller 2009). There are no reports in cats regarding efficacy of ASIT after treatment discontinuation.

## Allergen Selection

Similarly to what is reported in humans, the clinical response to ASIT in dogs and cats seems to be allergen-specific. Allergen selection should therefore be as accurate as possible. Allergens to be included in the ASIT should be selected based on the patient's clinical history, including allergen exposure and results of intradermal and/or allergy serum testing. Open-label trials have shown similar efficacy between ASIT based on intradermal and allergy serum testing (Griffin and Hillier 2001). However, controlled studies need to be conducted to determine the ideal allergy test methodology for formulation of ASIT.

The two most common forms of allergenic extract diluents or adjuvants used in veterinary medicine in the US and EU are aqueous and alum-precipitated, respectively. Aqueous allergens are rapidly absorbed and require smaller doses but necessitate multiple frequent injections. Alum-precipitated allergens are more slowly absorbed, requiring larger doses but fewer injections. There have been concerns regarding possible carcinogenic effects of alum-precipitated allergens, which may have led to its lower availability nowadays (Scott *et al*. 2001). An open study showed that patients receiving aqueous-based allergens may have a better improvement with ASIT than patients receiving alum-precipitated allergens (Kunkle 1980).

Cross-reactivity may be important in allergen selection for ASIT in dogs and cats, as it can potentially help simplify formulation practices and reduce inventory requirements by reducing the number of allergens included; however, most of the information used is extrapolated from humans (Esch 2008). Usually cross-reactivity is present within the same family or closer relationships, so that species of the same genus have higher cross-reactivity compared to genera of the same family. Grass antigens tend to be the most cross-reactive, as they have fewer families; however, the three main grass families do not often cross-react. Weeds are less cross-reactive than grasses, and tree antigens are the least cross-reactive. Companies providing allergens for ASIT can assist veterinarians with information regarding potential cross-reactivity among different allergens.

Another factor to be considered when selecting allergens for ASIT is the compatibility of allergen mixtures. Two problems that may occur with allergen mixtures are excessive dilution due to large numbers of allergens in the mixture, leading to suboptimal dosing, and more rapid allergen deterioration and loss of allergenicity as a result of the enzymatic activity of some allergen extracts. In humans, allergen extracts containing high concentrations of proteolytic enzymes, such as mold and insect extracts, have been implicated in reducing the potency of allergen mixtures and ultimately interfering with their efficacy when they are stored in the same vial, with grass pollens being among the most susceptible to proteolytic effects (Esch 2008). Most dogs with AD exhibit multiple hypersensitivities; therefore, allergen mixtures are often prescribed. The degradation of pollen allergens by mold proteases has also been reported in veterinary medicine (Rosenbaum *et al*. 1996). In addition, it has been shown that the success rate of ASIT increases with separation of mold allergens from other types of allergens (Mueller and Bettenay 1996). However, the true significance of allergen mixture and degradation on ASIT clinical response in dogs and cats is currently unknown. For specific guidelines used in humans when formulating mixtures with protease-containing mold, insect and mite extracts, the veterinarian can refer to (Esch 2008), and other human literature sources.

## Administration Route

In dogs and cats, subcutaneous injections are the standard route of administration of ASIT. Injections are usually administered in the nape of the neck. It is helpful to alternate injection sites so that the same site is not repeatedly injected.

Oral or sublingual immunotherapy, using a different allergen formulation than those used subcutaneously, has recently been investigated in dogs. A preliminary open study investigated the clinical response of 10 mite-sensitive dogs with AD

to sublingual immunotherapy (SLIT) (DeBoer *et al*. 2010a). Treatment consisted of 0.1 mL of allergen solution of increasing concentrations administered sublingually twice daily for 6 months. Concurrently, all dogs were treated with decreasing doses of oral methylprednisolone tapered to a minimum required dose. This study showed significant improvement in pruritus and clinical scores. Four of 10 dogs did not require oral glucocorticoid administration after 6 months of immunotherapy. In a separate report, mite-specific IgE and IgG levels in serial serum samples from the same mite-sensitive dogs were assayed by ELISA over the course of 6 months (DeBoer *et al*. 2010b). Median *Dermatophagoides farinae*-specific IgE levels declined significantly, while the median *D. farinae*-specific IgG levels increased, which generally correlated with successful SLIT. Conversely, another pilot placebo-controlled study using experimental atopic beagles showed that oral administration of 10 mg of *D. farinae* culture, mixed with cream cheese (applied inside the cheeks and on the hard palate), once daily for 7 months was safe but did not induce a significant decrease in clinical signs or allergen-specific IgE (Marsella 2010).

It is currently unknown if oral or sublingual immunotherapy would work in dogs that had not responded to conventional ASIT. Further studies are needed to investigate the efficacy of oral or sublingual immunotherapy in dogs with AD. To date, oral and sublingual allergen formulations are not commercially available for use in dogs.

## Allergen Vials and Treatment Protocols

There are many commercial companies that supply allergens for intradermal testing and ASIT. For those veterinarians initiating the practice of ASIT, the authors recommend consulting a dermatologist for suggestions of which company to use. Companies that provide allergens for ASIT usually supply the allergens in 2–3 vials. The recommended number of allergens per vial may vary according to the allergen provider and dermatology practice, but usually no more than 12 allergens should be included per vial to avoid over-dilution of antigens, which can interfere with response. Each vial contains a particular concentration of allergens mixed in a diluent or adjuvant, and it is often known as allergen solution. The patient is started on the most diluted allergen solution, and the allergen concentration is gradually increased to minimize the risk of adverse effects and achieve the desirable maintenance dose.

To date, the optimal allergen concentration for ASIT in veterinary medicine has not been identified. The initial concentration used may vary, but it is typically between 200 and 2000 PNU/mL (see chart below). The maintenance vial usually has a total allergen solution of 10,000–20,000 PNU/mL. Overall, the allergen amount injected at the initial loading phase varies from 0.05 to 1 mL, while the maintenance dose is typically 1 mL. A recent prospective double-blinded study in dogs found no significant difference between effectiveness of ASIT given at a low dose (0.1 mL) compared to the standard dose (1.0 mL) (Colombo *et al*. 2005).

Allergen manufacturers usually suggest a protocol; however, many dermatologists develop their own protocols. There are numerous ASIT protocols being used, with no standardization described for dogs and cats. Some protocols are based on body weight, and differ for small (≤20 lb) and large dogs (>20 lb) (Scott *et al*. 2001). The optimal dosing interval for both loading and maintenance

allergen injections has not been established. The interval between injections may vary from 2 to 7 days during the initial loading phase and from 5 to 20 days during the maintenance phase. When aqueous allergens are used, animals that require injections more frequently than every 10 days are usually given smaller volumes of allergens.

Included here is the protocol used in the authors' practice for many years, as an example.

### AQUEOUS HYPOSENSITIZATION

| | Day | Volume (mL) | Date | Itch level |
|---|---|---|---|---|
| Vial #1 (200 PNU/mL) | 2-day interval | | | |
| | 0 | 0.1 | _____ | _____ |
| | 2 | 0.2 | _____ | _____ |
| | 4 | 0.4 | _____ | _____ |
| | 6 | 0.8 | _____ | _____ |
| | 8 | 1.0 | _____ | _____ |
| Vial #2 (2000 PNU/mL) | 2-day interval | | | |
| | 10 | 0.1 | _____ | _____ |
| | 12 | 0.2 | _____ | _____ |
| | 14 | 0.4 | _____ | _____ |
| | 16 | 0.8 | _____ | _____ |
| | 18 | 1.0 | _____ | _____ |
| Vial #3 (20,000 PNU/mL) | 2-day interval | | | |
| | 20 | 0.1 | _____ | _____ |
| | 22 | 0.2 | _____ | _____ |
| | 24 | 0.4 | _____ | _____ |
| | 26 | 0.8 | _____ | _____ |
| | 28 | 1.0 | _____ | _____ |
| | 10-day interval | | | |
| | 38 | 1.0 | _____ | _____ |
| | 48 | 1.0 | _____ | _____ |
| | 20-day interval | | | |
| | 68 | 1.0 | _____ | _____ |
| | 88 | 1.0 | _____ | _____ |
| | 108 | 1.0 | _____ | _____ |

All protocols should be considered a starting point, and, in order to maximize the efficacy of ASIT, adjustments should be made according to each individual response. Thus, injection frequency and dose of allergen solution may be modified according to the patient's requirements. Experience with the patient allows the owner and the veterinarian to estimate how frequently the injections

should be administered to maximize response. For example, if a dog is receiving the injections every 20 days and the owner reports that the dog's itching level increases 3 days before each injection, the injections can be administered more often, every 17 days.

Another less conventional protocol reported in dogs and cats is rush immunotherapy (RIT), which is based on a short and intensive protocol of ASIT. The RIT uses a shorter initial loading phase, advancing the patient to the maintenance phase in 7 hours compared to the conventional 10–15 weeks. The benefits of such a protocol include the potential to obtain a clinical response sooner and avoid the frequent injections given initially by the owners. In dogs, one protocol using aqueous allergens involves subcutaneously administering increasing doses of allergens every 30 minutes for 7 hours (Mueller *et al*. 2004). Dogs are usually premedicated with an antihistamine for a few days prior to the RIT. An intravenous catheter is placed prior to the first allergen injection for administration of emergency drugs if needed. Dogs are monitored for side effects, with vital signs being evaluated frequently. Dogs are then discharged and continue on maintenance immunotherapy at home. A double-blinded randomized study in dogs with AD showed that RIT seems to be safe and associated with a higher success rate than conventional ASIT over a 12-month period, with improvement seen within the first 6 months of therapy (Mueller *et al*. 2004). However, further studies are needed to support or dispute these findings.

A pilot study showed that RIT appears to be safe for use in cats when aqueous allergens are administered subcutaneously at increasing doses every 30 minutes for 5 hours to a maintenance dose of 15,000 PNU/mL (Trimmer *et al*. 2005). However, there are no reports on the efficacy of RIT in atopic cats.

## Adverse Effects

Adverse reactions to conventional ASIT are reported to be rare to uncommon in dogs. The most common adverse event reported in dogs is pruritus (reported in about 25% of dogs) and exacerbation of clinical signs after administration of increasing concentrations of ASIT. Localized injection-site reactions are uncommon and include swelling, pain, erythema or pruritus. Systemic adverse reactions are rare in dogs and include weakness, depression, sleepiness, anxiety, panting, hyperactivity, diarrhea, vomiting, increased bowel sounds, urination changes, frequent swallowing, urticaria, angioedema, collapse, and anaphylaxis (Griffin and Hillier 2001). Anaphylaxis, although rare, is the most serious complication, and dogs should be treated as soon as possible.

There is very little information regarding ASIT adverse reactions in cats, with localized injection-site reactions, pruritus, and fatal anaphylaxis being anecdotally reported. Most adverse reactions occur immediately after an injection or up to 1–2 days later, and can persist for hours to days.

Pre-treatment with antihistamines or glucocorticoids, 1–2 hours prior to each allergen injection, is anecdotally reported in dogs and cats to prevent adverse reactions and recommended by the authors, mainly when administering more than 12–15 allergens. Factors influencing adverse effects of ASIT in dogs and cats have not been investigated.

RIT and oral or sublingual immunotherapy are reported to be generally safe in dogs and cats. Intradermal administration of allergen solution in 30 dogs with

AD receiving RIT showed increased pruritus in eight dogs and generalized wheal formation in one dog (Mueller and Bettenay 2001). However, another study, performed in 12 dogs with AD, did not show any side effects of RIT when administered subcutaneously (Mueller *et al*. 2004). One pilot study investigating the safety of RIT in atopic cats reported that two of four cats developed mild increase in grooming behavior, which was interpreted as mild pruritus, during the rapid loading phase, and two others developed dermal swelling at injection site 1 week after RIT (Trimmer *et al*. 2005).

Studies investigating oral or sublingual immunotherapy in dogs did not report any side effects (DeBoer *et al*. 2010a, 2010b).

Despite the uncommon to rare adverse reactions associated with conventional ASIT or RIT, it is important to ask clients to observe the pet closely for about 2 hours after administering the allergen solution, and to seek appropriate veterinary care if required.

## Concurrent Therapy and Drug Interactions

There have been conflicting opinions regarding the influence of glucocorticoids on the outcome of ASIT, with some dermatologists suggesting avoidance during the induction phase of ASIT and others suggesting no effect if glucocorticoids are used at low doses or on alternate days (Loewenstein and Muller 2009). Cyclosporine was shown to not interfere with intradermal or serum allergen-specific IgE reactivity when administered orally at 5 mg/kg/day for 30 days (Goldman *et al*. 2010). However, the effect of cyclosporine on the response to ASIT is currently unknown. Basically, there is no current evidence to suggest that concurrent administration of any topical or systemic anti-inflammatory/immunomodulatory drugs alters the clinical benefit of ASIT in dogs and cats (Olivry *et al*. 2010b). In fact, due to the possible delay in ASIT clinical response, anti-inflammatory/immunomodulatory drugs may be given temporarily, as needed, to maintain good quality of life until ASIT is reported to be effective. It is possible that concurrent administration of anti-inflammatory/immunomodulatory drugs could mask evaluation of the clinical response to ASIT and its adverse effects that would require modification of the ASIT protocol, mainly when used during the induction phase.

## Client Education

Client education is a very important aspect of ASIT administration. Prior to starting ASIT therapy, clients should be aware of the technique, reported success rate, and duration of ASIT, in addition to the cost and time commitment involved. The recommended protocol and how to administer the injections should be explained in detail. After drawing the solution, clients should allow the solution to reach room temperature prior to administration. They should also be informed about using new syringes and needles for each injection, and disposing of them properly.

It is very important to teach clients to train their pets to accept the allergy shots. Rewards should be given after each injection. The training is especially helpful when owners are nervous, as animals will often sense this apprehension. Clients should be well informed about potential side effects and receive

recommendations for what to do in case they occur. If clients understand the importance of following ASIT recommendations and have frequent communication and follow-up visits during the first year of therapy, they will likely be more compliant.

## Recheck Evaluations and Monitoring

Frequent follow-up visits and monitoring of patients during ASIT is crucial to maximize the potential benefits of ASIT. If possible, re-evaluation of patients at 1, 3, 6, and 12 months after starting ASIT can be helpful to try to reach optimal results. At these visits, veterinarians can modify ASIT protocols according to the patient's response and occurrence of adverse effects, and can check compliance, as compliance with ASIT by dog owners has been reported to be low. Additionally, complicating factors often associated with atopic dermatitis, such as skin and ear infections, are likely to recur and should be appropriately addressed at these follow-up visits.

# Section 4
# Skin Diseases and Suggested Treatment

## Hypersensitivity Disorders

### ATOPIC DERMATITIS

Atopic dermatitis is a chronic relapsing genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features that is associated with IgE antibodies, most commonly directed against environmental allergens. Epidermal barrier defects may also contribute to its pathogenesis. It appears to be more common in dogs than in cats. Symptoms may occur seasonally or year-round, depending on offending allergens, and are characterized by variable degrees of pruritus, erythema, and secondary skin lesions. It involves mostly the face, axillae, ventral neck, ventral abdomen, inguinal area, and feet (mostly interdigital areas). The age of onset is typically between 1 and 3 years, but symptoms can start at any age. Bacterial and/or yeast skin infections are common complicating problems.

**Treatment options**

- Antihistamines (amitriptyline hydrochloride, cetirizine hydrochloride, chlorpheniramine maleate, clemastine fumarate, cyproheptadine hydrochloride, diphenhydramine hydrochloride, doxepin hydrochloride, fexofenadine hydrochloride, hydroxyzine hydrochloride, loratadine, trimeprazine + prednisolone) – topical, oral
- Ceramides – topical
- Colloidal oatmeal – topical
- Cyclosporine – oral
- Essential fatty acids – oral, topical
- Glucocorticoids (betamethasone, dexamethasone, hydrocortisone, hydrocortisone aceponate, isoflupredone acetate, methylprednisolone, mometasone furoate, prednisolone, prednisone, triamcinolone acetonide) – topical, oral, injectable (cats only)
- Interferon gamma, recombinant canine – injectable
- Interferon omega, recombinant feline – injectable
- Masitinib mesylate – oral
- Neutralized zinc – topical
- Misoprostol – oral
- Pentoxifylline – oral

*Canine and Feline Dermatology Drug Handbook*, First Edition.
Sandra N. Koch, Sheila M.F. Torres and Donald C. Plumb.

Published 2012 by Blackwell Publishing Ltd.

- Phytosphingosine salicyloyl – topical
- Pimecrolimus – topical
- PO7P (Chinese herbal supplement) – oral
- Pramoxine hydrochloride – topical
- Tacrolimus – topical

### FELINE MOSQUITO-BITE HYPERSENSITIVITY

Mosquito-bite hypersensitivity is an uncommon disease of cats previously sensitized to mosquito bites. Symptoms are usually seasonal in temperate zones and year-round in subtropical and tropical areas and are characterized by variable degrees of pruritus, papules, erosions, and crusts on the dorsal aspect of the nose and pinnae. Footpads may be affected with hyperkeratosis, hyperpigmentation or hypopigmentation, fissures, swelling, ulcerations, and pain. Peripheral lymphadenopathy may be present.

**Treatment options**

- Glucocorticoids (betamethasone, dexamethasone, hydrocortisone, hydrocortisone aceponate, methylprednisolone, mometasone furoate, prednisolone) – topical, oral, injectable
- Repellents that do not contain permethrin – topical

### FLEA ALLERGY DERMATITIS

Flea allergy dermatitis is a hypersensitivity reaction of dogs and cats to allergens in flea saliva. Symptoms are usually seasonal in temperate zones and year-round in subtropical and tropical areas and are characterized by variable degrees of pruritus, a primary papular eruption, and secondary skin lesions. Most commonly affected areas include the dorsal-lumbosacral area, base of the tail, caudal aspects of the legs, ventral abdomen, inguinal and perineal areas. The face can also be affected in cats. Bacterial and/or yeast skin infections can be complicating factors.

**Treatment options**

- Colloidal oatmeal – topical
- Deltamethrin collar – topical
- Dinotefuran – topical
- Fipronil (± (S)-methoprene) – topical
- Glucocorticoids (betamethasone, dexamethasone, hydrocortisone, hydrocortisone aceponate, isoflupredone acetate, methylprednisolone, mometasone furoate, prednisolone, prednisone, triamcinolone acetonide) – topical, oral, injectable (cats only)
- Imidacloprid – topical
- Lufenuron – oral
- (S)-Methoprene combinations – topical
- Nitenpyram – oral
- Permethrin (dogs only) – topical
- Pyrethrin – topical
- Pyriproxyfen – topical
- Selamectin – systemic
- Spinetoram – topical
- Spinosad – oral

## Autoimmune Skin Diseases

### DISCOID LUPUS ERYTHEMATOSUS

Discoid lupus erythematosus is a relatively benign autoimmune skin disease. The pathogenesis of skin lesions in lupus erythematosus is unclear but may include photosensitivity, keratinocyte damage, autoantibody production, and immune-complex formation. It is common in dogs but rare in cats. Symptoms are characterized mostly by nasal depigmentation, erythema, scaling, crusting, erosion, and ulceration. It may also involve the dorsal aspect of the muzzle, lips, periocular skin, and pinnae, and less commonly the oral cavity, distal limbs, and genitalia.

**Treatment options**

- Cyclosporine – oral
- Essential fatty acids – oral, topical
- Glucocorticoids (betamethasone, dexamethasone, hydrocortisone, hydrocortisone aceponate, isoflupredone acetate, methylprednisolone, mometasone furoate, prednisolone, prednisone, triamcinolone acetonide) – topical, oral, injectable (cats only)
- Pimecrolimus – topical
- Sunscreen – topical
- Tacrolimus – topical
- Tetracycline (or doxycycline) and niacinamide – oral
- Vitamin E – topical, oral

### PEMPHIGUS FOLIACEUS

Pemphigus foliaceus is the most common autoimmune skin disease of dogs and cats. It is caused by the production of antibodies against a component of the adhesion molecules on keratinocytes, which leads to loss of keratinocyte adhesion or acantholysis. It is commonly idiopathic, but some cases may be drug-induced, or a sequela to chronic inflammatory skin diseases. Symptoms are characterized by superficial pustules and erosions, and crusts mostly on the dorsal aspect of the muzzle, pinnae, footpads, and nail folds (particularly in cats). Mucosal involvement is rare. Skin lesions are usually not pruritic; however, pruritus may be present if secondary skin infection develops.

**Treatment options**

- Auranofin – oral
- Aurothiomalate sodium – injectable
- Azathioprine – oral (dogs only)
- Chlorambucil – oral
- Cyclophosphamide – oral
- Cyclosporine – oral
- Essential fatty acids – oral, topical
- Glucocorticoids (betamethasone, dexamethasone, hydrocortisone, hydrocortisone aceponate, isoflupredone acetate, methylprednisolone, mometasone furoate, prednisolone, prednisone, triamcinolone acetonide) – topical, oral, injectable (cats only)
- Human intravenous immunoglobulin IgG (hIVIG) – injectable
- Mycophenolate mofetil – oral
- Pimecrolimus – topical

- Sunscreen – topical
- Tacrolimus – topical
- Tetracycline (or doxycycline) and niacinamide – oral

## Sterile Inflammatory/Immune-Mediated Skin Diseases

### CUTANEOUS VASCULITIS

Cutaneous vasculitis is an inflammatory skin disease of blood vessels, usually secondary to immune-complex deposition within the vessel walls. It is uncommon in dogs and rare in cats. Vasculitis may be associated with many underlying conditions such as infections (bacterial, fungal, viral, rickettsial), food hypersensitivity, insect/arthropod bites, drug reaction, vaccinations (mainly rabies), metabolic diseases (e.g., diabetes mellitus, uremia), immune-mediated diseases (e.g., systemic lupus erythematosus), exposure to cold (cold agglutinin disease), and malignancy, or it can be idiopathic. Symptoms may vary, but most commonly alopecia, crusting, purpura, necrosis, erosions, and crateriform (punched-out) ulcers are seen mainly on pinnae, lips, oral mucosa, footpads, tail, and scrotum. Other signs such as anorexia, depression, fever, arthropathy, myopathy, and pitting edema of extremities may be seen.

**Treatment options**

- Azathioprine – oral (dogs only)
- Chlorambucil – oral
- Cyclophosphamide – oral
- Cyclosporine – oral
- Dapsone – oral (dogs only)
- Glucocorticoids (betamethasone, dexamethasone, hydrocortisone, hydrocortisone aceponate, isoflupredone acetate, methylprednisolone, mometasone furoate, prednisolone, prednisone, triamcinolone acetonide) – topical, oral, injectable (cats only)
- Pentoxifylline – oral
- Sulfasalazine – oral
- Tetracycline (or doxycycline) and niacinamide – oral

### IDIOPATHIC STERILE PYOGRANULOMATOUS-GRANULOMATOUS SYNDROME

Idiopathic sterile pyogranulomatous-granulomatous syndrome is an inflammatory skin disease believed to be immune-mediated; however, the pathogenesis is unknown. It is uncommon in dogs and rare in cats. Clinical signs are characterized by non-painful and non-pruritic, firm, dermal plaques and/or nodules that may be alopecic and ulcerated. Lesions may wax and wane, and occur anywhere on the body, but most commonly on the muzzle, around the eyes, and on the pinnae and feet.

**Treatment options**

- Azathioprine – oral (dogs only)
- Chlorambucil – oral
- Cyclophosphamide – oral
- Cyclosporine – oral

- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral, injectable (cats only)
- Pentoxifylline – oral
- Tetracycline (or doxycycline) and niacinamide – oral

### JUVENILE CELLULITIS

Juvenile cellulitis is also known as juvenile sterile granulomatous dermatitis and lymphadenitis, juvenile pyoderma, or puppy strangles. It is an uncommon inflammatory skin disease of dogs affecting mostly puppies 3 weeks to 4 months old, with highest incidence in golden retrievers, Labrador retrievers, dachshunds, pointers, and Lhasa apsos. The etiology is unknown but it is believed to be immune-mediated. The disease is characterized by acute swelling, sterile papules, pustules, crusts, draining tracts, and/or small ulcers on the muzzle and periocular areas with marked submandibular and prescapular lymphadenopathy. Exudative otitis externa, fever, anorexia, and depression may be present.

**Treatment options**

- Cyclosporine – oral
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral
- Griseofulvin – oral

### REACTIVE HISTIOCYTOSIS

Cutaneous and systemic histiocytosis are uncommon reactive inflammatory skin diseases derived from dermal dendritic cells. The etiology is unknown but it is believed to be immune-mediated. The breed predilection (most commonly Bernese mountain dog, rottweiler, boxer, golden retriever, and Labrador retriever) suggests a genetic predisposition. Both conditions usually affect adult dogs and are associated with nodules or plaques, especially around the muzzle, head, neck, and extremities. Lesions may be alopecic, erythematous, and usually non-painful and non-pruritic. Cutaneous histiocytosis may wax and wane, and it may spontaneously resolve. Systemic histiocytosis carries a worse prognosis, as it may also involve the conjunctiva, sclera, retrobulbar tissues, nasal cavity, lymph nodes, and internal organs such as the liver, spleen, lungs, and bone marrow.

**Treatment options**

- Azathioprine – oral (dogs only)
- Chlorambucil – oral
- Cyclosporine – oral
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral
- Leflunomide – oral
- Tetracycline (or doxycycline) and niacinamide – oral

### SEBACEOUS ADENITIS

Sebaceous adenitis is an inflammatory skin disease. It is uncommon in dogs and rare in cats. The etiology is unknown but it is believed to be immune-mediated. It affects dogs between 1 and 5 years old; however, it may occur at any age. Breeds with the highest incidence include the standard poodle, akita, viszla, English springer spaniel, and Havanese dogs, but it can occur in any breed. It is characterized by variable degrees of scaling, follicular casting, and hair loss and

typically it is not associated with pruritus unless secondary infections occur. It affects most commonly the head, pinnae, and dorsum, and in certain breeds the ear canals, but sebaceous adenitis can affect any part of the body and may become generalized.

**Treatment options**
- Acitretin – oral
- Ceramides – topical
- Cyclosporine – oral, topical
- Essential fatty acids – oral, topical
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral
- Isotretinoin – oral
- Phytosphingosine hydrochloride – topical
- Salicylic acid – topical
- Sulfur, precipitated – topical
- Tetracycline (or doxycycline) and niacinamide – oral
- Vitamin A – oral

### STERILE NODULAR PANNICULITIS

Sterile nodular panniculitis is an inflammatory disease of the subcutaneous fat. Extracellular lipid undergoes hydrolysis into fatty acids, which can lead to inflammation and granulomatous reactions. Panniculitis may occur due to a foreign-body reaction, trauma, injection of vaccines or other medications, immune-mediated diseases (e.g., vasculitis, systemic lupus erythematosus), or nutrition deficiency (e.g., feline pansteatitis), or it may be idiopathic. It is a rare condition in dogs and cats. Symptoms are characterized by one or more subcutaneous nodules of variable sizes that may be erythematous, alopecic, painful, fluctuant to firm, and that may ulcerate and drain a yellowish, oily exudate. Lesions may wax and wane, and they can develop anywhere on the body, but most commonly over the ventrolateral neck, chest, and abdomen. Concurrent fever, anorexia, and depression may occur.

**Treatment options**
- Azathioprine – oral (dogs only)
- Chlorambucil – oral
- Cyclophosphamide – oral
- Cyclosporine – oral
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral, injectable (cats only)
- Pentoxifylline – oral
- Tetracycline (or doxycycline) and niacinamide – oral

## Parasitic Skin Diseases

### CANINE DEMODICOSIS

Demodicosis caused by *Demodex canis* is a common canine skin disease associated with the presence of larger than normal numbers of mites in the hair follicles. It may be localized (mostly to face and forelegs) or generalized, and is classified as juvenile-onset or adult-onset. The generalized juvenile-onset disease

and adult-onset forms have a guarded prognosis. Hereditary predisposition is likely associated with the generalized juvenile-onset form, and a deficiency in T-lymphocyte function is speculated to occur. Clinical signs include alopecia, erythema, scaling, follicular casts, crusts, hyperpigmentation, comedones, edema, papules, pustules, bullae, and draining tracts. Pruritus, lymphadenopathy, and fever may be present. In addition to *D. canis* (follicular mite), two less common species of *Demodex* mites have been reported in dogs: *D. cornei* (surface mite) and *D. injai* (follicular mite). The typical clinical sign associated with *D. cornei* is pruritus, and with *D. injai* is excessive oil along the dorsum, with or without pruritus.

**Treatment options**

- Amitraz – topical
- Benzoyl peroxide – topical
- Doramectin – oral, injectable, oral
- Ivermectin – oral
- Milbemycin oxime – oral
- Moxidectin – oral
- Moxidectin and imidacloprid – topical
- Rotenone – topical

### CANINE SARCOPTIC MANGE

Canine sarcoptic mange is a common skin disease caused by *Sarcoptes scabiei* var. *canis*, a superficial burrowing mite. Exposure to mites and their allergens induces a humoral and cell-mediated hypersensitivity reaction characterized by non-seasonal intense pruritus, usually associated with alopecia, erythema, scaling, crusts, papules, and excoriations affecting mostly pinnal margins, elbows, hocks, ventral abdomen, and thorax. With chronicity, lesions may become generalized. Sarcoptic mange is highly contagious to other dogs, can cause a temporary dermatitis in humans, and can rarely cause disease in cats.

**Treatment options**

- Amitraz – topical
- Doramectin – injectable
- Fipronil – topical
- Ivermectin – oral, injectable
- Lime sulfur – topical
- Milbemycin oxime – oral
- Moxidectin – oral, injectable
- Moxidectin and imidacloprid – topical
- Selamectin – topical

### CHEYLETIELLOSIS

Cheyletiellosis is an uncommon skin disease of dogs and cats caused by *Cheyletiella*, a non-burrowing mite, leading to variable levels of pruritus and excessive scaling, mostly over the dorsum. Hair loss, papules, and crusts may also be present. The mite is not host-specific and may readily transfer between dogs, cats, and rabbits. Humans can also develop a transient dermatitis after contact with affected animals.

**Treatment options**
- Fipronil – topical
- Ivermectin – oral, injectable
- Lime sulfur – topical
- Milbemycin oxime – oral
- Moxidectin and imidacloprid – topical
- Selamectin – topical

### FELINE DEMODICOSIS

Feline demodicosis is an uncommon skin disease caused by the presence of *Demodex* mites in the skin. It can be caused either by *D. cati* (follicular mite) or *D. gatoi* (surface mite). Skin disease may be localized or generalized. Demodicosis caused by *D. cati* is usually characterized by non-pruritic focal patchy or generalized alopecia and erythema, with or without scaling and crusts, and it typically affects middle-aged to older cats with an underlying disease. Demodicosis caused by *D. gatoi* is characterized by a pruritic focal patchy or generalized self-inflicted alopecia with or without erythema, scaling, and crusts. *D. gatoi* is contagious to other cats.

**Treatment options**
- Amitraz – topical
- Doramectin – injectable
- Ivermectin – injectable
- Lime sulfur – topical
- Milbemycin oxime – oral

### OTODECTIC MANGE (OTOACARIOSIS)

Otodectic mange is a common disease of dogs and cats, particularly puppies and kittens, caused by infestation of ear canals with *Otodectes cynotis*, a non-burrowing non-host-specific psoroptid mite, causing pruritus and a dark-brown ceruminous otitis externa. Ectopic infestations of the neck, head, tail, and rarely trunk can occur, but dermatitis rarely develops on these areas. Adult cats are often asymptomatic carriers. Transient infestation has been reported in humans.

**Treatment options**
- Fipronil – topical
- Ivermectin – topical, injectable
- Moxidectin – injectable
- Pyrethrin ± pyperonyl butoxide – topical
- Rotenone – topical
- Selamectin – topical
- Thiabendazole – topical

## Fungal Skin Disorders

### DERMATOPHYTOSIS

Dermatophytosis is a contagious fungal infection of the skin, hair, and nails that occurs more frequently in young or immunocompromised dogs and cats. Classical clinical signs include focal or multi-focal areas of well-demarcated alopecia or hypotrichosis, scaling, crusting, and erythema. The disease, however, can have quite variable clinical presentations such as draining tracts (kerion) or

nodules (dermatophytic mycetoma/pseudomycetoma), and it can become generalized. Areas more typically affected include the ears, face, and feet, but any body site can be involved. Cats are often asymptomatic carriers of dermatophyte organisms, complicating the zoonotic aspect of this disorder. Treatment can be challenging, because organisms may survive in the environment for more than 1 year.

**Treatment options**

- Chlorhexidine – topical
- Clotrimazole – topical
- Enilconazole – topical
- Fluconazole
- Griseofulvin – oral
- Itraconazole – oral
- Ketoconazole – oral or topical
- Lime sulfur – topical
- Lufenuron – oral
- Miconazole – topical
- Selenium sulfide – topical
- Terbinafine – oral

### *MALASSEZIA* DERMATITIS

*Malassezia* dermatitis is a very common skin condition of dogs and less frequently cats. It is typically secondary to an underlying disorder. The most common yeast causing infection/overgrowth in dogs is the non-lipid-dependent species *Malassezia pachydermatis*; however, a broad variety of species have been isolated from cats, such as *M. pachydermatis* and the lipid-dependent *M. sympodialis*. Clinical signs are not very specific and may include pruritus, erythema, scaling, oily skin, a rancid or "yeasty" odor, alopecia, and brownish discoloration of the skin, hair, or nail plate. Areas most commonly affected are the ears, feet, face (lips/muzzle/chin), axilla, ventral neck, perineum, and nail folds. *Malassezia* dermatitis in a middle-aged to older cat may indicate the presence of an internal disorder (e.g., thymoma, paraneoplastic alopecia, diabetes mellitus). It is important to remember that *Malassezia* organisms are normally present in the skin and mucosa of most dogs and cats.

**Treatment options**

- Chlorhexidine – topical
- Chloroxylenol – topical
- Clotrimazole – topical
- Fluconazole – oral
- Itraconazole – oral
- Ketoconazole – oral, topical
- Lime sulfur – topical
- Miconazole – topical
- Selenium sulfide – topical
- Terbinafine – oral

### SYSTEMIC FUNGAL DISEASES

Systemic mycotic infections caused by pathogenic organisms often affect the skin, and these include blastomycosis, sporotrichosis, cryptococcosis,

histoplasmosis, and coccidioidomycosis. Except for *Sporothrix schenckii*, which invades the organism via cutaneous inoculation or wound contamination, the infection typically occurs through inhalation of the vegetative form of the fungus, which lives under special conditions in the environment. The only one considered a true zoonosis is sporotrichosis. Cutaneous manifestations can vary, but they typically include multi-focal nodules/plaques that eventually become eroded to ulcerated and may drain a sanguineous-purulent exudate. Systemic signs will differ according to the internal organ affected, and non-organ-specific signs include fever and decreased appetite or anorexia.

**Treatment options**
- Amphotericin B – injectable
- Caspofungin acetate – injectable
- Fluconazole – oral
- Iodide, potassium – oral
- Itraconazole – oral
- Ketoconazole – oral
- Posoconazole – oral
- Voriconazole – oral

## Endocrine Skin Disorders

### CANINE ALOPECIA X

Alopecia X is a non-inflammatory alopecia that typically affects intact male dogs between 2 and 5 years of age. The cause of this disease is still unknown. Pomeranians are over-represented, but Alaskan malamutes, miniature poodles, akitas, chow chows, keeshonds, Siberian huskies, and samoyeds also appear to be predisposed. Clinical signs are limited to the skin and include non-inflammatory alopecia that gradually progresses to affect the neck, the trunk, and the caudal and lateral aspects of the hind legs and tail. Hyperpigmentation and scaling are also often present, and dogs may develop secondary bacterial and/or yeast infections at any time during the disease course.

**Treatment options**
- Melatonin – oral, implant
- Methyltestosterone – oral
- Mitotane – oral
- Somatotropin – injectable
- Trilostane – oral

### CANINE HYPERADRENOCORTICISM

Hyperadrenocorticism can be spontaneous or the result of inappropriate use of glucocorticoid therapy (iatrogenic). Most cases of spontaneous hyperadrenocorticism in dogs are due to a functional pituitary tumor (85%), with fewer cases caused by an adrenal tumor (15%). The iatrogenic form can affect dogs of any age; however, the spontaneous disease typically affects middle-aged to old dogs. Clinical signs include polydipsia, polyuria, polyphagia, panting, muscle atrophy, non-inflammatory alopecia that typically spares the head and extremities, atrophic skin, comedones, calcinosis cutis, distended abdomen, and/or exercise intolerance. About 5% of the patients may develop diabetes mellitus at some

point during the disease course, and bacterial and/or fungal skin infections or demodicosis may also complicate the disease. Surgery can be performed to remove the adrenal or pituitary tumor; however, most patients receive medical treatment because in general they are not good candidates for surgery, there is currently limited experience of performing pituitary surgeries, and the efficacy of the currently available medical therapies is very good.

**Diagnostic and treatment options**
- Corticotropin – diagnostic aid
- Cosyntropin – diagnostic aid
- Ketoconazole – oral
- Mitotane – oral
- Selegiline hydrochloride – oral
- Trilostane – oral

### CANINE HYPOTHYROIDISM

The most common causes of canine hypothyroidism are lymphocytic thyroiditis or idiopathic atrophy of the thyroid parenchyma. The disease progresses insidiously; therefore, middle-aged to old dogs are most commonly affected. Various breeds have been reported as predisposed to primary hypothyroidism, and sighthounds have been shown to have thyroid hormone concentrations below laboratory reference intervals. Clinical signs are non-specific and include lethargy, exercise intolerance, bradycardia, weight gain unaccompanied by appetite increase, cold intolerance, peripheral or central neurologic signs, non-inflammatory alopecia that typically affects the tail and spares the head and extremities, comedones, cutaneous hyperpigmentation, and/or scaling. Myxedema may be noticed in severe, chronic cases. Bacterial and/or yeast skin infections or demodicosis may complicate the disease.

**Diagnostic and treatment options**
- Levothyroxine sodium – oral
- Thyrotropin-releasing hormone – diagnostic aid
- Thyrotropin – diagnostic aid

## Keratinization Disorders

### ACNE

Acne is a poorly understood keratinization disorder of the hair follicles that occurs more often in cats than in dogs. Hyperplasia of sebaceous glands is also seen histologically in feline cases. Feline acne is characterized clinically by the presence of comedones and/or black keratinous debris on the chin and lips. Comedonic hair follicles can become inflamed and infected, resulting in the development of papules, small nodules, and/or draining tracts as a result of rupture of hair follicles (furunculosis). If furunculosis occurs, severe inflammation of the chin may develop. Canine acne is typically characterized by the presence of papules, nodules that may erode or ulcerate, and draining tracts (furunculosis) localized to the chin and lips. It typically affects young dogs of short-coated breeds. Feline and canine acne are often complicated by secondary superficial and/or deep pyoderma.

**Treatment options**
- Acitretin – oral
- Adapalene – topical
- Benzoyl peroxide – topical
- Chlorhexidine – topical
- Ethyl lactate – topical
- Isotretinoin – oral, topical
- Mupirocin – topical
- Salicylic acid, sulfur – topical
- Tazarotene – topical
- Tretinoin – topical

### CANINE ZINC-RESPONSIVE DERMATOSIS

Canine zinc-responsive dermatosis is an inflammatory skin disorder that may be associated with a true or relative dietary zinc deficiency (type 2) or altered absorption of zinc from the gastrointestinal tract despite consumption of a nutritionally balanced diet (type 1). Siberian huskies and Alaskan malamutes are prone to develop type 1 disease, possibly because of an autosomal recessive mode of inheritance. Type 1 is usually seen between 1 and 3 years of age, and type 2 occurs more frequently in fast-growing young dogs fed a home-made diet deficient in zinc or a diet with excess of vitamins, and minerals such as calcium or plant phytates that may interfere with zinc absorption. Clinical signs include well-demarcated alopecia to hypotrichosis associated with erythema, scaling, and crusting typically localized to the muzzle, chin, periocular area, other mucocutaneous sites, pinnae and pressure points. Footpads can become hyperkeratotic, and lymphadenopathy may occur in severe cases. Pruritus, when present, varies from mild to severe. Secondary bacterial and *Malassezia* skin infections often complicate the disease.

**Treatment options**
- Essential fatty acids – oral, topical
- Glucocorticoids (betamethasone, dexamethasone, hydrocortisone, hydrocortisone aceponate, isoflupredone acetate, methylprednisolone, mometasone furoate, prednisolone, prednisone, triamcinolone acetonide) – topical, oral
- Zinc – oral, injectable

## Pyodermas

### SUPERFICIAL PYODERMA

Superficial pyoderma in dogs is typically caused by *Staphylococcus pseudintermedius*, which frequently colonizes mucocutaneous areas such as the nasal mucosa, anal ring, and perineum. In the large majority of cases, it is a secondary problem complicating underlying diseases. Canine superficial pyoderma is often recurrent, because most associated underlying disorders, such as atopic dermatitis, are non-curable. Clinical signs in the dog are variable and include papules, pustules, epidermal colarettes, yellow-brown crusts, and/or moth-eaten alopecia (especially in short-coated breeds). The trunk, ventral abdomen, inguinal area, and/or inner thighs are commonly affected. Cats are generally much less often affected by superficial pyoderma than dogs, and this may partly reflect differences in the skin barrier between these species. Agents

most frequently associated with feline superficial pyoderma include S. *pseudintermedius*, *S. aureus*, and *S. felis*. Clinical signs include papules, pustules, and/or yellow-brown crusts. Self-inflicted, eroded to ulcerated lesions of cats often become over-colonized with coccus-shaped bacteria. Treatment includes topical therapy in the form of medicated shampoos and/or creams/ointments and systemic antibiotics. The treatment should be planned taking into consideration the etiologic agent, depth and extent of the lesions, the patient's age, body weight, and tolerance to drugs, and the owner's commitment to the designed treatment. If using a systemic antibiotic, remember to choose the appropriate antibiotic (ideally based on culture and susceptibility) and administer it at the correct dosage for the appropriate duration of time (i.e., at least 1 week past clinical resolution). Identifying the underlying disease will help prevent recurrences.

**Treatment options**

- Antibacterials (amoxicillin + clavulanic acid, bacitracin, cefadroxil, cefovecin sodium, cefpodoxime proxetil, cephalexin, chloramphenicol, ciprofloxacin hydrochloride, clarithromycin, clindamycin hydrochloride/palmitate, dicloxacillin sodium, difloxacin hydrochloride, enrofloxacin, lincomycin, marbofloxacin, moxifloxacin, norfloxacin, orbifloxacin, ormetropin + sulfadimethoxine, oxacillin, pradofloxacin, rifampin, sulfadiazine/sulfamethoxazole + trimethoprim) – oral
- Benzoyl peroxide – topical
- Chlorhexidine – topical
- Chloroxylenol – topical
- Elimiderm – topical
- Ethyl lactate – topical
- Fusidic acid – topical
- Gentamicin – topical
- Hypochlorous acid – topical
- Mupirocin – topical
- Nitrofurazone – topical
- Povidone iodine – topical
- Propionibacterium acnes – injectable
- Selenium sulfide – topical
- Silver sulfadiazine – topical
- Staphylococcal phage lysate – injectable

### DEEP PYODERMA

Deep pyoderma occurs when the bacteria reach the dermis and/or subcutaneous tissue via rupture of the hair follicle or penetrating wounds. *Staphylococcus pseudintermedius* is the most common etiologic agent in dogs, but *S. aureus*, *S. schleiferi*, and less commonly Gram-negative bacteria such as *Pseudomonas* or *Proteus* may also be involved. In cats, fight abscess is the most common form of deep bacterial infection, and bacteria from the oral cavity are typically involved, including *Pasteurela multocida*, *Bacteroides*, *Fusobacterium*, among others. Similarly to superficial pyoderma, the large majority of cases are secondary to an underlying disease. Clinical signs include erythema, ill-defined swelling, hemorrhagic bulla, papules, nodules, draining tracts, erosions, ulcerations, crusts, abscesses, and/or cellulitis. Lesions may be confined to one body region such as the face or feet, or they may

be generalized (e.g., German shepherd dog pyoderma). Treatment includes adjunctive topical therapy in the form of medicated shampoos and/or creams/ointments and systemic antibiotics. It is very important to select the antibiotic therapy based on culture and sensitivity, and to administer the treatment for at least 2 weeks past clinical resolution. Identifying the underlying disease will help prevent recurrences.

**Treatment options**
Refer to the superficial pyoderma list.

## Miscellaneous

### ACRAL LICK DERMATITIS

Acral lick dermatitis is one of the most challenging canine skin disorders that dermatologists have to manage. The inciting causes that stimulate dogs to compulsively lick and chew at the affected area are multiple and often not easy to identify, which contributes to the difficulty in successfully managing these cases. Large-breed dogs, especially Doberman pinschers, great Danes, golden retrievers, Labrador retrievers, German shepherd dogs, and boxers appear to be predisposed. The characteristic lesion is a well-demarcated plaque which is firm (fibrotic) and has an eroded or ulcerated surface. Lesions are typically single but can be multiple and usually develop on the dorsal aspect of the carpal/metacarpal region, but they can also be present on the tarsal/metatarsal area. Secondary superficial bacterial over-growth and deep bacterial infection are often present, and these should be addressed as part of the treatment regimen.

**Treatment options**
- Benzodiazepines (alprazolam, clonazepam, diazepam, lorazepam, oxazepam) – oral
- Capsaicin – topical
- Fluocinolone acetonide and DMSO – topical
- *LickGuard*® – topical
- Selective serotonin reuptake inhibitors (SSRIs) (fluoxetine hydrochloride, paroxetine hydrochloride, sertraline hydrochloride) – oral
- Tricyclic antidepressants (amitriptyline hydrochloride, clomipramine hydrochloride, doxepin hydrochloride) – oral

### CANINE FAMILIAL DERMATOMYOSITIS

Canine dermatomyositis is an inflammatory skin disorder that affects the skin and muscle. Its pathomechanism is not well understood, but the ischemic features characteristic of this disorder suggest an immunologic damage to blood vessels. It appears to be hereditary in collies and Shetland sheepdogs, and an autosomal dominant mode of inheritance with variable expressivity has been suggested for collies. Other breeds reported with this condition include kuvasz, chow chow, German shepherd dog, and Welsh corgi, but additional breeds can be infrequently affected. The age of onset is typically 6 months or less, but adult dogs can also be affected. Clinical signs include scarring alopecia, scaling, crusting, and erythema, and lesions are typically localized to

the face (dorsal muzzle, ears, periocular area), extremities, and tip of tail. Muscles more often affected are the masseter and temporalis, but involvement is usually minimal and may not be clinically evident. Disease progression is variable, and clinical signs often wax and wane, with spontaneous resolution occurring in some cases.

**Treatment options**
- Cyclosporine – oral
- Pentoxifylline – oral
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral
- Tetracycline (or doxycycline) and niacinamide – oral
- Vitamin E – oral

### CANINE PERIANAL FISTULAS

Perianal fistulas, also known as anal furunculosis, define a chronic disorder characterized by the development of multiple fistulas and draining tracts at the perianal region. The pathomechanism is currently unknown, but the good response to cyclosporine therapy suggests that an immune-mediated mechanism plays a role. This disorder occurs most frequently in German shepherd dogs, but other breeds can also be affected. Clinical signs are characterized by fibrotic fistulas and/or sinuses draining a serous-sanguineous to purulent exudate, and erosions to ulcerations. Lesions may involve various extents of the perianal region according to the degree of severity and chronicity. The animal often presents with tenesmus, straining to defecate, dyschezia, and reluctance to have the affected area examined or touched. Surgical removal of the affected tissue may be part of the treatment regimen in some cases.

**Treatment options**
- Cyclosporine – oral
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral
- Pimecrolimus – topical
- Sulfasalazine – oral
- Tacrolimus – topical

### CANINE SYMMETRICAL ONYCHODYSTROPHY

Symmetrical onychodystrophy is also known as symmetrical onychitis, symmetrical lupoid onychodystrophy, and symmetrical onychomadesis. The etiopathogenesis is currently unknown and German shepherd dogs, Norwegian Gordon setters, and English setters appear to be predisposed. Typically multiple or all nails present with sloughing of the plate (onychomadesis), fragmentation and horizontal detachment of the plate at the free edge (onychorrhexis), and separation of the plate from the bed (onycholysis). Serous-sanguineous to purulent exudate is often present, and the nails are typically very painful to the touch. Secondary bacterial infection and paronychia (inflammation of the nail fold) usually complicate this disorder. The first sign of response to therapy is pain/discomfort resolution. A newly formed nail plate is often misshapen and dry. Amputation of the third phalanx may be required in cases that do not respond to medical treatment.

**Treatment options**
- Essential fatty acids – oral
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone acetonide) – oral
- Tetracycline (or doxycycline) and niacinamide – oral

### FELINE EOSINOPHILIC GRANULOMA COMPLEX

Feline eosinophilic granuloma complex is not a disease entity per se, but it comprises a group of three skin reaction patterns including eosinophilic plaque, eosinophilic granuloma, and eosinophilic ulcer (synonyms: rodent ulcer, indolent ulcer). The pathogenesis is unknown, but some cases are associated with an allergic condition (food allergy, atopic dermatitis, flea allergy) or a genetic predisposition. Interestingly, bacterial infection appears to play a role in some cats, with antibiotic therapy completely resolving or significantly improving the condition. The eosinophilic plaque is characterized by an often eroded to ulcerated well-demarcated plaque, typically localized to the ventral abdomen and inner aspects of the thighs. The eosinophilic ulcer has an elevated border and often spans the upper lip, with variable severity. The eosinophilic granuloma has different clinical presentations but typically manifests as linear plaques that more often develop on the caudal aspects of the thighs but can also occur at other sites. Nodules or plaques (feet, tongue, ears, lip margin) or ill-defined swelling (chin and lower lip) are other clinical presentations of the eosinophilic granuloma. Some cats can have combination of various lesions. Pruritus can vary from absent to severe. Lesions can spontaneously resolve, recur, or become refractory to treatment. Identifying and controlling any underlying disease is an important part of the treatment regimen.

**Treatment options**
- Auranofin – oral
- Aurothiomalate sodium – injectable
- Chlorambucil – oral
- Cyclosporine – oral
- Doxycycline – oral
- Hydrocortisone aceponate – topical
- Glucocorticoids (dexamethasone, methylprednisolone, prednisolone, triamcinolone acetonide) – oral, injectable
- Interferon alpha, human recombinant – injectable
- Interferon omega, feline recombinant – injectable

### FELINE PSYCHOGENIC ALOPECIA

Feline psychogenic alopecia is an over-diagnosed compulsive disorder where the cat excessively grooms or pulls out the hair without inducing visible skin inflammation. The pathomechanism is not well understood, but it is believed to be triggered by environmental stressors and anxiety. The diagnosis should be based on a supportive history (e.g., moving, boarding, new cat or dog acquired, owner changed daily routine, etc.) and the exclusion of other causes of self-induced non-inflammatory alopecia such as surface demodicosis, food allergy, and atopic dermatitis. The alopecia has often a symmetrical pattern and develops on areas where the cat can easily reach such as the abdomen, groin, lumbo-

sacral area, and inner aspect of the legs. Owners may not always witness the cat's over-grooming behavior, but the presence of broken hairs at affected sites will support a presumptive diagnosis. Appropriate behavior modification is an important part of the treatment plan.

**Treatment options**

- Benzodiazepines (alprazolam, clonazepam, diazepam, lorazepam, oxazepam) – oral
- Selective serotonin reuptake inhibitors (SSRIs) (fluoxetine hydrochloride, paroxetine hydrochloride, sertraline hydrochloride) – oral
- Tricyclic antidepressants (amitriptyline hydrochloride, clomipramine hydrochloride, doxepin hydrochloride) – oral

# References

The authors performed an extensive veterinary and human literature search for elaboration of this book, including many scientific articles, proceedings, textbooks and formulary or drug books. Therefore, the references cited below are not all-inclusive, but they should serve the readers as a guideline. The references cited in the different sections of the book are listed below.

## General References


Allen DG, Dowling PM, Smith DA. *Handbook of Veterinary Drugs*, 3rd edn. Baltimore, MD and Philadelphia, PA: Lippincott Williams & Wilkins; 2005.

Gotthelf LN. *Small Animal Ear Diseases: An Illustrated Guide*, 2nd edn. St. Louis, MO: Elsevier Saunders; 2005.

Greene CE. *Infectious Diseases of the Dog and Cat*, 3rd edn. St. Louis, MO: Saunders; 2006.

Kerdel FA, Romanelli P, Trent JT. *Dermatologic Therapeutics: a Pocket Guide*. New York, NY: McGraw-Hill; 2005.

Papich MG. *Saunders Handbook of Veterinary Drugs*, 2nd edn. St. Louis, MO: Saunders; 2007.

Plumb D. *Plumb's Veterinary Drug Handbook*, 6th edn. Ames, IA: Blackwell; 2008.

Ramsey I. *British Small Animal Veterinary Association (BSAVA) Small Animal Formulary*, 6th edn. Replika Press Pvt, India; 2008.

Scott DW, Miller WH, Griffin CE. *Muller and Kirk's Small Animal Dermatology*, 6th edn. Philadelphia, PA: Saunders; 2001.


### ONLINE REFERENCES


Drug Information Online: www.drugs.com.

Thomson Reuters Micromedex: www.micromedex.com.

US National Library of Medicine (PubMed/Medline): www.ncbi.nlm.nih.gov/pubmed.

US Food and Drug Administration (FDA)/FDA Center for Veterinary Medicine: www.fda.gov/AnimalVeterinary/default.htm.

Veterinary Information Network: www.vin.com.

Wolters Kluwer Health Facts and Comparisons: www.factsandcomparisons.com.


## Section 1: Systemic Drugs

### ACITRETIN


Castillo V, Giacomini D, Paez-Pereda M, *et al*. Retinoic acid as a novel medical therapy for Cushing's disease in dogs. *Endocrinology* 147(9):4438–4444; 2006.



*Canine and Feline Dermatology Drug Handbook*, First Edition.
Sandra N. Koch, Sheila M.F. Torres and Donald C. Plumb.


Published 2012 by Blackwell Publishing Ltd.

### AMITRIPTYLINE HYDROCHLORIDE

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### CETIRIZINE HYDROCHLORIDE

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### CHLORPHENIRAMINE MALEATE

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### CIPROFLOXACIN

Abadia AR, Aramayona JJ, MJ Muñoz, *et al.* Ciprofloxacin pharmacokinetics in dogs following oral administration. *Journal of Veterinary Medicine* 42(8): 505–511; 1995.

Albarellos GA, Kreil VE, Landoni MF. Pharmacokinetics of ciprofloxacin after single intravenous and repeat oral administration to cats. *Journal of Veterinary Pharmacology and Therapeutics* 27:155–162; 2004.

### CLEMASTINE FUMARATE

Hansson H, Bergvall K, Bondesson U *et al.* Clinical pharmacology of clemastine in healthy dogs. *Veterinary Dermatology* 15:152–158.

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### CLINDAMYCIN HYDROCHLORIDE/PALMITATE

Scott DW, Beningo KE, Miller WH, Rothstein E. Efficacy of clindamycin hydrochloride capsules for the treatment of deep pyoderma due to *Staphylococcus intermedius* infection in dogs. *Canadian Veterinary Journal* 39(12):753–756; 1998.

### CLOMIPRAMINE HYDROCHLORIDE

Gulikers K, Panciera DL. Evaluation of the effects of clomipramine on canine thyroid function tests. *Journal of Veterinary Internal Medicine* 17(1):44–49; 2003.

Mertens PA, Torres S, Jessen C. Effects of clomipramine hydrochloride in cats with psychogenic alopecia: a prospective study. *Journal of the American Animal Hospital Association* 42(5):336–343; 2006.

### CYCLOSPORINE

Font A, Bardagi M, Mascort J, Fondevila D. Treatment with oral cyclosporin A of a case of vesicular cutaneous lupus erythematosus in a rough collie. *Veterinary Dermatology* 17(6):440–442; 2006.

Goldman C, Rosser E, Petersen A, Hauptman J. Investigation on the effects of ciclosporin (Atopica) on intradermal test reactivity and allergen-specific immunoglobulin (IgE) serology in atopic dogs. *Veterinary Dermatology* 21(4):393–399; 2010.

Irwin KE, Beale KM, Fadok VA. Comparison of modified cyclosporine to chlorambucil in the management of feline pemphigus foliaceus. *North American Veterinary Dermatology Forum Proceedings*: 200; 2011.

Kovalik M, Thoday KL, Handel IG, *et al*. Ciclosporin A therapy is associated with disturbances in glucose metabolism in dogs with atopic dermatitis. *Veterinary Dermatology* 22(2):173–180; 2011.

Mauldin EA, Morris DO, Brown DC, Casal ML. Exfoliative cutaneous lupus erythematosus in German shorthair pointer dogs: disease development, progression and evaluation of three immunomodulatory drugs (ciclosporin, hydroxychloroquine, and adalimumab) in a controlled environment. *Veterinary Dermatology* 21(4):373–382; 2010.

Paterson S. Successful therapy of sebaceous adenitis with topical cyclosporine in 20 dogs. *Veterinary Dermatology* 15(Suppl.1):64; 2004.

Rosenkrantz WS, Aniya JS. Cyclosporine, ketoconazole and azathioprine combination therapy in three cases of refractory canine pemphigus foliaceus. *North American Veterinary Dermatology Forum Proceedings*: 220; 2007.

Rosenkrantz WS, Griffin CE, Barr RJ. Clinical evaluation of cyclosporine in animal models with cutaneous immune-mediated disease and epitheliotropic lymphoma. *Journal of the American Animal Hospital Association* 25:377–384; 1989.

Santoro D, Campbell KL. Use of ciclosporin in a dog with canine juvenile sterile granulomatous dermatitis and lymphadenitis (letter to the editor). *Veterinary Dermatology* 22(3):287–288; 2011.

Thelen A, Mueller RS, Linek M. Influence of food intake on the clinical response to cyclosporine A in canine atopic dermatitis. *Veterinary Record* 159:854–856; 2006.

### CYPROHEPTADINE HYDROCHLORIDE

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### DEXAMETHASONE

Ployngam T, Tobias AH, Smith SA, Torres SM, Ross SJ. Hemodynamic effects of methylprednisolone acetate administration in cats. *American Journal of Veterinary Research* 67(4):583–587; 2006.

Smith SA, Tobias AH, Fine DM, Jacob KA, Ployngam T. Corticosteroid-associated congestive heart failure in 12 cats. *International Journal of Applied Research in Veterinary Medicine* 2(3):159–170; 2004.

### DIPHENHYDRAMINE HYDROCHLORIDE

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### FEXOFENADINE HYDROCHLORIDE

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### GRISEOFULVIN

Shibata K, Nagata M. Efficacy of griseofulvin for juvenile cellulitis in dogs. *Veterinary Dermatology* 15(Suppl.1):20–40; 2004.

### HYDROXYCHLOROQUINE SULFATE

Mauldin EA, Morris DO, Brown DC, Casal ML. Exfoliative cutaneous lupus erythematosus in German shorthair pointer dogs: disease development, progression and evaluation of three immunomodulatory drugs (ciclosporin, hydroxychloroquine, and adalimumab) in a controlled environment. *Veterinary Dermatology* 21(4):373–382; 2010.

Oberkirchner U, Linder K, Olivry T. Successful treatment of a novel variant of canine chronic cutaneous lupus erythematosus with oral hydroxychloroquine, topical tacrolimus and prednicarbate. *North American Veterinary Dermatology Forum Proceedings*: 235; 2011.

### HYDROXYZINE HYDROCHLORIDE/PALMOATE

Bizikova P, Papich MG, Olivry T. Hydroxyzine and cetirizine pharmacokinetics and pharmacodynamics after oral and intravenous administration of hydroxyzine to healthy dogs. *Veterinary Dermatology* 19(6):348–357; 2008.

Olivry T, DeBoer D, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010.

### INTERFERON ALPHA, RECOMBINANT HUMAN

Thompson LA, Grieshaber TL, Glickman L, Glickman N. Human recombinant interferon-alpha-2b for management of idiopathic recurrent superficial pyoderma in dogs: a pilot study. *Veterinary Therapeutics* 5(1):75–81; 2004.

Tzannes S, Ibarrola P, Batchelor DJ, Burrow RD, Blackwood L. Use of recombinant human interferon alpha-2a in the management of a dog with epitheliotropic lymphoma. *Journal of the American Animal Hospital Association* 44(5): 276–282; 2008.

### INTERFERON GAMMA, RECOMBINANT CANINE

Yasukawa K, Saito S, Kubo T, *et al*. Low-dose recombinant canine interferon-gamma for treatment of canine atopic dermatitis: An open randomized comparative trial of two doses. *Veterinary Dermatology* 21(1):42–49; 2010.

### INTERFERON OMEGA, RECOMBINANT FELINE

Carlotti DN, Boulet M, Ducret J, *et al*. The use of recombinant omega interferon therapy in canine atopic dermatitis: a double-blind controlled study. *Veterinary Dermatology* 20(5–6):405–411; 2009.

Gutzwiller MER, Brachelente C, Taglinger K, *et al*. Feline herpes dermatitis treated with interferon omega. *Veterinary Dermatology* 18(1):50–54; 2007.

### ISOTRETINOIN

Castillo V, Giacomini D, Paez-Pereda M, *et al*. Retinoic acid as a novel medical therapy for Cushing's disease in dogs. *Endocrinology* 147(9):4438–4444; 2006.

### ITRACONAZOLE

Bensignor E. Oral itraconazole as a pulse therapy for the treatment of canine *Malassezia* dermatitis: a randomized, blinded, comparative trial. *European Journal of Companion Animal Practice* 18(1):69–72; 2008 (reprint).

**KETOCONAZOLE**

Lien YH, Huang HP. Use of ketoconazole to treat dogs with pituitary-dependent hyperadrenocorticism: 48 cases (1994–2007). *Journal of the American Veterinary Medical Association* 233(12): 1896–1901; 2008.

**LEVOTHYROXINE SODIUM**

Traon GL, Brennan SF, Burgaud S, *et al*. Clinical evaluation of a novel liquid formulation of L-thyroxine for once daily treatment of dogs with hypothyroidism. *Journal of Veterinary Internal Medicine* 23(1):43–49; 2009.

**LOMUSTINE**

Cooper M, Tsai X, Bennett P. Combination CCNU and vinblastine chemotherapy for canine mast cell tumours 57 cases. *Veterinary and Comparative Oncology* 7(3):196–206; 2009.

Kristal O, Rassnick KM, Gliatto JM, *et al*. Hepatotoxicity associated with CCNU (lomustine) chemotherapy in dogs. *Journal of Veterinary Internal Medicine* 18(1):75–80; 2004.

Rassnick KM, Moore AS, Williams LE, *et al*. Treatment of canine mast cell tumors with CCNU (Lomustine). *Journal of Veterinary Internal Medicine* 13(6): 601–605; 1999.

Rassnick KM, Williams LE, Kristal O, *et al*. Lomustine for treatment of mast cell tumors in cats: 38 cases (1999–2005). *Journal of the American Veterinary Medical Association* 232(8):1200–1205; 2008.

Risbon RE, de Lorimier LP, Skorupski K, *et al*. Response of canine cutaneous epitheliotropic lymphoma to lomustine (CCNU): a retrospective study of 46 cases (1999–2004). *Journal of Veterinary Internal Medicine* 20(6):1389–1397; 2006.

Skorupski KA, Clifford CA, Paoloni MC, *et al*. CCNU for the treatment of dogs with histiocytic sarcoma. *Journal of Veterinary Internal Medicine* 21(1): 121–126; 2007.

Williams LE, Rassnick KM, Power HT, *et al*. CCNU in the treatment of canine epitheliotropic lymphoma. *Journal of Veterinary Internal Medicine* 20(1): 136–143; 2006.

Skorupski K. Prospective randomized clinical trial assessing the efficacy of Denamarin® for prevention of CCNU induced hepatopathy in tumor-bearing dogs. In: *Proceedings of the 30th Annual Conference of the Veterinary Cancer Society*. San Diego, CA: 75; 2010.

**LORATADINE**

Paradis M. Nonsteroidal antipruritic drugs in dogs and cats: an update. *Bulletin of the Canadian Academy of Veterinary Dermatology*: 3–7; 1996.

**LUFENURON ± MILBEMYCIN OXIME**

Ben-Ziony Y, Arzi B. Use of lufenuron for treating fungal infection of dogs and cats: 297 cases (1997–1999). *Journal of the American Veterinary Medical Association* 217(10):1510–1513; 2000.

**MASITINIB MESYLATE**

Cadot P, Hensel P, Bensignor E, *et al*. Masitinib decreases signs of canine atopic dermatitis: a multicentre, randomized, double-blind, placebo-controlled phase 3 trial. *Veterinary Dermatology* 22(6):554–564;2011.

Hahn KA, Oglivie TR, Devauchelle P et al. Masitinib is safe and effective for the treatment of canine mast cell tumors. *Journal of Veterinary Internal Medicine* 22(6):1301–1309; 2008.

### METHYLPREDNISOLONE/METHYLPREDNISOLONE ACETATE

Ployngam T, Tobias AH, Smith SA, Torres SM, Ross SJ. Hemodynamic effects of methylprednisolone acetate administration in cats. *American Journal of Veterinary Research* 67(4):583–587; 2006.

Smith SA, Tobias AH, Fine DM, Jacob KA, Ployngam T. Corticosteroid-associated congestive heart failure in 12 cats. *International Journal of Applied Research in Veterinary Medicine* 2(3):159–170; 2004.

### MILBEMYCIN OXIME

Mueller R. Treatment protocols for demodicosis: an evidence-based review. *Veterinary Dermatology* 15(2):75–89, 2004.

### MINOCYCLINE HYDROCHLORIDE

Jang SJ, Hirsh DC. Rapidly growing members of the genus mycobacterium affecting dogs and cats. *Journal of the American Animal Hospital Association* 38(3):217–220; 2002.

### MISOPROSTOL

Olivry T, Dunston SM, Rivierre C, *et al*. A randomized controlled trial of misoprostol monotherapy for canine atopic dermatitis: effects on dermal cellularity and cutaneous tumour necrosis factor-alpha. *Veterinary Dermatology* 14(1):37–46; 2003.

### MOXIDECTIN

Mueller R. Treatment protocols for demodicosis: an evidence-based review. *Veterinary Dermatology* 15(2):75–89; 2004.

Wagner R, Wendlberger U. Field efficacy of moxidectin in dogs and rabbits infested with *Sarcoptes* spp., *Demodex* spp. and *Psoroptes* spp mites. *Veterinary Parasitology* 93(2):149–158; 2000.

### MOXIFLOXACIN

Govendir M, Hansen T, Kimble B, *et al*. Susceptibility of rapidly growing mycobacteria isolated from cats and dogs to ciprofloxacin, enrofloxacin and moxifloxacin. *Veterinary Microbiology* 147(1–2):113–118; 2011.

### MYCOPHENOLATE MOFETIL

Byrn KP, Morris DO. Study to determine the usefulness of mycophenolate mofetil for the treatment of pemphigus foliaceus in dogs (abstract). *Veterinary Dermatology* 12(4):226; 2001.

### NALTREXONE HYDROCHLORIDE

Schwartz S. Naltrexone-induced pruritus in a dog with tail chasing behavior. *Journal of the American Veterinary Medical Association* 202(2):278–280; 1993.

White DS. Naltrexone for treatment of acral lick dermatitis. *Journal of the American Veterinary Medical Association* 196(7):1073–1076; 1990.

**PO7P**

Schmidt V, McEwan, Volk A, *et al*. The glucocorticoid sparing efficacy of Phytopica in the management of canine atopic dermatitis. *Veterinary Dermatology* 21(1):97–105; 2010.

**POSACONAZOLE**

McLellan GJ, Aquino SM, Mason DR, Kinyon JM, Myers RK. Use of posaconazole in the management of invasive orbital aspergillosis in a cat. *Journal of the American Animal Hospital Association* 42(4):302–307; 2006.

**PREDNISOLONE/PREDNISONE**

Ployngam T, Tobias AH, Smith SA, Torres SM, Ross SJ. Hemodynamic effects of methylprednisolone acetate administration in cats. *American Journal of Veterinary Research* 67(4):583–587; 2006.

Smith SA, Tobias AH, Fine DM, Jacob KA, Ployngam T. Corticosteroid-associated congestive heart failure in 12 cats. *International Journal of Applied Research in Veterinary Medicine* 2(3):159–170; 2004.

**PROPIONIBACTERIUM ACNES INJECTION**

Becker AM, Janik TA, Smith EK. *Propionibacterium acnes* immunotherapy in chronic recurrent canine pyoderma. *Journal of Veterinary Internal Medicine* 3(1):26–30; 1989.

**TEPOXALIN**

Horvath-Ungerboeck C, Thoday KL, Shaw DJ, van den Broek AH. Tepoxalin reduces pruritus and modified CADESI-01 scores in dogs with atopic dermatitis: a prospective, randomized, double-blinded, placebo-controlled, cross-over study. *Veterinary Dermatology* 20(4):233–242; 2009.

**TERBINAFINE HYDROCHLORIDE**

Foust AL, Marsella R, Akucewich LH, *et al*. Evaluation of persistence of terbinafine in the hair of normal cats after 14 days of daily therapy. *Veterinary Dermatology* 18(4):246–251; 2007.

Sakai MR, May ER, Imerman PM, *et al*. Terbinafine pharmacokinetics after single dose oral administration in the dog. *Veterinary Dermatology* 22(6):528–534; 2011.

**THYROTROPIN**

Boretti FS, Sieber-Ruckstuhl NS, Wenger-Riggenbach B, *et al*. Comparison of 2 doses of recombinant human thyrotropin for thyroid function testing in healthy and suspected hypothyroid dogs. *Journal of Veterinary Internal Medicine* 23(4):856–861; 2009.

**TICARCILLIN DISODIUM + CLAVULANATE POTASSIUM**

Nuttall TJ. Use of ticarcillin in the management of canine otitis externa complicated by *Pseudomonas aeruginosa*. *Journal of Small Animal Practice* 39(4):165–168; 1998.

**TRIAMCINOLONE ACETONIDE**

Ployngam T, Tobias AH, Smith SA, Torres SM, Ross SJ. Hemodynamic effects of methylprednisolone acetate administration in cats. *American Journal of Veterinary Research* 67(4):583–587; 2006.

Preziosi DE, Goldschmidt MH, Greek JS, *et al*. Feline pemphigus foliaceus: a retrospective analysis of 57 cases. *Veterinary Dermatology* 14(6):313–321; 2003.

Smith SA, Tobias AH, Fine DM, Jacob KA, Ployngam T. Corticosteroid-associated congestive heart failure in 12 cats. *International Journal of Applied Research in Veterinary Medicine* 2(3):159–170; 2004.

### TRILOSTANE

Cerundolo R, Lloyd DH, Persechino A, Evans H, Cauvin A. Treatment of canine alopecia X with trilostane. *Veterinary Dermatology* 15(5):285–293; 2004.

Cook AK, Bond KG. Evaluation of the use of baseline cortisol concentration as a monitoring tool for dogs receiving trilostane as a treatment for hyperadrenocorticism. *Journal of the American Veterinary Medical Association* 237(7):801–805; 2010.

Feldman EC. Evaluation of twice-daily lower-dose trilostane treatment administered orally in dogs with naturally occurring hyperadrenocorticism. *Journal of the American Veterinary Medical Association* 238(11):1441–1451; 2011.

Leone F, Cerundolo R, Vercelli A, Lloyd DH. The use of trilostane for the treatment of alopecia X in Alaskan malamutes. *Journal of the American Animal Hospital Association* 41(5):336–342; 2005.

### VITAMIN A

Lam ATH, Affolter VK, Outerbridge CA, Gericota B, White SD. Oral vitamin A as an adjunct treatment for canine sebaceous adenitis. *Veterinary Dermatology* 22(4):305–311; 2011.

## Section 2: Topical Agents

### HYDROCORTISONE ACEPONATE

Bizikova P, Linder KE, Paps J, Olivry T. Effect of a novel topical diester glucocorticoid spray on immediate- and late-phase cutaneous allergic reactions in Maltese-beagle atopic dogs: a placebo-controlled study. *Veterinary Dermatology* 21:71–80; 2010.

Bonneau S, Skowronski V, Sanquer A, Maynard L, Eun HM. Therapeutic efficacy of topical hydrocortisone aceponate in experimental flea allergy in dogs. *Australian Veterinary Journal* 87(7):287–291; 2009.

Bryden SL, Burrows AK, Rème CA, Kelman M. Efficacy of a 0.0584% hydrocortisone aceponate spray (Cortavance) for the management of pedal pruritus in atopic dogs: a pilot study. *Veterinary Dermatology* 19(Suppl.1):40–41; 2008.

Nuttall T, Mueller R, Bensignor E, *et al*. Efficacy of a 0.0584% hydrocortisone aceponate spray in the management of canine atopic dermatitis: a randomised, double blind, placebo-controlled trial. *Veterinary Dermatology* 20(3):191–198; 2009.

Nuttall TJ, McEwan NA, Bensignor E *et al*. Comparable efficacy of a topical 0.0584% hydrocortisone aceponate spray and oral cyclosporine in treating canine atopic dermatitis. *Veterinary Dermatology*; 2011; doi: 10.1111/j.1365-3164.2011.00992.x

Rème CA, Dufour P. Effects of repeated topical application of 0.0584% hydrocortisone aceponate spray on skin thickness in beagle dogs. *The International Journal of Applied Research in Veterinary Medicine* 8(1):1–6; 2010.

Schmidt V, Buckley LM, McEwan NA, Rème CA, Nuttall TJ. Efficacy of a 0.0584% hydrocortisone aceponate spray in presumed feline allergic dermatitis: an open labeled pilot study. *Veterinary Dermatology* 2011; doi: 10.1111/j.1365-3164.2011.00993.x

**ENILCONAZOLE**

Hnilica KA, Medleau L. Evaluation of topically applied enilconazole for the treatment of dermatophytosis in a Persian cattery. *Veterinary Dermatology* 13(1):23–28; 2002.

**PIMECROLIMUS/TACROLIMUS**

Marsella R, Nicklin CF, Saglio S, Lopez J. Investigation on the effects of topical therapy with 0.1% tacrolimus ointment (Protopic®) on intradermal skin test reactivity in atopic dogs. *Veterinary Dermatology* 15(4):218–224; 2004.

**AMITRAZ**

Saari SAM, Juuti KH, Palojarvi JH, *et al. Demodex gatoi*-associated contagious pruritic dermatosis in cats: a report from six households in Finland. *Acta Veterinaria Scandinavica* 51:40–48; 2009.

**FIPRONIL ± (S)-METHOPRENE**

Chadwick AJ. Use of a 0.25 per cent fipronil pump spray formulation to treat canine cheyletiellosis. *Journal of Small Animal Practice* 38:261–262; 1997.

Curtis CF. Use of 0.25 per cent fipronil spray to treat sarcoptic mange in a litter of five-week-old puppies. *Veterinary Record* 139(2):43–44; 1996.

Koutinas AF, Saridomichelakis MN, Soubasis N, Bornstein S, Koutinas CK. Treatment of sarcoptic mange with fipronil spray: a field trial. *Australian Veterinary Practitioner* 31(3):115–119; 2001.

Nuttall TJ, French AT, Cheetham HC, Proctor FJ. Treatment of Trombicula autumnalis infestation in dogs and cats with a 0.25 per cent fipronil pump spray. *Journal of Small Animal Practice* 39(5): 237–239; 1998.

**IMIDACLOPRID COMBINATIONS**

Paterson TE, Halliwell RE, Fields PF, *et al*. Treatment of canine generalized demodicosis: a blind, randomized clinical trial comparing the efficacy of Advocate (Bayer Animal Health) with ivermectin. *Veterinary Dermatology* 20:447–455; 2009.

**OTOTOXICITY**

Barlow DW, Duckert LG, Kreig CS, Gates GA. Ototoxicity of topical otomicrobial agents. *Acta Otolaryngol* 115(2):231–235; 1995.

Brown RD, Penny JE, Henley CM, *et al*. Ototoxic drugs and noise. *Ciba Foundation Symposium* 85: 151–171; 1981.

Brummett RE, Harris RF, Lindgren JA. Detection of ototoxicity from drugs applied topically to the middle ear space. *Laryngoscope* 86(8):1177–1187; 1976.

Cole LK, Kwochka KW, Kowalski JJ, Hillier A. Microbial flora and antimicrobial susceptibility patterns of isolated pathogens from the horizontal ear canal and middle ear in dogs with otitis. *Journal of the American Veterinary Medical Association* 212(4):534–538; 1998.

Gotthelf LN. Ototoxicity. In: *Small Animal Ear Diseases: An Illustrated Guide*, 2nd edn. St. Louis, MO: Elsevier Saunders, 329–337; 2005.

Huizing EH, de Groot JCMJ. Human cochlear pathology in aminoglycoside ototoxicity: a review. *Acta Otolaryngologica Supplementum* 436:117–125; 1987.
Igarashi Y, Oka Y. Vestibular ototoxicity following intratympanic applications of chlorhexidine gluconate in the cat. *Archives of Otorhinolaringology* 245(4):210–217; 1988.
Igarashi Y, Suzuki J. Cochlear ototoxicity of chlorhexidine gluconate in cats. *Archives of Otorhinolaringology* 242(2):167–176; 1985.
Leake PA, Hradek GT. Cochlear pathology of long term neomycin induced deafness in cats. *Hearing Research* 33(1):11–33; 1988.
Mansfield PD, Steiss JE, Boosinger TR, Marshall AE. The effect of four commercial ceruminolytic agents on the middle ear. *Journal of the American Animal Hospital Association* 33(6):479–486; 1997.
Merchant SR, Neer TM, Tedford BL, *et al*. Ototoxicity assessment of a chlorhexidine otic preparation in dogs. *Progress in Veterinary Neurology* 4(3): 72–75; 1995.
Morizono T, Johnstone BM. Ototoxicity of chloramphenicol ear drops with propylene glycol as solvent. *Medical Journal of Autralia* 2(16):634–638; 1975.
Nuttall TJ, Paterson S. Topical and systemic antimicrobial therapy for ear infections. *Advances in Veterinary Dermatology* (workshop) 6:402–407; 2008.
Paterson S. Ototoxicity. *World Congress of Veterinary Dermatology Proceedings*: 227–230; 2008.
Perez R, Freeman S, Sohmer H, Sichel JY. Vestibular and cochlear ototoxicity of topical antiseptics assessed evoked potentials. *Laryngoscope* 110(9): 1522–1527; 2000.
Rybak LP, Krishna S. Chloramphenicol, colymycin, and polymyxin. In: Roland PS, Rutka JA, eds., *Ototoxicity*. Hamilton, ON: Decker, 128–133; 2004.
Strain GM, Merchant SR, Neer TM, Tedford BL. Ototoxicity assessment of a gentamicin sulfate otic preparation in dogs. *American Journal of Veterinary Research* 56(4):532–538; 1995.
Vassalli L, Harris DM, Gradini R, Applebaum EL. Propylene glycol-induced cholesteatoma in chinchilla middle ears. *American Journal of Otolaringology* 9(4): 180–188; 1988.
Weidong Qi, Dalian D, Salvi RJ. Cytotoxic effects of dimethyl sulphoxide (DMSO) on cohlear organotypic cultures. *Hearing Research* 236(1–2):52–60; 2008.

## Section 3: Allergen-Specific Immunotherapy

Bousquet J, Lockey R, Malling HJ, *et al*. Allergen immunotherapy: therapeutic vaccines for allergic diseases. World Health Organization. *American Academy of Allergy, Asthma and Immunology* 81(5:1):401–405; 1998.
Colombo S, Hill PB, Shaw DJ, Thoday KL. Effectiveness of low dose immunotherapy in the treatment of canine atopic dermatitis: a prospective double-blinded, clinical study. *Veterinary Dermatology* 16(3):162–170; 2005.
DeBoer DJ, Verbrugge M, Morris M. Pilot trial of sublingual immunotherapy (SLIT) in mite-sensitive atopic dogs. *Veterinary Dermatology* 21(3):325; 2010a.
DeBoer DJ, Verbrugge M, Morris M. Changes in mite-specific IgE and IgG during sublingual immunotherapy (SLIT) in dust mite-sensitive dogs with atopic dermatitis. *Veterinary Dermatology* 21(5):531–532; 2010b.

Esch RE. Allergen immunotherapy: what can and cannot be mixed? *Journal of Allergy and Clinical Immunology* 122:659–660; 2008.

Foster AP, Jackson HA, Stedman K, *et al*. Serological responses to house dust mite antigens in atopic dogs while receiving allergen-specific immunotherapy. *Veterinary Dermatology* 13:216; 2002.

Fraser MA, McNeil PE, Gettinby G. Examination of serum total IgG1 concentration in atopic and non-atopic dogs. *Journal of Small Animal Practice* 45(4): 186–190; 2004.

Goldman C, Rosser E, Petersen A, Hauptman J. Investigation on the effects of ciclosporin (Atopica) on intradermal test reactivity and allergen-specific immunoglobulin (IgE) serology in atopic dogs. *Veterinary Dermatology* 21(4): 393–399; 2010.

Griffin CE, Hillier A. The ACVD task force on canine atopic dermatitis (XXIV): allergen-specific immunotherapy Veterinary Immunology and Immunopathology 81(3–4):363–383; 2001.

Hites MJ, Kleinbeck ML, Loker JL, Lee KW. Effect of immunotherapy on the serum concentrations of allergen-specific IgG antibodies in dog sera. *Veterinary Immunology and Immunopathology* 22(1):39–51; 1989.

Keppel KE, Campbell KL, Zuckermann FA, *et al*. Quantification of canine regulatory T cell populations, serum interleukin-10 and allergen-specific IgE concentrations in healthy control dogs and canine atopic dermatitis patients receiving allergen-specific immunotherapy. *Veterinary Immunology and Immunopathology* 123(3–4):337–344; 2008.

Kunkle GA. The treatment of canine atopic disease. In: Kirk RW, ed., *Current Veterinary Therapy VII*, Philadelphia, PA: Saunders, 453–458; 1980.

Loewenstein C, Muller RS. A review of allergen-specific immunotherapy in human and veterinary medicine. *Veterinary Dermatology* 20(2):84–98, 2009.

Marsella R. Tolerability and clinical efficacy of oral immunotherapy with house dust mites in a model of canine atopic dermatitis: a pilot study. *Veterinary Dermatology* 21(6):566–571; 2010.

Mueller RS, Bettenay S. Long-term immunotherapy of 146 dogs with atopic dermatitis: a retrospective study. *Australian Veterinary Practitioner* 26:126–132; 1996.

Mueller RS, Bettenay SV. Evaluation of the safety of an abbreviated course of injections of allergen extracts (rush immunotherapy) for the treatment of dogs with atopic dermatitis. *American Journal of Veterinary Research* 62(3): 307–310; 2001.

Mueller RS, Fieseler KV, Zabel S, *et al*. Conventional and rush allergen-specific immunotherapy in the treatment of canine atopic dermatitis. *Advances in Veterinary Dermatology* 5:60–69; 2004.

Nuttall TJ. A retrospective survey on hyposensitization therapy. *Advances in Veterinary Dermatology* 3:507–508; 1998.

Olivry T, Foster AP, Muller RS, *et al*. Interventions for atopic dermatitis in dogs: a systematic review of controlled randomized trials. *Veterinary Dermatology* 21(1):4–22; 2010a.

Olivry T, DeBoer DJ, Favrot C, *et al*. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from The International Task Force on Canine Atopic Dermatitis. *Veterinary Dermatology* 21(3):233–248; 2010b.

Reinero CR, Byerly JR, Nishifuji K, *et al*. Rush immunotherapy in an experimental model of feline allergic asthma. *Veterinary Immunology and Immunopathology* 110(1–2):141–153; 2006.

Rosenbaum MR, Esch RE, Schwartzman RM. Effects of mold proteases on the biological activity of allergenic pollen extracts. *American Journal of Veterinary Research* 57(10):1447–1452; 1996.

Schnabl B, Bettenay SV, Dow K, Mueller RS. Results of allergen-specific immunotherapy in 117 dogs with atopic dermatitis. *Veterinary Record* 158(3):81–85; 2006.

Scott DW. Observations on canine atopy. *Journal of the American Animal Hospital Association* 17(1):91–100; 1981.

Scott DW, Miller WH, Griffin CE. Skin immune system and allergic skin diseases. In: *Muller and Kirk's Small Animal Dermatology*, 6th edn. Philadelphia, PA: Saunders, 574–608; 2001.

Shida M, Kadoya M, Park SJ, *et al*. Allergen-specific immunotherapy induces Th1 shift in dogs with atopic dermatitis. *Veterinary Immunology and Immunopathology* 102(1–2):19–31; 2004.

Trimmer AM, Griffin CE, Boord MJ *et al*. Rush allergen specific immunotherapy in feline atopic dermatitis: a pilot study of four cats. *Veterinary Dermatology* 16(5):324–329; 2005.

Walton Angorano D, MacDonald JM. Immunotherapy in canine atopy. In: Kirk RW, Bonagura JD, eds., *Current Veterinary Therapy XI*. Philadelphia, PA: Saunders, 505–508; 1991.

# Index



*Canine and Feline Dermatology Drug Handbook*, First Edition.
Sandra N. Koch, Sheila M.F. Torres and Donald C. Plumb.

Published 2012 by Blackwell Publishing Ltd.