■ **BIRDS:**

a) As an antipruritic and to suppress ovulation: 0.025–1 mL (3 mg/100 grams body weight) IM once every 4–6 weeks. May cause obesity, fatty liver, polydipsia/polyuria and lethargy if used repeatedly. (Clubb 1986)

Monitoring

- Weight
- Blood glucose (draw baseline before therapy)
- Mammary gland development
- Adrenocortical function
- Efficacy

Chemistry/Synonyms

A synthetic progestin, medroxyprogesterone acetate (MPA) occurs as an odorless, white to off-white, crystalline powder. It is insoluble in water and sparingly soluble in alcohol. It has a melting range of 200°–210°C.

Medroxyprogesterone acetate may also be known as: MPA, MAP, acetoxymethylprogesterone, medroxyprogesteroni acetas, methylacetoxyprogesterone, metipregnone, and NSC-26386; many trade names are available.

Storage/Stability

Medroxyprogesterone acetate suspensions for injection should be stored at room temperature (15–30°C); avoid freezing and temperatures above 40°C. MPA tablets should be stored in well-closed containers at room temperature.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Medroxyprogesterone Acetate Tablets (scored): 2.5 mg, 5 mg & 10 mg; *Provera*® (Pharmacia & Upjohn); generic; (Rx)

Medroxyprogesterone Acetate Injection: 104 mg (160 mg/mL) in 0.65 mL prefilled syringes & 1 mL vials; 150 mg/mL in 1 mL; 400 mg/mL in 2.5 mL and 10 mL vials and 1 mL U-ject; *Depo-Sub Q Provera 104*® (Pfizer); *Depo-Provera*® (Pharmacia); (Rx)

MEGESTROL ACETATE

(me-***jess***-trole) Ovaban®, Megace®

PROGESTIN

Prescriber Highlights

- **Synthetic progestin used in DOGS (FEMALE): for postponement of estrus & the alleviation of false pregnancy; DOGS (MALE): benign prostatic hypertrophy. CATS: Many dermatologic & behavior-related conditions**
- **Contraindications: Pregnant animals or with uterine disease, diabetes mellitus, or mammary neoplasias; should not be used treat bitches with pseudo-pregnancy; females should not be treated during diestrus, or with uterine hemorrhage**
- **Caution: Thrombophlebitis**
- **Adverse Effects: CATS: Profound adrenocortical suppression, adrenal atrophy, transient diabetes mellitus, polydipsia/polyuria, personality changes, increased weight, endometritis, cystic endometrial hyperplasia, mammary hypertrophy, neoplasias, & hepatotoxicity possible. DOGS: Increased appetite & weight gain, lethargy, change in behavior or hair color, mucometra, endometritis, cystic endometrial hyperplasia, mammary enlargement & neoplasia, acromegaly, adrenocortical suppression, or lactation (rare)**

Uses/Indications

Megestrol acetate (*Ovaban*®—Schering) is approved by FDA for use in dogs only for the postponement of estrus and the alleviation of false pregnancy. In male dogs, it has been used for benign prostatic hypertrophy. It is used clinically for many dermatologic and behavior-related conditions, primarily in the cat. See the Dosage section for specific indications and dosages for both dogs and cats.

Megestrol acetate is indicated in humans for the palliative treatment of advanced carcinoma of the breast or endometrium.

Pharmacology/Actions

Megestrol acetate possesses the pharmacologic actions expected of the other progestationals discussed (*e.g.*, medroxyprogesterone acetate). It has significant anti-estrogen and glucocorticoid activity (with resultant adrenal suppression). It does not have anabolic or masculinizing effects on the developing fetus.

Pharmacokinetics

Megestrol acetate is well absorbed from the GI tract and appears to be metabolized completely in the liver to conjugates and free steroids.

The half-life of megestrol acetate is reported to be 8 days in the dog.

Contraindications/Precautions/Warnings

Megestrol acetate is contraindicated in pregnant animals or in animals with uterine disease, diabetes mellitus, or mammary neoplasias. It has been recommended that MA not be used in dogs prior to their first estrous cycle or for anestrus therapy in dogs with abnormal cycles. The manufacturer (Schering) recommends that mating be prevented should estrus occur within 30 days of cessation of MA therapy.

This agent should not be used during pregnancy or to treat bitches with pseudo-pregnancy. Females should not be treated during diestrus, or with uterine hemorrhage. Do not use in females with prolonged heat unless cystic ovarian disease is confirmed and surgery or GNRH or hCG are not viable options. Animals with diabetes should not receive megestrol.

Because this drug can suppress adrenal function, exogenous steroids may need to be administered if the patient is stressed (*e.g.*, surgery, trauma).

For estrus control, the manufacturer recommends that drug must be given for the full treatment regimen to be effective. The package insert states that "*Ovaban*® should not be given for more than two consecutive treatments," but the reasons for this are unclear; some theriogenologists question the need for this precaution.

In humans, megestrol acetate is to be used with caution in patients with thrombophlebitis and is contraindicated as a test for pregnancy.

Adverse Effects

In cats, megestrol acetate can induce a profound adrenocortical suppression, adrenal atrophy, and an iatrogenic "Addison's" syndrome can develop at "standard" dosages (2.5–5 mg every other day) within 1–2 weeks. Once the drug has been discontinued, serum cortisol levels (both resting and ACTH-stimulated) will return to normal levels within a few weeks. Clinical signs of adrenocortical insufficiency (*e.g.*, vomiting, lethargy) are uncommon, but exogenous steroid support should be considered if the animal is stressed (surgery, trauma, etc.). Cats may develop a transient diabetes mellitus while receiving MA. Polydipsia/polyuria, personality changes, increased weight, endometritis, cystic endometrial hyperplasia, mammary hypertrophy and neoplasias may also occur. Increased appetite and weight gain is not consistently seen, but MA is occasionally used as an appetite stimulant. Rarely, megestrol acetate can cause hepatotoxicity (increased alkaline phosphatase) in cats.

Limited clinical studies have suggested that megestrol acetate may cause less cystic endometrial hyperplasia than other progestational agents, but cautious use and vigilant monitoring is still warranted.

In dogs, increased appetite and weight gain, lethargy, change in behavior or hair color, mucometra, endometritis, cystic endometrial hyperplasia, mammary enlargement and neoplasia, acromegaly, adrenocortical suppression or lactation (rare) may occur. One dog reportedly developed diabetes mellitus after use.

Reproductive/Nursing Safety

No effects were noted in either the bitch or litter when pregnant dogs received 0.25 mg/kg/day for 32 days during the first half of pregnancy; reduced litter sizes and puppy survival were detected when the dose was given during the last half of pregnancy. Fetal hypospadias are possible if progestational agents are administered during pregnancy.

During the *first 4 months of pregnancy* in humans, the FDA categorizes this drug as category ***X*** for use during pregnancy (*Studies in animals or humans demonstrate fetal abnormalities or adverse reaction; reports indicate evidence of fetal risk. The risk of use in pregnant women clearly outweighs any possible benefit.*) During *the last 5 months* of pregnancy in humans, the FDA categorizes this drug as category ***D*** for use during pregnancy (*There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.*)

Detectable amounts of progestins enter the milk of mothers receiving these agents. Effects on nursing infants have not been established.

Overdosage/Acute Toxicity

No information was located regarding acute overdosage of megestrol acetate. In humans, dosages of up to 800 mg/day caused no observable adverse reactions.

Toxicity studies performed in dogs at dosages of 0.1–0.25 mg/kg/day PO for 36 months yielded no gross abnormalities in the study population. Histologically, cystic endometrial hyperplasia was noted at 36 months, but resolved when therapy was discontinued. At dosages of 0.5 mg/kg/day PO for 5 months, a reversible uterine hyperplasia was seen in treated dogs. Dosages of 2 mg/kg/day demonstrated early cystic endometritis in biopsies done on dogs at 64 days.

Drug Interactions

- **CORTICOSTEROIDS**: Megestrol used with corticosteroids (long-term) may exacerbate adrenocortical suppression and diabetes mellitus.
- **RIFAMPIN**: May decrease progestin activity if administered concomitantly. This is presumably due to microsomal enzyme induction with resultant increase in progestin metabolism. The clinical significance of this potential interaction is unknown.

Doses

- **DOGS:**

For estrus control:

a) To halt cycle in proestrus: 2.2 mg/kg once daily for 8 days starting during the first 3 days of proestrus. While the timing of the next cycle is variable, it may be prolonged with 2.2 mg/kg/day for 4 days, then 0.55 mg/kg/day for 16–20 days.

To postpone an anticipated cycle**:** 0.55 mg/kg/day for 32 days, beginning at least 7 days prior to proestrus (Burke 1985)

b) For suppression during proestrus (first 3 days): 2.2 mg/kg once daily for 8 days (92% efficacy). Bitch must be controlled until behavioral signs of estrus disappear. If mating occurs during first 3 days of therapy, stop treatment and consider mismating therapy. There is an increased likelihood of pyometra developing if progestins are used concomitantly with estrogens. If mating occurs after 3 or more days of therapy continue at a dosage rate of 3–4 mg/kg PO.

To delay an anticipated heat during anestrus: 0.55 mg/kg PO for 32 days initiated 7 days prior to proestrus. Recommend doing vaginal cytology prior to therapy. If no erythrocytes are seen, initiate therapy if cycle time frame is appropriate. If erythrocytes are seen, delay therapy until proestrus therapy can be instituted. Do not repeat therapy more often than once every 6 months. (Woody 1988)

c) 2 mg/kg (or less) administered for ≤2 weeks in proestrus, or ≤2 mg/kg administered for a longer duration in anestrus. A typical dose for estrus suppression is 2 mg/kg PO once daily for 8 consecutive days, while a typical dose for temporary postponement is 0.5 mg/kg PO once daily in late anestrus. (Romagnoli 2002b), (Romagnoli 2006a)

For benign prostatic hypertrophy:

a) 0.5 mg/kg PO daily for 4–8 weeks (Root Kustritz and Klausner 2000)

b) 0.55 mg/kg PO daily (Purswell 1999)

c) 0.1–0.5 mg/kg per day for 3–8 weeks; best used to maintain breeding potential for short time prior to castration; use with caution. (Lane 2006b)

For pseudocyesis (false pregnancy):

a) 0.5 mg/kg PO once daily for 8 days (Barton and Wolf 1988)

To prevent vaginal hyperplasia development:

a) 2.2 mg/kg PO for 7 days early in proestrus (Wykes 1986)

For treatment of severe galactorrhea:
a) 0.55 mg/kg PO once daily for 7 days (Olson and Olson 1986)

For behavior disorders:
a) For adjunctive treatment of aggressive or unacceptable masculine behavior: 1.1–2.2 mg/kg PO once daily for 2 weeks, then 0.5–1.1 mg/kg once daily for 2 weeks. Should be used with behavior modification. (Voith and Marder 1988a)

■ **CATS:**

For suppression of estrus:
a) In anestrus: 5 mg/cat PO every 2 weeks or 2.5 mg/cat per week (better if divided into 2 doses given every 3.5 days); In proestrus: 5 mg/cat per day for 4 days, then 5 mg PO every 2 weeks. (Romagnoli 2006a)
b) If in behavioral estrus, signs may be inhibited by giving 5 mg/day PO until estrus stops (generally within 3–5 days), then 2.5–5 mg PO once weekly for 10 weeks

   Postponement of estrus (if started during diestrus): 2.5 mg PO daily for 8 weeks

   Postponement of estrus (if started during anestrus): 2.5 mg PO once weekly for up to 18 months. Recommend allowing cat to have a cycle (unmedicated) before beginning another treatment cycle. (Woody 1988)
c) If started in diestrus: 2.5 mg per day PO for up to 2 months

   If started in anestrus: 2.5 mg per week for up to 18 months

   For prevention of estrus: 5 mg daily PO for 3 days as soon as behavioral signs of estrus are seen; next estrus period will occur in approximately 4 weeks (Romatowski 1989) (information from package insert; *Ovarid*®—Glaxovet)

For treatment of idiopathic feline miliary dermatitis:
a) 2.5–5 mg once every other day, followed by weekly maintenance dosages. May be necessary to treat for animal's lifetime. Reserve use for severe cases; explain risks to owner and do not exceed 2.5 mg per week during maintenance phase. (Kwochka 1986)

As appetite stimulant:
a) 0.25–0.5 mg/kg q24h for 3–5 days, then q48–72h (Smith 2003a)

As an alternative treatment for immune-mediated skin diseases:
a) 2.5–5 mg PO once daily for 10 days, then every other day (Giger and Werner 1988)

For adjunctive therapy of eosinophilic granulomas:
a) 0.5 mg/kg PO once daily for 2 weeks, then twice weekly as needed (Coppoc 1988)

For eosinophilic ulcers:
a) Alone or in combination with methylprednisolone acetate (*Depo-Medrol*®): 5–10 mg PO every other day for 10–14 doses, then every 2 weeks as needed (DeNovo, Potter, and Woolfson 1988)

For eosinophilic keratitis (feline proliferative keratitis):
a) 0.5 mg/kg PO daily until a response is noted, then reduce dose to 1.25 mg PO 2–3 times weekly as required (Nelson 1986)

For feline plasma cell gingivitis:
a) 2.5 mg PO once daily for 10 days, then once every other day for 5 treatments, then as needed (Morgan 1988)

As a secondary therapy (thyroid hormone replacement first choice) for treatment of feline endocrine alopecia (FEA):
a) 5 mg PO every second to third day initially, then 2.5 mg PO once to twice weekly (Thoday 1986)

For feline psychogenic alopecia and dermatitis:
a) 2.5–5 mg every other day initially, then taper to the lowest maintenance dosage possible, given weekly as needed (Walton 1986)

For adjunctive therapy (with urine acidification, increased urine crystalloid solubility, and antispasmodics if required) for persistent hematuria and urethritis in a non-obstructed cat:
a) 2.5–5 mg PO once daily to every other day (with prednisone: 2.5–5 mg PO daily) (Lage, Polzin, and Zenoble 1988)

For urine marking, intraspecies aggression, anxiety:
a) 2 mg/kg/day for 5 days, then 1 mg/kg/day for 5 days, then 0.5 mg/kg/day for 5 days (Romatowski 1989) (information from package inserts; *Ovarid*®—Glaxovet)
b) To reduce marking in neutered male cats when all other drugs have been unsuccessful: megestrol acetate at 2.5–10 mg (total dose) per cat PO once daily for one week, then reduce to once or twice weekly. (Landsberg 2007)

Monitoring

- Weight
- Blood glucose (draw baseline before therapy)
- Mammary gland development and appearance
- Adrenocortical function
- Liver enzymes if long-term treatment
- Efficacy

Client Information

- The client should fully understand the potential risks of therapy (see Adverse Effects above) before starting therapy and should report changes in mammary glands or other signs associated with adverse reactions (*e.g.*, PU/PD, extreme lethargy, behavior changes, etc.) to the veterinarian.

Chemistry/Synonyms

A synthetic progestin, megestrol acetate (MA) occurs as an essentially odorless, tasteless, white to creamy white, crystalline powder that is insoluble in water, sparingly soluble in alcohol, and slightly soluble in fixed oils. It has a melting range of 213°–219°C over a 3° range and a specific rotation of +8° to +12°.

Megestrol acetate may also be known as: BDH-1298, compound 5071, megestroli acetas, NSC-71423, SC-10363, *Acestrol*®, *Borea*®, *Endace*®, *Gynodal*®, *Maygace*®, *Megace*®, *Megastrol*®, *Megefren*®, *Megestat*®, *Megestil*®, *Megestin*®, *Megostat*®, *Meltonar*®, *Meprogest*®, *Mestrel*®, *Nia*®, *Niagestin*®, *Niagestine*®, *Ovaban*®, *Prazoken*®, and *Varigestrol*®.

Storage/Stability

Megestrol acetate tablets should be stored in well-closed containers at a temperature of less than 40°C. The tablets may be crushed and administered with food. The veterinary manufacturer recommends storing the tablets from 2°–30°C (36°–86°F).

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Megestrol Acetate Oral Tablets: 5 mg, 20 mg; available in bottles of 250 and 500 tablets, and in 30 foil strips of 8 and packaged in cartons of 240 tablets; *Ovaban*® (Schering-Plough); (Rx). Approved for use in dogs only.

HUMAN-LABELED PRODUCTS:

Megestrol Acetate Tablets: 20 mg & 40 mg; *Megace*® (Bristol-Meyers Oncology); generic; (Rx)

Megestrol Acetate Suspension: 40 mg/mL in 240 mL; 125 mg/mL in 150 mL; *Megace*® (Bristol-Meyers Oncology); *Megace ES*® (Par Pharmaceutical Inc); (Rx)

MEGLUMINE ANTIMONIATE

(***meg***-loo-meen an-tih-***mohne***-ee-ate)
Glucantime®, Gulcantim®

PENTAVALENT ANTIMONY ANTILEISHMANIAL

Prescriber Highlights

- Pentavalent antimony compound used for treating leishmaniasis (with or without allopurinol) in dogs
- Not available in USA
- Extreme caution (relatively contraindicated) in patients with cardiac, hepatic or renal insufficiency
- Primary adverse effects noted in dogs with meglumine antimoniate are injection site reactions, lethargy & gastrointestinal effects (inappetance, vomiting)
- Treatment is prolonged & cost may be substantial

Uses/Indications
Meglumine antimoniate is used alone or in combination with allopurinol to treat leishmaniasis in dogs. It is available commercially in some Mediterranean and South American countries but not in the USA.

Pharmacology/Actions
Pentavalent antimony compounds such as meglumine antimoniate and sodium stibogluconate selectively inhibit the leishmanial enzymes required for glycolytic and fatty acid oxidation. Pentavalent antimony compounds rarely are successful in eradicating *Leishmania* organisms completely in infected dogs.

Pharmacokinetics
After subcutaneous or intramuscular injections in dogs systemic bioavailability is about 92%; highest tissue concentrations are found in the liver, spleen, and skin. Within 9 hours of dosing, 80% of the antimony is excreted in the urine.

Contraindications/Precautions/Warnings
Patients with renal, hepatic or cardiac failure are more likely to develop serious adverse effects with this agent; weigh the potential risks versus benefits carefully before treating. Hypersensitivity reactions have been reported in people, and any patient with previous hypersensitivity to meglumine antimoniate should not receive the drug.

Adverse Effects
Primary adverse effects noted in dogs are injection site reactions, lethargy, and gastrointestinal effects (inappetance, vomiting). Transient increases in liver enzymes have been reported.

In humans, increased serum lipase, amylase, creatinine, urea nitrogen, and increased QT interval on ECG, have been reported. Occasionally, decreases in white blood cell counts and hemoglobin have been reported in humans.

Reproductive/Nursing Safety
There is limited information available. Pregnant rats given up to 300 mg/kg on days 6–15 caused increased fetal resorptions and increased rates of abnormalities of the atlas bone. Weigh the risks versus benefits when deciding to treat during pregnancy. It is unknown if the drug enters maternal milk.

Overdosage/Acute Toxicity
No specific overdose information was located. Depending on the dosage, a single overdose could potentially cause renal, hepatic, pancreatic, and hematologic effects, but gastrointestinal effects (vomiting) and lethargy would be the most likely outcomes. It is recommended to observe the patient and contact an animal poison control center for further guidance with an overdose situation.

Drug Interactions
The following drug interactions have either been reported or are theoretical in humans or animals receiving meglumine antimoniate and may be of significance in veterinary patients (dogs):

- **AGENTS THAT CAN PROLONG QT INTERVAL** (*e.g.*, **tricyclic antidepressants, disopyramide, quinidine, procainamide**, etc.): meglumine antimoniate may prolong QT interval further with increased risk for arrhythmias

Laboratory Considerations
No specific laboratory interactions or considerations noted

Doses
- **DOGS:**

For leishmaniasis:

a) Meglumine antimoniate at a minimum dosage of 100 mg/kg SC daily for 3–4 weeks; better results are obtained with longer durations (4–6 weeks) of treatment. Protocol with allopurinol may reduce relapse rates: meglumine antimoniate as above with allopurinol at 20–40 mg/kg PO daily for a minimum of 3 weeks. Followed with long-term treatment with allopurinol (alone) at 20–40 mg/kg PO daily or intermittently (one week treatment per month). (Noli and Auxilia 2005)

b) Meglumine antimoniate (100 mg/kg/day SC) until resolution; with allopurinol at 20 mg/kg PO q12h for 9 months. (Brosey 2005)

Monitoring
- Efficacy (PCR preferred)
- CBC (baseline and periodic)
- Liver enzymes; renal function tests (serum creatinine, BUN); serum lipase and amylase (baseline and periodic)
- Urinalysis (baseline and periodic)

Client Information
- Clients should understand that treatment with this drug can be prolonged and expensive, and that a "cure" (complete eradication) is unlikely

Chemistry/Synonyms
Meglumine antimoniate is 1-Deoxy-1-methylamino-D-glucitol antimoniate. It has a molecular weight of 366. One gram contains approximately 272 mg of antimony.

Meglumine antimoniate may also be known as: meglumine antimonate, N-methylglucamine antimoniate, RP-2168, antimony meglumine, Protostib, 1-Deoxy-1-methylamino-D-glucitol antimoniate, *Glucantime*® and *Glucantim*®.

Storage/Stability
Unless otherwise specified by the manufacturer, commercially available ampules should be stored below 40°C, preferably between 15°–30°C; protect from freezing.