withdrawal (at labeled doses) = 21 days (cattle), a withdrawal period has not been established for pre-ruminating calves. Not for use in calves intended to be processed for veal.

Sulfadimethoxine Soluble Powder: 94.6 g/packet (for addition to drinking water); *Albon*® (Pfizer), *Di-Methox*® *Soluble Powder* (AgriLabs), generic; (AgriPharm, Aspen, Durvet, Phoenix Scientific, Vedco), *Sulfasol*® (Med-Pharmex); (OTC) Approved for use in dairy calves, dairy heifers, beef cattle, broiler and replacement chickens only, and meat-producing turkeys. Slaughter withdrawal (at labeled doses) = 7 days (cattle); 5 days (poultry—do not use in chickens over 16 weeks old or in turkeys over 24 weeks old).

Sulfadimethoxine 12.5% Concentrated Solution (for addition to drinking water): *Albon*® (Pfizer), *Amtech*® generic; (Phoenix Scientific), *Di-Methox*® *12.5% Oral Solution* (AgriLabs), *SDM*® *Solution* (Phoenix Pharmaceutical), generic; (AgriPharm, Aspen, Butler, Durvet, Vedco), *Sulforal*® (Med-Pharmex); (OTC). Approved for use in chickens, turkeys and cattle. Slaughter withdrawal (at labeled doses) = 7 days (for dairy calves, dairy heifers and beef cattle only. Withdrawal for pre-ruminating calves has not been established) Not to be used in calves to be processed for veal; 5 days (poultry—do not use in chickens over 16 weeks old or in turkeys over 24 weeks old).

HUMAN-LABELED PRODUCTS: None

SULFADIMETHOXINE/ ORMETOPRIM

(or-me-*toe*-prim) Primor®

POTENTIATED SULFONAMIDE ANTIMICROBIAL

Prescriber Highlights

- Potentiated sulfa similar to trimethoprim/sulfa. The following apply to TMP/Sulfa & may correlate to this agent as well:
- Contraindications: Hypersensitive to sulfas, thiazides, or sulfonylurea agents; severe renal or hepatic impairment
- Caution: Diminished renal or hepatic function, or urinary obstruction or urolithiasis
- Adverse Effects: DOGS: Keratoconjunctivitis sicca, hypersensitivity (type 1 or type 3) acute neutrophilic hepatitis with icterus, vomiting, anorexia, diarrhea, fever, hemolytic anemia, urticaria, polyarthritis, facial swelling, polydipsia, crystalluria, hematuria, polyuria, cholestasis, hypothyroidism, anemias, agranulocytosis, idiosyncratic hepatic necrosis in dogs. CATS: Anorexia, crystalluria, hematuria, leukopenias & anemias
- Potentially teratogenic, weigh risk vs. benefit

Uses/Indications

Sulfadimethoxine/ormetoprim is approved for the treatment of skin and soft tissue infections in dogs caused by susceptible strains of *Staphylococcus aureus* and *E. coli*.

Pharmacology/Actions

Sulfadimethoxine/ormetoprim shares mechanisms of action and probably the bacterial spectrum of activity with trimethoprim/sulfa. Alone, sulfonamides are bacteriostatic agents, but in combination with either ormetoprim or trimethoprim, the potentiated sulfas are bactericidal. Potentiated sulfas sequentially inhibit enzymes in the folic acid pathway, thereby inhibiting bacterial thymidine synthesis. The sulfonamide blocks the conversion of para-aminobenzoic acid (PABA) to dihydrofolic acid (DFA) and ormetoprim blocks the conversion of DFA to tetrahydrofolic acid by inhibiting dihydrofolate reductase.

The potentiated sulfas have a fairly broad spectrum of activity. Gram-positive bacteria that are generally susceptible include most streptococci, many strains of staphylococcus, and Nocardia. Many gram-negative organisms of the family Enterobacteriaceae are susceptible to the potentiated sulfas, but not *Pseudomonas aeruginosa*. Some protozoa (*Pneumocystis carinii*, Coccidia and Toxoplasma) are also inhibited by the combination. Potentiated sulfas reportedly have little activity against most anaerobes, but opinions on this vary.

Resistance will develop more slowly to the combination of drugs, than to either one alone. In gram-negative organisms, resistance is usually plasmid-mediated.

Pharmacokinetics

The pharmacokinetics of sulfadimethoxine are outlined in the previous monograph. Pharmacokinetic data for ormetoprim is not available at the time of this writing, but the manufacturer states that therapeutic levels are maintained over 24 hours at recommended doses.

Contraindications/Precautions/Warnings

The manufacturer states that ormetoprim/sulfadimethoxine should not be used in dogs showing marked liver parenchymal damage, blood dyscrasias, or in those with a history of sulfonamide sensitivity.

This combination should be used with caution in patients with pre-existing hepatic or thyroid disease.

Adverse Effects

This combination would be expected to exhibit an adverse reaction profile in dogs similar to that seen with trimethoprim/sulfa, including: keratoconjunctivitis sicca (which may be irreversible), acute neutrophilic hepatitis with icterus, vomiting, anorexia, diarrhea, fever, hemolytic anemia, urticaria, polyarthritis, facial swelling, polydipsia, polyuria, and cholestasis. Acute hypersensitivity reactions manifesting as Type I, (anaphylaxis) or Type III reaction (serum sickness) can also be seen. Hypersensitivity reactions appear to be more common in large breed dogs; Doberman Pinschers may possibly be more susceptible to this effect than other breeds. Other hematologic effects (anemias, agranulocytosis) are possible, but fairly rare.

Long-term (8 weeks) therapy at recommended doses with ormetoprim/sulfadimethoxine (27.5 mg/kg once daily) resulted in elevated serum cholesterol, thyroid and liver weights, mild follicular thyroid hyperplasia, and enlarged basophilic cells in the pituitary. The manufacturer states that the principal treatment-related effect of extended or excessive usage is hypothyroidism.

Reproductive/Nursing Safety

Safety of ormetoprim/sulfadimethoxine has not been established in pregnant animals. Reports of teratogenicity (cleft palate) have been reported in some lab animals with trimethoprim/sulfa.

Overdosage/Acute Toxicity

In experimental studies in dogs, doses greater than 80 mg/kg resulted in slight tremors and increased motor activity in some dogs. Higher doses may result in depression, anorexia, or seizures.

It is suggested that very high oral overdoses be handled by emptying the gut using standard precautions and protocols and by treating clinical signs supportively and symptomatically.

Drug Interactions; Laboratory Considerations
None have been noted for this combination, but it would be expected that the potential interactions outlined for the trimethoprim/sulfa monograph would also apply to this combination; refer to that monograph for more information.

Doses
- **DOGS:**

For susceptible infections:

a) Initially 55 mg/kg (combined drug) PO on the first day of therapy, then 27.5 mg/kg PO once daily for at least 2 days after remission of clinical signs. Not approved for treatment longer than 21 days. (Package insert; *Primor*®—Pfizer)

Monitoring
- Clinical efficacy
- Adverse effects

Client Information
- Animals must be allowed free access to water and must not become dehydrated while on therapy.

Chemistry/Synonyms
A diaminopyrimidine structurally related to trimethoprim, ormetoprim occurs as a white, almost tasteless powder. The chemistry of sulfadimethoxine is described in the previous monograph.

Sulfadimethoxine may also be known as: solfadimetossina, solfadimetossipirimidina, sulphadimethoxine, *Chemiosalfa®, Deltin®, Risulpir®, Ritarsulfa®, Sulfadren®, Sulfastop®,* or *Sulfathox®.*

Ormetoprim may also be known as NSC-95072, ormetoprima, ormétoprime, ormetoprimum, or Ro-5-9754.

Storage/Stability
Unless otherwise instructed by the manufacturer, store tablets in tight, light resistant containers at room temperature.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS:

Sulfadimethoxine/Ormetoprim Tablets (scored)

120's: 100 mg Sulfadimethoxine, 20 mg Ormetoprim

240's: 200 mg Sulfadimethoxine, 40 mg Ormetoprim

600's: 500 mg Sulfadimethoxine, 100 mg Ormetoprim

1200's: 1000 mg Sulfadimethoxine, 200 mg Ormetoprim; *Primor®* (Pfizer); (Rx) Approved for use in dogs.

Sulfadimethoxine/Ormetoprim medicated premix: 113.5 g sulfadimethoxine and 68.1 g ormetoprim per pound in 50 lb bags. Approved for use in chickens [broilers, replacements (breeders and layers)], turkeys, ducks, & Chukar partridges. Slaughter withdrawal (at labeled doses) = 5 days. Do not feed to chickens over 16 weeks or age, turkeys or ducks producing eggs for food. *Rofenaid® 40* (Alpharma), *Romet® 30* (Alpharma)—Approved for use in salmonids (trout and salmon) and catfish. Slaughter or release as stocker fish = 42 days. (OTC)

HUMAN-LABELED PRODUCTS: None

SULFASALAZINE

(sul-fa-***sal***-a-zeen) Azulfidine®

SULFONAMIDE/SALICYLATE ANTIBACTERIAL/ IMMUNOSUPPRESSIVE

Prescriber Highlights
- Sulfa-analog that has GI antibacterial & antiinflammatory activity used for inflammatory bowel disease; has also been used for vasculitis
- Contraindications: Hypersensitivity to it, sulfas or salicylates; intestinal or urinary obstructions
- Caution: Liver, renal or hematologic diseases; cats
- Adverse Effects: DOGS: Keratoconjunctivitis sicca, anorexia, vomiting, cholestatic jaundice, hemolytic anemia, leukopenia, vomiting, decreased sperm counts & an allergic dermatitis. CATS: Anorexia, vomiting, anemias

Uses/Indications
Sulfasalazine is used for the treatment of inflammatory bowel disease in dogs and cats. It has also been suggested for adjunctive use in treating vasculitis in dogs.

Pharmacology/Actions
While the exact mechanism of action for its therapeutic effects in treating colitis in small animals has not been determined, it is believed that after sulfasalazine is cleaved into sulfapyridine and 5-aminosalicylic acid (5-ASA, mesalamine) by bacteria in the gut the antibacterial (sulfapyridine) and/or antiinflammatory (mesalamine) activity alters the clinical signs/course of the disease. Levels of both drugs in the colon are higher then by giving them orally as separate agents.

Pharmacokinetics
Only about 10–33% of an orally administered dose of sulfasalazine is absorbed. Apparently, some of this absorbed drug is then excreted unchanged in the bile. Unabsorbed and biliary excreted drug is cleaved into 5-ASA and sulfapyridine in the colon by bacterial flora. The sulfapyridine component is rapidly absorbed, but only a small percentage of the 5-ASA is absorbed.

Absorbed sulfapyridine and 5-ASA are hepatically metabolized and then renally excreted.

Contraindications/Precautions/Warnings
Sulfasalazine is contraindicated in animals hypersensitive to it, sulfonamides or salicylates. It is also contraindicated in patients with intestinal or urinary obstructions. It should be used with caution in animals with preexisting liver, renal or hematologic diseases. Because cats can be sensitive to salicylates (see the aspirin monograph), use caution when using this drug in this species.

Adverse Effects
Although adverse effects do occur in dogs, with keratoconjunctivitis sicca (KCS) reported most frequently, they are considered to occur relatively uncommonly. Other potential adverse effects include anorexia, vomiting, cholestatic jaundice, hemolytic anemia, leukopenia, vomiting, decreased sperm counts and an allergic dermatitis. Should decreased tear production be noted early, either reducing the dose or discontinuing the drug may prevent progression of KCS or increase tear production.