SULFONAMIDES (Veterinary—Systemic)

This monograph includes information on the following:
Sulfachlorpyridazine†, Sulfadimethoxine, Sulfamerazine, Sulfamethazine, Sulfanilamide*, Sulfaquinoxaline, Sulfathiazole*.

Some commonly used *brand names* are:
For veterinary-labeled products—

Albon Boluses [Sulfadimethoxine]
Albon 12.5% Concentrated Solution [Sulfadimethoxine]
Albon Oral Suspension 5% [Sulfadimethoxine]
Albon SR [Sulfadimethoxine]
Albon Tablets [Sulfadimethoxine]
Calfspan [Sulfamethazine]
Di-Methox Injection-40% [Sulfadimethoxine]
Di-Methox 12.5% Oral Solution [Sulfadimethoxine]
Di-Methox Soluble Powder [Sulfadimethoxine]
Poultry Sulfa [Sulfamerazine, Sulfamethazine and Sulfaquinoxaline]
Powder 21 [Sulfamethazine and Sulfathiazole]
S-125 [Sulfadimethoxine]
S-250 [Sulfadimethoxine]
SDM Injection [Sulfadimethoxine]
SDM Solution [Sulfadimethoxine]
S-M-T [Sulfamethazine and Sulfathiazole]
SMZ-Med 454 [Sulfamethazine]
Sulfadived 12.5% Oral Solution [Sulfadimethoxine]
SulfaMed-G [Sulfadimethoxine]
Sulfa-MT [Sulfamethazine and Sulfathiazole]
Sulfasol [Sulfadimethoxine]
Sulforal [Sulfadimethoxine]
Sulmet Drinking Water Solution 12.5% [Sulfamethazine]
Sulmet Oblets [Sulfamethazine]
Sulmet Soluble Powder [Sulfamethazine]
Suprasulfa III Calf Bolus [Sulfamethazine]
Suprasulfa III Cattle Bolus [Sulfamethazine]
Sustain III [Sulfamethazine]
Sustain III Calf Bolus [Sulfamethazine]
Sustain III Cattle Bolus [Sulfamethazine]
Triple Sulfa Bolus [Sulfamethazine, Sulfanilamide, and Sulfathiazole]
Vetisulid Injection [Sulfachlorpyridazine]
Vetisulid Powder [Sulfachlorpyridazine]

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

*Not commercially available in the U.S. †Not commercially available in Canada.

Category: Antibacterial (systemic); antiprotozoal.

Indications

Note: The text between [EL-US] and [EL] describes uses that are not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling. The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

General considerations

Sulfonamides are broad-spectrum antimicrobials inhibiting both gram-positive and gram-negative bacteria, as well as some protozoa, such as coccidia.{R-17; 18} They are considered ineffective against most obligate anaerobes and should not be used to treat serious anaerobic infections.{R-86; 90; 93} However, they may affect aerobic organisms that contribute to the lowered oxygen tension in the microenvironment and, as such, they may be useful in certain diseases involving *Fusobacteria*, although the organism itself is often resistant. The activity of sulfonamides is very sensitive to environment, and this limitation affects the activity of sulfonamides in particular fluids and tissues, such as purulent material, as well as the ability of laboratories to standardize minimum inhibitory concentrations (MIC) of sulfonamides necessary *in vivo* to inhibit specific cultured bacteria.{R-17}

Resistance of animal pathogens to sulfonamides is widespread as a result of more than 50 years of therapeutic use{R-17; 19} and this limits their effectiveness; however, sulfonamides are still widely used in combination with other medications, as in the case of the potentiated sulfonamides. They are also utilized in herd management of disease and some individual animal applications. Cross-resistance between sulfonamides is considered complete.{R-17}

Accepted

Coccidiosis (treatment)—Resistance to sulfonamides by coccidia has been reported in several species, including cattle, chickens,{R-22} and sheep.{R-106} It also should be noted that sulfonamides aid in reducing the number of oocysts shed, but they may not alter the clinical course of a susceptible coccidial infection.{R-106}

[EL-CAN]*Calves* and *cattle*[EL]: Sulfamethazine extended-release boluses are indicated in the treatment of *Eimeria bovis* and *Eimeria zuernii*.{R-11} Sulfaquinoxaline is indicated in the control and treatment of susceptible *E. bovis* and *E. zuernii*.{R-14}

Chickens: [EL-CAN]Sulfadimethoxine oral solution and powder for oral solution[EL] are indicated in the treatment of outbreaks of coccidiosis caused by susceptible coccidia.{R-2; 4} Sulfamethazine oral solution; [EL-CAN]sulfamethazine powder for oral solution[EL]; and [EL-CAN]sulfamerazine, sulfamethazine, and sulfaquinoxaline combination powder for oral solution[EL] are indicated in the control of susceptible *Eimeria necatrix* and *Eimeria tenella*.{R-9; 12; 109} Sulfaquinoxaline is indicated in the control of outbreaks of coccidiosis caused by susceptible *Eimeria acervulina, Eimeria brunetti, Eimeria maxima, E. necatrix,* and *E. tenella*.{R-14}

Dogs: Sulfadimethoxine oral suspension and tablets are indicated in the treatment of enteritis associated with coccidiosis caused by susceptible organisms.{R-3; 6}

Turkeys: [EL-CAN]Sulfadimethoxine oral solution and powder for oral solution[EL] are indicated in the treatment of outbreaks of coccidiosis caused by susceptible coccidia.{R-2; 4} Sulfamethazine oral solution; [EL-CAN]sulfamethazine powder for oral solution[EL]; and [EL-CAN]sulfamerazine, sulfamethazine, and sulfaquinoxaline combination powder for oral solution[EL] are indicated in the control of susceptible *Eimeria adenoeides* and *Eimeria meleagrimitis*.{R-9; 12; 109} Sulfaquinoxaline is indicated in the control of outbreaks of susceptible *E. adenoeides* and *E. meleagrimitis*.{R-14}

Coryza, infectious (treatment)—*Chickens:* [EL-CAN]Sulfadimethoxine oral solution and powder for oral solution[EL] are indicated in the treatment of outbreaks of infectious coryza caused by susceptible *Haemophilus gallinarum*.{R-2; 4} Sulfamethazine oral solution and [EL-CAN]powder for oral solution[EL] are indicated in the control of

infectious coryza caused by susceptible *H. gallinarum*.{R-9; 12}

Cystitis, bacterial (treatment)—*Cats* and *dogs:* Sulfadimethoxine [EL CAN]oral suspension[EL] and tablets are indicated in the treatment of cystitis caused by susceptible organisms; however, the potentiated sulfonamides and other antimicrobials have generally replaced sulfonamides administered alone.{R-3; 6}

Diphtheria (treatment)—*Cattle:* Sulfonamides are not directly effective against most obligate anaerobes, but may affect aerobic organisms that create the microenvironment in which *Fusobacteria* thrive; therefore, sulfonamides may be useful in the treatment of diphtheria but are not recommended in advanced or serious infections.{R-86; 90; 93} [EL CAN]Sulfadimethoxine boluses, extended-release boluses, injection, oral solution, and powder for oral solution[EL]; and sulfamethazine boluses, extended-release boluses, oral solution, and [EL CAN]powder for oral solution[EL] are indicated in the treatment of calf diphtheria caused by susceptible *Fusobacterium necrophorum*.{R-1-5; 7; 9; 10; 12; 13} [EL US]Sulfamethazine, sulfanilamide, and sulfathiazole combination is indicated as an aid in the treatment of diphtheria in calves.[EL]{R-97}

Enteritis, bacterial (treatment)—The primary treatment for enteritis in many cases, including those involving colibacillosis in calves, is aggressive fluid replacement. Treatment of enteritis with antimicrobials should rely on a specific diagnosis and knowledge of pathogen susceptibility.

- [EL CAN]*Calves*, less than 1 month of age[EL]: Sulfachlorpyridazine injection and powder for oral solution are indicated in the treatment of diarrhea caused or complicated by *Escherichia coli*.{R-89}
- *Calves* and *cattle:* Sulfamethazine boluses, extended-release boluses, oral solution, and [EL CAN]powder for oral solution[EL]; and [EL US]sulfamethazine and sulfathiazole combination[EL] are indicated in the treatment of enteritis (colibacillosis, scours) caused by susceptible *E. coli*.{R-7; 9; 10; 12; 13; 15}
- *Dogs:* Sulfadimethoxine boluses and [EL CAN]oral suspension[EL] are indicated in the treatment of enteritis caused by susceptible *Salmonella* species.{R-3; 6}
- *Foals:* Sulfamethazine boluses are indicated in the treatment of enteritis caused by susceptible *E. coli*.{R-13}
- *Pigs:* [EL CAN]Sulfachlorpyridazine powder for oral solution[EL], and sulfamethazine oral solution and [EL CAN]powder for oral solution[EL] are indicated in the treatment of enteritis caused by susceptible *E. coli*.{R-9; 12; 89} [EL US]Sulfamethazine and sulfathiazole combination is indicated to aid in the treatment of enteritis.[EL]{R-15}
- [EL US]*Sheep*[EL]: Sulfamethazine oral solution is indicated in the treatment of enteritis caused by susceptible organisms.{R-16}

Fowl cholera (treatment)—

- *Chickens:* [EL CAN]Sulfadimethoxine oral solution and powder for oral solution[EL] are indicated in the treatment of acute fowl cholera caused by susceptible *Pasteurella multocida*.{R-2; 4} Sulfamethazine oral solution and [EL CAN]powder for oral solution; sulfamerazine, sulfamethazine, and sulfaquinoxaline combination powder for oral solution[EL]; and sulfaquinoxaline oral solution are indicated in the control of acute fowl cholera caused by susceptible *P. multocida*.{R-9; 12; 14; 109}
- *Turkeys:* [EL CAN]Sulfadimethoxine oral solution and powder for oral solution[EL] are indicated in the treatment of acute fowl cholera caused by susceptible *P. multocida*.{R-2; 4} [EL CAN]Sulfamerazine, sulfamethazine, and sulfaquinoxaline combination powder for oral solution[EL]; and sulfaquinoxaline oral solution are indicated in the control of acute fowl cholera caused by susceptible *P. multocida*.{R-14; 109}

Fowl typhoid (treatment)—*Chickens* and *turkeys:* Sulfaquinoxaline oral solution is indicated in the control of acute fowl typhoid caused by susceptible *Salmonella gallinarum*.{R-14}

Pneumonia, bacterial (treatment)—

- *Calves:* Sulfamethazine boluses and extended-release boluses are indicated in the treatment of pneumonia and bovine respiratory disease complex caused by susceptible *Pasteurella* species.{R-7; 11; 13} However, *in vitro* studies have shown high levels of resistance to sulfamethazine by *Mannheimia (Pasteurella) haemolytica* and *P. multocida;*{R-23} therefore, sulfamethazine generally has been replaced by antimicrobials known to be effective against the specific pathogens involved.
- *Cats* and *dogs:* Sulfadimethoxine [EL CAN]oral suspension[EL] and tablets are indicated in the treatment of bacterial pneumonia caused by susceptible organisms;{R-3; 6} however, sulfadimethoxine generally has been replaced by antimicrobials known to be effective against the specific pathogens involved.
- *Cattle:* Sulfamethazine extended-release boluses, oral solution, and [EL CAN]powder for oral solution[EL]; [EL CAN]sulfadimethoxine boluses, extended-release boluses, injection, oral solution, and powder for oral solution[EL]; and [EL US]sulfamethazine and sulfathiazole combination[EL] are indicated in the treatment of bacterial pneumonia and bovine respiratory disease complex caused by susceptible organisms.{R-1-5; 9; 10; 12; 15; 96} [EL US]Sulfamethazine, sulfanilamide, and sulfathiazole combination is indicated as an aid in the treatment of pneumonia.[EL]{R-97} However, *in vitro* studies have shown high levels of resistance to sulfamethazine by *M. haemolytica* and *P. multocida*,{R-23} and the sulfonamides generally have been replaced by antimicrobials known to be effective against the specific pathogens involved.
- *Foals:* Sulfamethazine boluses are indicated in the treatment of pneumonia caused by susceptible *Pasteurella* species; however, sulfamethazine generally has been replaced by antimicrobials known to be effective against the specific pathogens involved.{R-13}
- *Pigs:* Sulfamethazine oral solution and [EL CAN]powder for oral solution[EL] are indicated in the treatment of pneumonia caused by susceptible organisms;{R-9; 12} however, sulfamethazine generally has been replaced by antimicrobials known to be effective against the specific pathogens involved.

Pododermatitis, necrotic (treatment)—*Cattle:* Sulfonamides are not directly effective against most obligate anaerobes,{R-86; 90; 93} but may affect aerobic organisms that create the microenvironment in which *Fusobacteria* thrive; therefore, they may be useful in the treatment of pododermatitis but are not recommended in advanced or serious infections. [EL CAN]Sulfadimethoxine boluses, extended-release boluses[EL], injection, oral solution, and powder for oral solution; and sulfamethazine extended-release boluses, oral solution, and [EL CAN]powder for oral solution[EL] are indicated in the treatment of pododermatitis caused by susceptible *Fusobacterium necrophorum*.{R-1-5; 9; 10; 12} [EL US]Sulfamethazine and sulfathiazole combination and sulfamethazine, sulfanilamide, and sulfathiazole combination are indicated as aids in the treatment of necrotic pododermatitis caused by susceptible *F. necrophorum*.[EL]{R-15; 96; 97}

Pullorum disease (treatment)—*Chickens:* Sulfamethazine oral solution and [EL CAN]powder for oral solution[EL] are indicated in the control of susceptible *Salmonella pullorum*.{R-9; 12}

Respiratory infections, bacterial (treatment)—

- *Cats* and *dogs:* Sulfadimethoxine oral suspension and tablets are indicated in the treatment of respiratory infections, such as bronchitis, caused by susceptible organisms.{R-3; 6}
- [EL US]*Pigs*[EL]: Sulfamethazine and sulfathiazole combination is indicated as an aid in the treatment of respiratory infections caused by susceptible organisms.{R-15}
- [EL US]*Sheep*[EL]: Sulfamethazine oral solution is indicated in the treatment of acute respiratory infections caused by susceptible organisms.{R-16}

Skin and soft tissue infections (treatment)—*Cats* and *dogs:* Sulfadimethoxine [EL CAN]oral suspension[EL] and tablets are indicated in the treatment of skin and soft tissue infections;{R-3; 6} however, sulfonamides are not effective in infections associated with purulent debris, such as abscesses.

Potentially effective

Note: The following indications continue to be included on product labeling, but have not been classified as *Accepted* by the USP

Expert Veterinary Medicine Information Committee:

Cats, *cattle*, *dogs*, and *sheep:* Although product labeling in the U.S. and Canada includes the use of sulfonamides in the treatment of *metritis* in cats, dogs, and cattle, and *pyometra* in cats and dogs, and Canadian labeling also includes the treatment of metritis in sheep, the efficacy of these uses is not established based on current knowledge.{R-3; 6; 9; 10; 15; 16; 97} Sulfonamides are poorly distributed into the uterus and their activity may be decreased in the presence of purulent debris; sulfonamides rarely are recommended in the treatment of metritis.{R-103}

Cattle and *sheep:* Although product labeling in the U.S. and Canada for cattle and, in Canada, for sheep includes use of sulfonamides in the treatment of *mastitis*, the efficacy of this use is not established, based on current knowledge.{R-12; 15; 16} Many sulfonamides, including most of those labeled for treatment of mastitis, are poorly distributed into milk. Considering also the high incidence of pathogen resistance reported, sulfonamides rarely are recommended in the treatment of mastitis.{R-103}

Horses: Although product labeling in the U.S. and Canada includes the use of sulfonamides in the treatment of *equine strangles* (*Streptococcus equi* infection), the efficacy of this use is not established based on current knowledge.{R-13; 16} The activity of sulfonamides may be decreased in the presence of purulent debris; therefore, they rarely are recommended in the treatment of strangles.{R-103; 107}

Regulatory Considerations

U.S.—

Federal law prohibits the extra-label use of sulfonamides in lactating dairy cattle (21 CFR 530.41).{R-104}

Withdrawal times have been established for sulfachlorpyridazine; sulfadimethoxine; sulfamethazine; sulfaquinoxaline; and sulfamerazine, sulfamethazine, and sulfaquinoxaline combination. See the *Dosage Forms* section.

Canada—

Withdrawal times have been established for sulfamethazine; sulfamethazine and sulfathiazole combination; and sulfamethazine, sulfanilamide, and sulfathiazole combination. See the *Dosage Forms* section.

Chemistry

Chemical name:

Sulfachlorpyridazine—N^1-(6-Chloro-3-pyridazinyl)sulfanilamide.{R-36}

Sulfadimethoxine—Benzenesulfonamide, 4-amino-*N*-(2,6-dimethoxy-4-pyrimidinyl)-.{R-36}

Sulfamerazine—Benzenesulfonamide, 4-amino-*N*-(4-methyl-2-pyrimidinyl)-.{R-36}

Sulfamethazine—Benzenesulfonamide, 4-amino-*N*-(4,6-dimethyl-2-pyrimidinyl)-.{R-36}

Sulfanilamide—*p*-Aminobenzenesulfonamide.{R-36}

Sulfaquinoxaline—N^1-2-Quinoxalinylsulfanilamide.{R-36}

Sulfathiazole—Benzenesulfonamide, 4-amino-*N*-2-thiazolyl-.{R-36}

Molecular formula:

Sulfachlorpyridazine—$C_{10}H_9ClN_4O_2S$.{R-36}

Sulfadimethoxine—$C_{12}H_{14}N_4O_4S$.{R-36}

Sulfamerazine—$C_{11}H_{12}N_4O_2S$.{R-36}

Sulfamethazine—$C_{12}H_{14}N_4O_2S$.{R-36}

Sulfanilamide—$C_6H_8N_2O_2S$.{R-36}

Sulfaquinoxaline—$C_{14}H_{12}N_4O_2S$.{R-36}

Sulfathiazole—$C_9H_9N_3O_2S_2$.{R-36}

Molecular weight:

Sulfachlorpyridazine—284.72.{R-36}

Sulfadimethoxine—310.33.{R-36}

Sulfamerazine—264.30.{R-36}

Sulfamethazine—278.33.{R-36}

Sulfanilamide—172.20.{R-36}

Sulfaquinoxaline—300.34.{R-36}

Sulfathiazole—255.32.{R-36}

Description:

Sulfadimethoxine USP—Practically white, crystalline powder.{R-56}

Sulfamethazine USP—White to yellowish white powder, which may darken on exposure to light. Practically odorless.{R-56}

Sulfanilamide—White, odorless, crystalline powder.{R-98}

Sulfaquinoxaline—Yellow, odorless powder.{R-94}

Sulfathiazole USP—Fine, white or faintly yellowish white, practically odorless powder.{R-56}

pKa:

Sulfadimethoxine—6.15.{R-33; 35}

Sulfamethazine—2.65, 7.4.{R-19}

Sulfanilamide—10.5.{R-19; 35}

Sulfaquinoxaline—5.5.{R-19; 46}

Sulfathiazole—7.1.{R-19}

Solubility:

Sulfadimethoxine USP—Soluble in 2 *N* sodium hydroxide; sparingly soluble in 2 *N* hydrochloric acid; slightly soluble in alcohol, in ether, in chloroform, and in hexane; practically insoluble in water.{R-56}

Sulfamethazine USP—Very slightly soluble in water and in ether; soluble in acetone; slightly soluble in alcohol.{R-56}

Sulfanilamide—Slightly soluble in water, in alcohol, in acetone, in glycerin, in propylene glycol, in hydrochloric acid, and in solutions of potassium and sodium hydroxide; practically insoluble in chloroform, in ether, and in petroleum ether.{R-98}

Sulfaquinoxaline—Practically insoluble in water; very slightly soluble in alcohol; practically insoluble in ether; freely soluble in aqueous solutions of alkalis.{R-94}

Sulfathiazole USP—Very slightly soluble in water; soluble in acetone, in dilute mineral acids, in solutions of alkali hydroxides, and in 6 *N* ammonium hydroxide; slightly soluble in alcohol.{R-56}

Pharmacology/Pharmacokinetics

Note: Unless otherwise noted, pharmacokinetic values are based on a single intravenous administration of medication.

Mechanism of action: Bacteriostatic. Sulfonamides interfere with the biosynthesis of folic acid in bacterial cells; they compete with para-aminobenzoic acid (PABA) for incorporation in the folic acid molecule. By replacing the PABA molecule and preventing the folic acid formation required for DNA synthesis, the sulfonamides prevent multiplication of the bacterial cell. Only organisms that synthesize their own folic acid are susceptible; mammalian cells use preformed folic acid and, therefore, are not susceptible. Cells that produce excess PABA or environments with PABA, such as necrotic tissues, allow for resistance by competition with the sulfonamide.{R-17; 18}

Absorption: Most sulfonamides are well absorbed orally with the exception of the enteric sulfonamides, such as sulfaquinoxaline, which are minimally absorbed.{R-19} Delays in absorption may occur in adult ruminants or when sulfonamides are administered with food to monogastric animals.{R-17; 20}

Bioavailability: Oral—Sulfadimethoxine:

Cattle—59% (107 mg per kg of body weight [mg/kg] dose).{R-44}

Dogs—48.8% (55 mg/kg dose).{R-41}

Sulfamethazine:

Pigs—86% (50 mg/kg dose).{R-66}

Ponies—84% (160 mg/kg dose).{R-57}

Distribution: Sulfonamides are widely distributed throughout the body. They cross the placenta, and a few penetrate into the cerebrospinal fluid.{R-20} Sulfonamides may be distributed into milk; however, they vary greatly in their ability to do so. The

process depends on several factors, including protein binding and pKa values.[R-102]

Volume of distribution—
- Sulfadimethoxine:
  - *Goats*—Area: 0.49 ± 0.095 liters per kg (L/kg).[R-35]
  - *Pigs*—Area:
    - Suckling (1 to 2 weeks)—0.483 ± 0.078 L/kg.[R-45]
    - Growing (11 to 12 weeks)—0.345 ± 0.016 L/kg.[R-45]
  - *Rabbits*—Steady state: 0.213 ± 0.007 L/kg.[R-40]
- Sulfamethazine:
  - *Buffalo*—Area: 0.44 ± 0.17 L/kg.[R-55]
  - *Cattle*—Extrapolated: 0.35 L/kg.[R-82]
  - *Goats*—Area: 0.28 to 0.39 L/kg; 0.44 L/kg.[R-35]
  - *Horses*—Steady state: 0.63 ± 0.074 L/kg.[R-57]
  - *Lambs*—Area: 0.334 ± 0.031 L/kg.[R-61]
  - *Pigs*—Area: 0.5;[R-66; 67] 0.77 ± 0.06 L/kg.[R-70]
    - Administered in conjunction with sulfathiazole: Area—1.01 ± 0.12 L/kg.[R-70]
  - *Sheep*—Area: 0.4 L/kg;[R-62; 63] 0.6 L/kg.[R-58]
- Sulfanilamide: *Goats*—Area: 1.3 ± 0.13 L/kg.[R-35]
- Sulfathiazole: *Pigs*—Area: 1.16 ± 0.16 L/kg.[R-70]

Protein binding: Binding can vary depending on serum concentration and other factors.[R-43]
- Sulfachlorpyridazine—*Cows:* 80 to 85%.[R-34]
- Sulfadimethoxine—
  - *Cats:* 87.5%.[R-42]
  - *Chickens:* 40%.[R-43]
  - *Dogs:* >75%.[R-39]
  - *Goats:* 94%.[R-35]
- Sulfamethazine—
  - *Cows:*
    - When plasma concentration is less than 50 mcg per mL (mcg/ mL)—79%.[R-79]
    - When plasma concentration is more than 50 mcg/mL—51%.[R-79]
  - *Goats:* 86%.[R-35]
  - *Horses:* 70%.[R-37]
  - *Sheep:* 77%.[R-58]
- Sulfanilamide—*Cows:* <20%.[R-34] Sulfathiazole—*Cows:* 65 to 76%.[R-34]

Biotransformation: Sulfonamides are primarily metabolized in the liver but metabolism also occurs in other tissues. Biotransformation occurs mainly by acetylation, glucuronide conjugation, and aromatic hydroxylation in many species.[R-17] The types of metabolites formed and the amount of each varies depending on the specific sulfonamide administered; the species, age, diet, and environment of the animal; the presence of disease; and, with the exception of pigs and ruminants, even the sex of the animal.[R-53; 54; 71; 79] Dogs are considered to be unable to acetylate sulfonamides to any significant degree.[R-108]

N_4-acetyl metabolites have no antimicrobial activity and hydroxymetabolites have 2.5 to 39.5% of the activity of the parent compound.[R-37] Metabolites may compete with the parent drug for involvement in folic acid synthesis but have little detrimental effect on the bacterial cell, and so could lower the activity of the remaining parent drug.[R-37]

In pigs, sulfamethazine is metabolized into N_4-acetylsulfamethazine, desaminosulfamethazine and the N_4-glucose conjugate of sulfamethazine.[R-72] In general, metabolites of sulfonamides are cleared more quickly than the parent drug;[R-78] however, the desaminosulfamethazine half-life of elimination can vary from 1 to 9 days, while sulfamethazine and other metabolites have a shorter half-life of 10 to 20 hours.[R-73] It has been theorized that diets containing nitrate, which is then reduced by bacteria to nitrite, will greatly increase the amount of sulfamethazine biotransformed to the desaminosulfamethazine metabolite and prolong tissue residues of metabolite,[R-71] but there is no conclusive evidence.

Half-life:

Absorption—Sulfadimethoxine: *Dogs*—Oral dose of 55 mg/kg: 1.9 hours.[R-39]

Elimination—
- Sulfachlorpyridazine: *Cows*—1.2 hours.[R-34]
- Sulfadimethoxine:
  - *Cats*—10.2 hours.[R-42]
  - *Cattle*—12.5 hours.[R-38]
  - *Dogs*—13.1 hours.[R-39]
  - *Goats*—8.6 hours.[R-34]
  - *Pigs*—
    - Single dose:
      - Suckling pig (1 to 2 weeks of age)—16.2 hours.[R-45]
      - Growing pig (11 to 12 weeks of age)—9.4 hours.[R-45]
    - After 5 days of once-daily intravenous dosing: 9.2 hours.[R-40]
  - *Rabbits*—After 6 days of once-daily intravenous dosing: 5.2 hours.[R-40]
- Sulfamethazine:
  - *Buffalo*—5.5 hours.[R-55]
  - *Calves*, 2 to 3 months of age—5.2 to 5.7 hours.[R-78; 79]
  - *Cattle*—5 to 11.3 hours.[R-34; 78; 79; 82]
  - *Goats*—2.4 to 4.1 hours;[R-35] 8.5 to 9.6 hours.[R-35; 82]
  - *Horses*—5.4 hours;[R-37] 11.4 hours.[R-57]
  - *Lambs*—7.2 hours.[R-61]
  - *Pigs*—9.8 hours;[R-70] 16.9 hours.[R-66; 67]
  - *Sheep*—4.5 hours;[R-58] 9.5 to 10.8 hours.[R-62; 63]
- Sulfanilamide:
  - *Cows*—6.2 hours.[R-34]
  - *Goats*—7.7 hours.[R-34]
- Sulfathiazole:
  - *Cows*—1.5 hours.[R-34]
  - *Pigs*—9 hours.[R-70]
  - *Sheep*—1.3 hours.[R-84]

Peak serum concentration:
- Sulfadimethoxine—Oral:
  - *Cattle*—114 ± 10 mcg/mL at 10 hours (107 mg/kg dose).[R-44]
  - *Chickens*—106.3 mcg/mL at 12 hours (100 mg/kg dose).[R-43]
  - *Dogs*—67 ± 16 mcg/mL of serum at 3.75 hours (55 mg/kg dose).[R-39]
- Sulfamethazine—Oral: *Ponies*—301.4 mcg/mL of serum at 0.83 hour (160 mg/kg dose).[R-57]

Duration of action:

The sulfonamides have been loosely categorized according to their plasma concentration versus time profiles:[R-19; 24]
- Short-acting—Sulfathiazole.
- Intermediate-acting—Sulfachlorpyridazine.
- Intermediate- to long-acting—Sulfadimethoxine, sulfamethazine.
- Enteric (minimally absorbed)—Sulfaquinoxaline.

Note: Duration of action may be estimated by the length of time target serum concentrations are maintained. Target concentrations are generally based on minimum inhibitory concentrations for each organism. Many sources use 50 mcg sulfonamide per mL (5 mg per decaliter) of blood as the minimum effective concentration for sulfonamides in animals.[R-64; 76; 80]
- Sulfadimethoxine—Oral: *Chickens*—A single dose of 100 mg/kg maintained plasma concentration of greater than or equal to 50 mcg/mL for 36 hours.[R-43]
- Sulfamethazine—
  - Intravenous: *Lambs*—An intravenous dose of 107.3 mg/kg maintained a plasma concentration of greater than 50 mcg/mL for 18 to 24 hours.[R-64]
  - Oral (powder for oral solution): *Calves*, 8 months of age—[R-

[R-76]

An oral dose of 214.3 mg/kg a day (1848 mg/L of water) administered in the only source of drinking water maintained a serum concentration of at least 50 mcg/mL from 18 hours to at least 120 hours after start of treatment.[R-76]

An oral dose of 142.9 mg/kg a day (1028 mg/L of water) administered in the only source of drinking water maintained a serum concentration of at least 50 mcg/mL from 24 to 180 hours after the start of treatment.[R-76]

An oral dose of 71.4 mg/kg a day (572 mg/L of water) administered in the only source of drinking water maintained a serum concentration of at least 50 mcg/mL from only 72 to 96 hours after the start of treatment.[R-76]

Oral (extended-release boluses):

Calves, 3 to 5 days of age: An oral dose of 396 mg/kg, administered as a single extended-release bolus, maintained a serum concentration of at least 50 mcg/mL from 4 to 96 hours post-administration.[R-80]

Calves and *cattle:* An oral dose of 264 mg/kg maintained a serum concentration greater than 50 mcg/mL from 12 to 48 or 72 hours post-administration.[R-81]

Elimination: Renal excretion is the primary route of elimination for most nonenteric sulfonamides and it occurs by glomerular filtration of parent drug, tubular excretion of unchanged drug and metabolites, and passive reabsorption of nonionized drug.[R-17; 20] Alkalization of the urine increases the fraction of the dose that is eliminated in the urine.[R-20] In general, the metabolites of the parent drug are more quickly eliminated by the kidney than the original sulfonamide is,[R-78] but the proportions of metabolites formed can vary, depending on many factors.

Sulfonamides are also distributed in relatively small amounts into milk, saliva, and into the gastrointestinal tract.[R-77; 79]

Sulfadimethoxine—*Cattle:* 17.9% of an intravenous dose of 107 mg per kg of sulfadimethoxine is excreted into the urine unchanged and at least 58.4% is excreted as metabolites into urine.[R-44] Only 6.3% of an oral dose of 107 mg of sulfadimethoxine per kg is excreted unchanged in the urine and 37.7% as metabolites in the urine.[R-44]

Total clearance:

Cats—0.31 mL per minute per kg (mL/min/kg).[R-42]

Dogs—0.36 mL/min/kg.[R-39]

Goats—0.65 mL/min/kg.[R-35]

Pigs—

Suckling pig (1 to 2 weeks): 0.35 mL/min/kg.[R-45]

Growing pig (11 to 12 weeks): 0.44 mL/min/kg.[R-45]

Sulfamethazine—

Cattle: 11 to 37% of a dose of sulfamethazine is excreted into the urine as parent drug.[R-78; 82]

Horses: Only 43% of the administered dose is eliminated in the urine and only 7.8% of it is in the form of parent drug.[R-37]

Pigs: 24.5% of a sulfamethazine dose is excreted in the urine as unchanged drug and 52.1% as measured metabolites.[R-67]

Sheep: 18% of a sulfamethazine dose is excreted into the urine as parent compound and 53% as metabolites.[R-64]

Total clearance:

Buffalo—0.93 mL/min/kg.[R-55]

Calves, 5 days of age—0.33 mL/min/kg.[R-79]

Calves, 2 to 3 months of age—0.57 mL/min/kg.[R-79]

Cows—0.73 mL/min/kg.[R-79]

Goats—0.55 to 0.65 mL/min/kg; 1.13 to 1.4 mL/min/kg.[R-35]

Horses—0.92 mL/min/kg.[R-37]

Pigs—0.35 mL/min/kg.[R-66]

Ponies—0.7 mL/min/kg.[R-57]

Sheep—1.6 mL/min/kg.[R-58]

Sulfathiazole—Total clearance: *Pigs*—1.5 mL/min/kg.[R-70]

Precautions to Consider

Species sensitivity

Dogs: An idiosyncratic sulfonamide toxicosis can occur in any breed of dog, but has been reported more frequently in the Doberman Pinscher than in other breeds. This specific type of drug reaction includes blood dyscrasias, nonseptic polyarthritis, and skin rash.[R-26; 27] Dogs given sulfonamides may also develop cutaneous eruptions, hepatitis, or keratitis sicca.[R-17; 27] Dogs have been reported to develop a hemorrhagic syndrome when doses of sulfaquinoxaline that are tolerated by many chickens are administered in their drinking water.[R-47-50]

Cross-sensitivity and/or related problems

Patients allergic to one sulfonamide may be allergic to other sulfonamides also.

Carcinogenicity

For sulfamethazine—High doses have been shown to induce follicular cell hyperplasia of the thyroid gland and splenic changes in specific–pathogen-free mice. When the highest doses (4800 parts per million in the diet) were fed for 24 months, 26 to 33% of the mice developed thyroid gland adenomas.[R-51] The applicability of these results to other species with recommended doses is unclear at this time.

Pregnancy/Reproduction

Sulfonamides cross the placenta in pregnant animals.[R-20; 60] Some teratogenic effects have been seen when very high doses were given to pregnant mice and rats.[R-20]

Lactation

Sulfonamides are distributed into milk; however, the sulfonamides that are clinically relevant to food-producing animals are distributed into milk in concentrations too low to be therapeutic but high enough to produce residues.[R-103; 105] For many sulfonamides, 0.5 to 2% of the total dose is found in the milk.[R-31; 32] Distribution into milk varies depending on the amount of non–protein-bound sulfonamide present in the blood and the amount of the nonionized and therefore liposoluble form of the medication present. Sulfonamides with higher pKa values produce a higher proportion of drug in the blood that is non-ionized,[R-31] and if other factors, such as the rate of biotransformation, also support it, may be distributed more easily into milk. For lactating dairy cattle, concentration of the active parent compound of sulfamethazine, measured at a specific time in milk, is about 20% of the concentration in the blood.[R-77]

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Drug interactions relating specifically to the use of sulfonamides in animals are rarely reported in veterinary literature. Human drug interactions have been reported and are included in the following section.

Human drug interactions[R-69]

The following drug interactions have been reported in humans, and are included in the human monograph *Sulfonamides (Systemic)* in *USP DI Volume I;* these drug interactions are intended for informational purposes only and may or may not be applicable to the use of sulfonamides in the treatment of animals:

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Anticoagulants, coumarin- or indandione-derivative, or

Anticonvulsants, hydantoin, or
Antidiabetic agents, oral
(these medications may be displaced from protein binding sites and/or their metabolism may be inhibited by some sulfonamides, resulting in increased or prolonged effects and/or toxicity; dosage adjustments may be necessary during and after sulfonamide therapy)
Bone marrow depressants
(concurrent use of bone marrow depressants with sulfonamides may increase the leukopenic and/or thrombocytopenic effects; if concurrent use is required, close observation for myelotoxic effects should be considered)
Cyclosporine
(concurrent use with sulfonamides may increase the metabolism of cyclosporine, resulting in decreased plasma concentrations and potential transplant rejection, and additive nephrotoxicity; plasma cyclosporine concentrations and renal function should be monitored)
Hemolytics, other
(concurrent use with sulfonamides may increase the potential for toxic side effects)
Hepatotoxic medications, other
(concurrent use with sulfonamides may result in an increased incidence of hepatotoxicity; patients, especially those on prolonged administration or those with a history of liver disease, should be carefully monitored)
Methenamine
(in acid urine, methenamine breaks down into formaldehyde, which may form an insoluble precipitate with certain sulfonamides, especially those that are less soluble in urine, and may also increase the danger of crystalluria; concurrent use is not recommended)
Methotrexate or
Phenylbutazone
(the effects of methotrexate may be potentiated during concurrent use with sulfonamides because of displacement from plasma protein binding sites; phenylbutazone may displace sulfonamides from plasma protein binding sites, increasing sulfonamide concentrations)
Penicillins
(since bacteriostatic drugs may interfere with the bactericidal effect of penicillins in the treatment of meningitis or in other situations where a rapid bactericidal effect is necessary, it is best to avoid concurrent therapy)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Laboratory value alterations relating specifically to the use of sulfonamides in animals are rarely reported in veterinary literature. Human laboratory value alterations have been reported and are included in the following section.

Human laboratory value alterations[R-69]

The following laboratory value alterations have been reported in humans, and are included in the human monograph *Sulfonamides (Systemic)* in *USP DI Volume I;* these laboratory value alterations are intended for informational purposes only and may or may not be applicable to the use of sulfonamides in the treatment of animals:

With diagnostic test results
Benedict's test
(sulfonamides may produce a false-positive Benedict's test for urine glucose)
Jaffé alkaline picrate reaction assay
(sulfamethoxazole may interfere with the Jaffé alkaline picrate reaction assay for creatinine, resulting in overestimations of approximately 10% in the normal values for creatinine)
Sulfosalicylic acid test
(sulfonamides may produce a false-positive sulfosalicylic acid test for urine protein)
Urine urobilinogen test strip (e.g., Urobilistix)
(sulfonamides may interfere with the [Urobilistix] test for urinary urobilinogen)
With physiology/laboratory test values
Alanine aminotransferase (ALT [SGPT]), serum, and
Aspartate aminotransferase (AST [SGOT]), serum, and
Bilirubin, serum
(values may be increased)
Blood urea nitrogen (BUN) and
Creatinine, serum
(concentrations may be increased)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problem exists:

» Hypersensitivity to sulfonamides
(animals that have had a previous reaction to sulfonamides may be much more likely to react on subsequent administration)

Risk-benefit should be considered when the following medical problems exist:

Hepatic function impairment
(systemically absorbed sulfonamides are metabolized by the liver; delayed biotransformation may increase the risk of adverse effects)
Renal function impairment
(systemically absorbed sulfonamides are renally excreted; delayed elimination could cause accumulation of sulfonamide and metabolites, increasing the risk of adverse effects)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = major clinical significance):

Culture and susceptibility, *in vitro,* and
Minimum inhibitory concentration (MIC)
(*in vitro* cultures and MIC test should be done on samples collected prior to sulfonamide administration to determine pathogen susceptibility)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

Incidence unknown

All species

Crystallization in the urinary tract

Note: *Crystallization* of sulfonamides can occur in the kidneys or urine with high doses of sulfonamide or when an animal is dehydrated. Solubility in the urine is dependent on the concentration of drug in the urine, urinary pH (less soluble in an acidic pH), the patient's hydration, and the amount of drug in the acetylated form. Because dogs do not produce acetylated metabolites, they may be less susceptible to this adverse effect.[R-85] It can be minimized in susceptible

animals by maintaining a high urine flow and, if necessary, alkalinizing the urine.

Dogs

Cutaneous drug eruption;[R-27] ***hepatitis; hypothyroidism;***[R-100; 101] ***idiosyncratic toxicosis***[R-26; 27] (blood dyscrasias, including anemia, leukopenia or thrombocytopenia; fever; focal retinitis; lymphadenopathy; nonseptic polyarthritis; polymyositis; skin rash); ***keratoconjunctivitis sicca***[R-28-30]

Note: Iatrogenic *hypothyroidism* may occur and thyroid function test values may be lowered in dogs administered sulfonamides.[R-100; 101] Although studies have looked at this reaction with potentiated sulfonamides,[R-100; 101] sulfonamides administered alone have been reported to impair thyroid function.[R-100] With administration of sulfamethoxazole and trimethoprim combination at high doses or of ormetoprim and sulfadimethoxine, thyrotropin stimulation test values and serum thyroxine values have been significantly reduced.[R-100] Sulfadiazine and trimethoprim combination, administered at labeled doses (25 mg of sulfadiazine and 5 mg of trimethoprim per kg every 24 hours), has not affected thyroid test values in studies performed.

Idiosyncratic toxicosis can occur 8 to 20 days after initiation of treatment and is believed to be caused either by an immune-mediated syndrome or by an idiosyncratic reaction in dogs, perhaps due to toxic metabolites of the sulfonamide. Of 22 reported cases compiled in one study, 7 involved Doberman Pinschers, and it has been theorized that they are more susceptible to this toxicosis.[R-26] A large majority of the animals in which idiosyncratic toxicosis occurs have had a previous exposure to a sulfonamide. Most cases involve a trimethoprim and sulfonamide combination.[R-27] When sulfonamide therapy is discontinued, recovery generally occurs within 2 to 5 days.[R-27]

Keratoconjunctivitis sicca is considered a possible side/adverse effect in any dog on sulfonamide therapy for more than a month; however, it can occur at any time after therapy is initiated. Reports conflict over whether this is a dose-related or idiosyncratic reaction.[R-108] The most frequent reports have been with sulfasalazine or trimethoprim and sulfonamide combination,[R-28-30] perhaps because these medications are most commonly used for long-term therapy in dogs. Lacrimation may not return to normal after discontinuation of sulfonamide treatment.

For sulfaquinoxaline

Chickens and *dogs*

Hemorrhagic syndrome (anorexia, epistaxis, hemoptysis, lethargy, pale mucous membranes, possibly death)[R-46-50]

Note: *Hemorrhagic syndrome* has been reported in chickens and dogs but may occur in other species. It is most often reported with the addition of sulfaquinoxaline to feed for chickens, but in dogs has been reported to follow administration in the water supply of products labeled for poultry.[R-47-50] Sulfaquinoxaline is a vitamin K antagonist that inhibits vitamin K eposide and vitamin K quinone reductase and causes an effect similar to that of coumarin anticoagulants.[R-46] Rapid hypoprothrombinemia occurs in dogs, and sulfaquinoxaline may have an additional adverse effect on specific cell types; this may explain why supplementation of chicken feeds with vitamin K has not always prevented the syndrome in chickens.[R-46-47] Rapid discontinuation of medication and initiation of therapy with vitamin K_1 may reverse the effects.

Human side/adverse effects[R-69]

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monograph *Sulfonamides (Systemic)* in *USP DI Volume I;* these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of sulfonamides in the treatment of animals:

Incidence more frequent

Central nervous system effects; gastrointestinal disturbances; hypersensitivity; photosensitivity

Incidence less frequent

Blood dyscrasias; hepatitis; Lyell's syndrome (difficulty in swallowing; redness, blistering, peeling, or loosening of skin); ***Stevens-Johnson syndrome*** (aching joints and muscles; redness, blistering, peeling, or loosening of skin; unusual tiredness or weakness)

Incidence rare

Central nervous system toxicity; Clostridium difficile colitis; crystalluria or hematuria; goiter or thyroid function disturbance; interstitial nephritis or tubular necrosis

Note: *C. difficile colitis* may occur up to several weeks after discontinuation of these medications.

Fatalities have occurred, although rarely, due to severe reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Therapy should be discontinued at the first appearance of skin rash or any serious side/adverse effects.

The multiorgan toxicity of sulfonamides is thought to be the result of the way sulfonamides are metabolized in certain patients. It is probably due to the inability of the body to detoxify reactive metabolites. Sulfonamides are metabolized primarily by acetylation. Patients can be divided into slow and fast acetylators. Slow acetylation of sulfonamides makes more of the medication available for metabolism by the oxidative pathways of the cytochrome P450 system. These pathways produce reactive toxic metabolites, such as hydroxylamine and nitroso compounds. The metabolites are normally detoxified by scavengers, such as glutathione. However, some populations, such as human immunodeficiency virus (HIV)–infected patients, have low concentrations of glutathione and these metabolites accumulate, producing toxicity. Patients who are slow acetylators have a higher incidence of sulfonamide hypersensitivity reactions, although severe toxicity has also been seen in fast acetylators. Acetylation status alone cannot fully explain sulfonamide toxicity since approximately 50% of North American blacks and whites are slow acetylators and severe reactions occur in less than 1% of patients treated with sulfonamides. However, decreased acetylation may increase the amount of sulfonamide metabolized to toxic metabolites.

Overdose

For more information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer.**

Toxicities secondary to acute overdose of sulfonamides are not typically reported. Side effects may be more likely to occur with high doses and long-term administration, but are seen at recommended doses as well.

Client Consultation

Dosage and length of treatment recommendations should be followed; high doses or long-term use can increase the risk of side effects. Animals should have a good water supply and should be monitored to ensure adequate water consumption during treatment.

General Dosing Information

Residue avoidance: Management practices can affect depletion of residues in pigs. When pigs have environmental access to urine and manure from pigs treated with sulfamethazine, the residues are easily recycled and can cause these animals to have positive urine tests for sulfonamide and violative tissue residues. Hot or cold environmental temperatures do not appear to inactivate sulfamethazine in the environment.{R-70; 74}

For oral dosage forms only

Intestinal parasites, among other factors, can affect the pharmacokinetics of sulfamethazine in lambs and probably in other species also. In parasitized lambs given a single dose of 99 mg per kg of body weight (mg/kg), sulfamethazine's half-life of elimination and time to peak concentration were doubled.{R-65}

For treatment of adverse effects

Recommended treatment consists of the following:

For anaphylaxis

- Parenteral epinephrine.
- Oxygen administration and respiratory support.

SULFACHLORPYRIDAZINE

Summary of Differences

Pharmacology/pharmacokinetics: Intermediate duration of action.{R-19; 24}

Oral Dosage Forms

Note: The text between [EL]US and [EL] describes uses not included in U.S. product labeling. Text between [EL]CAN and [EL] describes uses that are not included in Canadian product labeling.

The [EL]US or [EL]CAN designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFACHLORPYRIDAZINE POWDER FOR ORAL SOLUTION

Usual dose: [EL]CAN Enteritis (diarrhea associated with *E. coli*)[EL]—

Calves, less than 1 month of age: Oral, 33 to 49.5 mg per kg of body weight every twelve hours.{R-89}

Withdrawal times—US: Meat—7 days.{R-89}

Pigs: Oral, 22 to 38.5 mg per kg of body weight, administered as a drench every twelve hours or 44 to 77 mg per kg of body weight a day administered in the only source of drinking water.{R-89}

Withdrawal times—US: Meat—4 days.{R-89}

Strength(s) usually available:{R-92}

U.S.—

Veterinary-labeled product(s):

50 grams per bottle (OTC) [*Vetisulid Powder*].{R-89}

Canada—

Veterinary-labeled product(s):

Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

Parenteral Dosage Forms

Note: The text between [EL]US and [EL] describes uses not included in U.S. product labeling. Text between [EL]CAN and [EL] describes uses that are not included in Canadian product labeling.

The [EL]US or [EL]CAN designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFACHLORPYRIDAZINE INJECTION

Usual dose: [EL]CAN Enteritis (diarrhea associated with *E. coli*)[EL]—

Calves, less than 1 month of age: Intravenous, 33 to 49.5 mg per kg of body weight every twelve hours.{R-87}

Withdrawal times—US: Meat—5 days.{R-87} This withdrawal applies when medication is administered for a maximum of 5 days. This product is not labeled for use in calves intended for human food production.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

200 mg per mL (OTC) [*Vetisulid Injection*].

Canada—

Veterinary-labeled product(s):

Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86°F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.{R-87}

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFADIMETHOXINE

Summary of Differences

Pharmacology/pharmacokinetics: Intermediate to long duration of action.{R-19; 24}

Oral Dosage Forms

Note: The text between [EL]US and [EL] describes uses not included in U.S. product labeling. Text between [EL]CAN and [EL] describes uses that are not included in Canadian product labeling.

The [EL]US or [EL]CAN designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFADIMETHOXINE BOLUSES

Usual dose:

[EL]CAN Calf diphtheria[EL];

[EL]CAN Pneumonia, bacterial[EL]; or

[EL]CAN Pododermatitis[EL]—*Cattle:* Oral, 55 mg per kg of body weight as the initial dose, followed by 27.5 mg per kg of body weight every twenty-four hours for five days.{R-1}

Withdrawal times—US: Meat—7 days, Milk—60 hours.{R-1} A withdrawal period has not been established for preruminating calves; these products are not labeled for use in calves to be used in the production of human food.{R-1}

Strength(s) usually available:{R-1}

U.S.—

Veterinary-labeled product(s):

5000 mg (5 grams) (OTC) [*Albon Boluses*].

15,000 mg (15 grams) (OTC) [*Albon Boluses*].

Canada—

Veterinary-labeled product(s):
Not commercially available.

Additional information: Animals should maintain an adequate water intake during the treatment period.{R-1}

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

USP requirements: Not in USP.{R-56}

SULFADIMETHOXINE EXTENDED-RELEASE BOLUSES

Usual dose:

ELCAN Bacterial pneumonia EL;
ELCAN Calf diphtheria EL; or
ELCAN Pododermatitis EL—*Cattle:* Oral, 137.5 mg per kg of body weight as a single dose.{R-5}
Withdrawal times—US: Meat—21 days.{R-5} This product is not labeled for use in lactating dairy cattle. A withdrawal period has not been established for preruminating calves; these products are not labeled for use in calves to be used in the production of human food.{R-5}

Note: To maintain sustained release of medication, boluses should not be divided; it is recommended that animals should receive a tablet for the nearest 91 kg (200 pounds) of body weight.{R-5}

Strength(s) usually available:{R-92}
U.S.—
Veterinary-labeled product(s):
12.5 grams (Rx) [*Albon SR*].
Canada—
Veterinary-labeled product(s):
Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFADIMETHOXINE ORAL SOLUTION

Usual dose:

ELCAN Calf diphtheria EL;
ELCAN Pneumonia, bacterial EL; or
ELCAN Pododermatitis EL—*Calves* and *cattle:* Oral, 55 mg per kg of body weight (2.4 to 3.75 grams per gallon of water) as an initial dose, followed by 27.5 mg per kg of body weight (1.2 to 1.8 grams per gallon of water) a day for four days.{R-2}
Withdrawal times—US: Meat—7 days.{R-2} Products are not labeled for use in lactating dairy cattle or preruminating calves.
ELCAN Coccidiosis EL; or
ELCAN Fowl cholera EL—
Chickens, broiler and replacement: Oral, 1875 mg per gallon of water (0.05% solution), administered as the only source of drinking water for six days.{R-2}
Withdrawal times—US: Meat—5 days.{R-2} Products are not labeled for use in chickens older than 16 weeks of age.
Turkeys: Oral, 938 mg per gallon of water (0.025% solution), administered as the only source of drinking water for six days.{R-2}
Withdrawal times—US: Meat—5 days.{R-2} Products are not labeled for use in turkeys older than 24 weeks of age.
ELCAN Infectious coryza outbreaks EL—*Chickens,* broiler and replacement: Oral, 1875 mg per gallon of water (0.05% solution), administered as the only source of drinking water for six days.{R-2}
Withdrawal times—US: Meat—5 days.{R-2} Products are not labeled for use in chickens older than 16 weeks of age.
Note: Administration of sulfadimethoxine for longer than the recommended time can result in slowed growth rates and other adverse effects.{R-83}

Strength(s) usually available:{R-92}
U.S.—
Veterinary-labeled product(s):
125 mg per mL (OTC) [*Albon 12.5% Concentrated Solution; Di-Methox 12.5% Oral Solution; SDM Solution; Sufladived 12.5% Oral Solution; Sulforal;* GENERIC].
Canada—
Veterinary-labeled product(s):
Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light.{R-2}

Stability: Freezing or discoloration does not affect stability. Medication should be thawed before using.{R-2}

Preparation of dosage form: Prepare fresh drinking water daily.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFADIMETHOXINE ORAL SUSPENSION USP

Usual dose:

ELCAN Bacterial pneumonia and other respiratory infections EL;
ELCAN Cystitis EL; or
ELCAN Skin and soft tissue infections EL—*Cats* and *dogs:* Oral, 55 mg per kg of body weight as an initial dose, followed by 27.5 mg per kg of body weight every twenty-four hours.{R-3}
ELCAN Enteritis associated with coccidiosis or *Salmonella* EL—*Dogs:* Oral, 55 mg per kg of body weight as an initial dose, followed by 27.5 mg per kg of body weight every twenty-four hours.{R-3}

Strength(s) usually available:
U.S.—
Veterinary-labeled product(s):
50 mg per mL (Rx) [*Albon Oral Suspension 5%*].{R-3}
Canada—
Veterinary-labeled product(s):
Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Preserve in tight, light-resistant containers, and store at controlled room temperature. Label it to indicate that it is for veterinary use only. Contains the labeled amount, within

±10%. Meets the requirements for Identification and pH (5.0–7.0).{R-56}

SULFADIMETHOXINE SOLUBLE POWDER USP

Usual dose:

EL CAN Bacterial pneumonia EL;
EL CAN Calf diphtheria EL; or
EL CAN Pododermatitis EL—*Calves* and *cattle:* Oral, 55 mg per kg of body weight (2.4 to 3.3 grams per gallon) as an initial dose, followed by 27.5 mg per kg of body weight (1.2 grams per gallon) every twenty-four hours for four days.{R-4}
Withdrawal times—US: Meat—7 days.{R-4} Products are not labeled for use in lactating dairy cattle. A withdrawal period has not been established for preruminating calves; these products are not labeled for use in calves to be used in the production of human food.
EL CAN Coccidiosis EL; or
EL CAN Fowl cholera EL—
Chickens, broiler and replacement: Oral, 1892 mg per gallon of water (0.05% solution), administered as the only source of drinking water for six days.{R-4}
Withdrawal times—US: Meat—5 days.{R-4} Products are not labeled for use in chickens older than 16 weeks of age.
Turkeys: Oral, 946 mg per gallon of water (0.025% solution), administered as the only source of drinking water for six days.{R-4}
Withdrawal times—US: Meat—5 days.{R-4} Products are not labeled for use in turkeys older than 24 weeks of age.
EL CAN Infectious coryza outbreaks EL—*Chickens,* broiler and replacement: Oral, 1892 mg per gallon of water (0.05% solution), administered as the only source of drinking water for six days.{R-4}
Withdrawal times—US: Meat—5 days.{R-4} Products are not labeled for use in chickens older than 16 weeks of age.

Strength(s) usually available:{R-92}

U.S.—
Veterinary-labeled product(s):
28.3 grams per ounce of powder (OTC) [*Di-Methox Soluble Powder; SulfaMed-G; Sulfasol;* GENERIC].
Canada—
Veterinary-labeled product(s):
Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Preserve in tight, light-resistant containers, and store at controlled room temperature. Label it to indicate that it is for veterinary use only. Contains the labeled amount, within ±10%. Meets the requirements for Identification, Minimum fill, and pH (7.0–8.0, in a solution [1 in 20]).{R-56}

SULFADIMETHOXINE TABLETS USP

Usual dose:

Bacterial pneumonia and other respiratory infections; Cystitis; or
Skin and soft tissue infections—*Cats* and *dogs:* Oral, 55 mg per kg of body weight as an initial dose, followed by 27.5 mg per kg of body weight every twenty-four hours.{R-6; 91}
Enteritis associated with coccidiosis or *Salmonella—Dogs:* Oral, 55 mg per kg of body weight as an initial dose, followed by 27.5 mg per kg of body weight every twenty-four hours.{R-6}

Strength(s) usually available:{R-6}

U.S.—
Veterinary-labeled product(s):
125 mg (Rx) [*Albon Tablets*].
250 mg (Rx) [*Albon Tablets*].
500 mg (Rx) [*Albon Tablets*].
Canada—{R-91}
Veterinary-labeled product(s):
125 mg (OTC) [*S-125*].
250 mg (OTC) [*S-250*].

Additional information: Animals should maintain an adequate water intake during the treatment period.{R-91}

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.{R-91}

USP requirements: Preserve in tight, light-resistant containers, and store at controlled room temperature. Label the Tablets to indicate that they are for veterinary use only. Contains the labeled amount, within ±10%. Meets the requirements for Identification, Disintegration (30 minutes), and Uniformity of dosage units.{R-56}

Parenteral Dosage Forms

SULFADIMETHOXINE INJECTION

Usual dose:

EL CAN Calf diphtheria EL;
EL CAN Pneumonia, bacterial EL; or
EL CAN Pododermatitis EL—*Cattle:* Intravenous, 55 mg per kg of body weight as an initial dose, followed by 27.5 mg per kg of body weight every twenty-four hours.{R-88}
Withdrawal times—US: Meat—5 days, Milk—60 hours.{R-88} A withdrawal period has not been established for preruminating calves; these products are not labeled for use in calves to be used in the production of human food.

Strength(s) usually available:{R-92}

U.S.—
Veterinary-labeled product(s):
400 mg per mL (Rx) [*Di-Methox Injection-40%; SDM Injection;* GENERIC].
Canada—
Veterinary-labeled product(s):
Not commercially available.

Stability: Crystallization does not change the potency of sulfadimethoxine injection.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light.

USP requirements: Not in USP.{R-56}

SULFAMERAZINE, SULFAMETHAZINE, AND SULFAQUINOXALINE

Oral Dosage Forms

Note: The text between EL US and EL describes uses not included in U.S. product labeling. Text between EL CAN and EL describes uses that are not included in Canadian product labeling.

The EL US or EL CAN designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFAMERAZINE, SULFAMETHAZINE, AND SULFAQUINOXALINE POWDER FOR ORAL SOLUTION

Usual dose:

[EL CAN]Coccidiosis[EL]—

Chickens: Oral, 609 mg of sulfamerazine, 609 mg of sulfamethazine, and 305 mg of sulfaquinoxaline per gallon of water (a 0.04% solution), administered as the only source of drinking water for two to three days, followed by unmedicated water for three days.{R-109} Then, administer 379 mg of sulfamerazine, 379 mg of sulfamethazine, and 189 mg of sulfaquinoxaline per gallon of water (0.025% solution), administered as the only source of drinking water for two days. If bloody droppings appear, repeat the 0.025% solution for an additional 2 days.{R-109}

Withdrawal times—US: Meat—14 days.{R-109} This product is not labeled for use in chickens laying eggs for human consumption.

Turkeys: Oral, 379 mg of sulfamerazine, 379 mg of sulfamethazine, and 189 mg of sulfaquinoxaline per gallon of water (a 0.025% solution), administered as the only source of drinking water for two days, followed by unmedicated drinking water for three days.{R-109} Then, administer the 0.025% solution as drinking water for two days, followed by unmedicated drinking water for three days, followed by two more days of the 0.025% solution. Repeat the treatment, if necessary.{R-109}

Withdrawal times—US: Meat—14 days.{R-109} This product is not labeled for use in turkeys laying eggs for human consumption.

[EL CAN]Fowl cholera, acute[EL]—*Chickens* and *turkeys:* Oral, 609 mg of sulfamerazine, 609 mg of sulfamethazine, and 305 mg of sulfaquinoxaline per gallon of water (a 0.04% solution), administered as the only source of drinking water for two to three days.{R-109}

Withdrawal times—US: Meat—14 days.{R-109} This product is not labeled for use in chickens or turkeys laying eggs for human consumption.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

400 mg sulfamerazine, 400 mg sulfamethazine, and 200 mg sulfaquinoxaline per gram (OTC) [*Poultry Sulfa*].

Canada—

Veterinary-labeled product(s):

Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from moisture.

Preparation of dosage form: Medication should not be mixed or administered in galvanized containers.{R-109}

Additional information: Product labeling states that litter should not be changed during treatment.{R-109}

Keep out of the reach of children.{R-109}

USP requirements: Not in USP.{R-56}

SULFAMETHAZINE

Summary of Differences

Pharmacology/pharmacokinetics: Intermediate to long duration of action.{R-19; 24}

Oral Dosage Forms

Note: The text between [EL US] and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL US] or [EL CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFAMETHAZINE BOLUSES

Usual dose:

Calf diphtheria—*Calves:* Oral, 220 mg per kg of body weight as an initial dose, followed by 110 mg per kg of body weight every twenty-four hours.{R-13}

Enteritis associated with *Escherichia coli*—*Calves* and *foals:* Oral, 220 mg per kg of body weight as an initial dose, followed by 110 mg per kg of body weight every twenty-four hours.{R-13}

Pneumonia, bacterial—*Calves* and *foals:* Oral, 220 mg per kg of body weight as an initial dose, followed by 110 mg per kg of body weight every twenty-four hours.{R-13}

Withdrawal times—US: Meat—10 days.{R-13} This withdrawal time applies when the medication is administered for a maximum of five days. Products are not labeled for use in lactating dairy cattle or preruminating calves to be used in human food production. Canada: Meat—10 days, Milk—96 hours.{R-8} Products are not labeled for use in preruminating calves or horses to be used in human food production.

Strength(s) usually available:{R-92}

U.S.—

Veterinary-labeled product(s):

2.5 grams (OTC) [*Sulmet Oblets*].

5 grams (OTC) [*Sulmet Oblets*].

Canada—

Veterinary-labeled product(s):

15 grams (OTC) [GENERIC].

15.6 grams (OTC) [GENERIC].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFAMETHAZINE EXTENDED-RELEASE BOLUSES

Usual dose:

Calf diphtheria;

[EL CAN]Coccidiosis[EL];

Enteritis, bacterial; or

Pneumonia, bacterial—

Calves, 1 month of age or older: Oral, 350 to 400 mg per kg of body weight, administered as a single dose.{R-7; 11} The dose may be repeated in three days, if necessary.{R-7; 11}

Cattle: Oral, 330 to 350 mg per kg of body weight as a single dose.{R-10} The dose may be repeated in three days, if necessary.{R-10}

Pododermatitis—*Cattle:* Oral, 330 to 350 mg per kg of body weight as a single dose.{R-10} The dose may be repeated in three days, if necessary.{R-10}

Withdrawal times—US: Meat—8 or 12 days, depending on the product.{R-10; 11} Withdrawal times apply when medication is administered for a maximum of two doses. Products are not labeled for use in lactating dairy cattle or preruminating calves intended for the production of human food. Canada: Meat—12

or 28 days, depending on the product. Products are not labeled for use in lactating dairy cattle.{R-7}

Strength(s) usually available:{R-92}
U.S.—{R-10; 11}
Veterinary-labeled product(s):
8 grams (OTC) [*Sustain III Calf Bolus*].
8.25 grams (OTC) [*Suprasulfa III Calf Bolus*].
30 grams (OTC) [*Suprasulfa III Cattle Bolus*].
32.1 grams (OTC) [*Sustain III Cattle Bolus*]
Canada—{R-7}
Veterinary-labeled product(s):
8 grams (OTC) [*Calfspan*].
32.1 grams (OTC [*Sustain III*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Additional information: Boluses can be broken at the score line, but should not be crushed.
Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFAMETHAZINE ORAL SOLUTION

Usual dose:
Calf diphtheria; or
Pododermatitis—*Calves* and *cattle:* Oral, 247.5 mg per kg of body weight as an initial dose, followed by 123.8 mg per kg of body weight every twenty-four hours for three days, administered in the only source of drinking water.{R-12}
Withdrawal times—US: Meat—10 days.{R-12} Withdrawal times apply when medication is administered for a maximum of five days. This product is not labeled for use in lactating dairy cows or preruminating calves to be used in the production of human food. Canada: Meat—10 or 12 days, depending on the product, Milk—96 hours.
Coccidiosis—
Chickens: Oral, 134 to 196 mg per kg of body weight a day for two days, followed by 67 to 98 mg per kg of body weight for four days, administered in the only source of drinking water.{R-12}
Withdrawal times—This product is not labeled for use in chickens laying eggs for human consumption. US: Meat—10 days.{R-12} Canada: Meat—12 days.
Turkeys: Oral, 117 to 286 mg per kg of body weight a day for two days, followed by 58.5 to 143 mg per kg of body weight for four days, administered in the only source of drinking water.{R-12}
Withdrawal times—This product is not labeled for use in turkeys laying eggs for human consumption. US: Meat—10 days.{R-12} Canada: Meat—12 days.
Enteritis, bacterial—
Calves, cattle, and *pigs:* Oral, 247.5 mg per kg of body weight as an initial dose, followed by 123.8 mg per kg of body weight every twenty-four hours for three days, administered in the only source of drinking water.{R-12}
Withdrawal times—US: *Cattle*—Meat: 10 days. *Pigs*—Meat: 15 days.{R-12} Withdrawal times apply when medication is administered for a maximum of five days. This product is not labeled for use in lactating dairy cows or preruminating calves to be used in the production of human food. Canada: *Cattle*—Meat: 10 or 12 days, depending on the product, Milk—96 hours. *Pigs*—Meat: 10 or 12 days, depending on the product.
EL[US] *Sheep* [EL]: Oral, 225 mg per kg of body weight the first day, followed by 112.5 mg per kg of body weight for three days, administered in the only source of drinking water.{R-16}
Withdrawal times—Canada: Meat—10 days, depending on the product.{R-16}
Fowl cholera, acute; or
Pullorum disease—*Chickens:* Oral, 134 to 196 mg per kg of body weight a day for six days, administered in the only source of drinking water.{R-12}
Withdrawal times—This product is not labeled for use in chickens laying eggs for human consumption. US: Meat—10 days.{R-12} Canada: Meat—12 days.
Infectious coryza—*Chickens:* Oral, 134 to 196 mg per kg of body weight a day for two days, administered in the only source of drinking water.{R-12}
Withdrawal times—This product is not labeled for use in chickens laying eggs for human consumption. US: Meat—10 days.{R-12} Canada: Meat—12 days.
Pneumonia, bacterial—*Calves, cattle,* and *pigs:* Oral, 247.5 mg per kg of body weight as an initial dose, followed by 123.8 mg per kg of body weight every twenty-four hours for three days, administered in the only source of drinking water.{R-12}
Withdrawal times—US: *Cattle*—Meat: 10 days. *Pigs*—Meat: 15 days.{R-12} These withdrawal times apply when the medication is administered for a maximum of five days. This product is not labeled for use in lactating dairy cows or preruminating calves to be used in the production of human food. Canada: *Cattle*—Meat: 10 or 12 days, depending on the product, Milk—96 hours. *Pigs*—Meat: 10 or 12 days, depending on the product.
Respiratory infections, bacterial—EL[US] *Sheep* [EL]: Oral, 225 mg per kg of body weight the first day, followed by 112.5 mg per kg of body weight for three days, administered in the only source of drinking water.{R-16}
Withdrawal times—Canada: Meat—10 days, depending on the product.{R-16}

Strength(s) usually available:{R-92}
U.S.—
Veterinary-labeled product(s):
125 mg per mL (OTC) [*Sulmet Drinking Water Solution 12.5%*].
Canada—
Veterinary-labeled product(s):
125 mg per mL (OTC) [GENERIC].
250 mg per mL (OTC) [GENERIC].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFAMETHAZINE POWDER FOR ORAL SOLUTION

Usual dose:
EL[CAN] Calf diphtheria [EL]; or
EL[CAN] Pododermatitis [EL]—*Cattle:* Oral, 237.6 mg per kg of body weight as an initial dose, followed by 118.8 mg per kg of body weight every twenty-four hours for three days, administered as an individual animal drench or in the only source of drinking water.{R-9}
Withdrawal times—US: Meat—10 days.{R-9} Withdrawal times apply when the medication is administered for a maximum of five days. Products are not labeled for use in lactating dairy cows or preruminating calves to be used in the production of human food.

[EL CAN] Coccidiosis [EL]—
Chickens: Oral, 128 to 187 mg per kg of body weight a day for two days, followed by 64 to 93.5 mg per kg of body weight for four days, administered in the only source of drinking water.{R-9}
Withdrawal times—US: Meat—10 days.{R-9} Products are not labeled for use in chickens laying eggs for human consumption.
Turkeys: Oral, 110 to 273 mg per kg of body weight a day for two days, followed by 55 to 136.5 mg per kg of body weight for four days, administered in the only source of drinking water.{R-9}
Withdrawal times—US: Meat—10 days.{R-9} Products are not labeled for use in turkeys laying eggs for human consumption.
[EL CAN] Enteritis, bacterial [EL]; or
[EL CAN] Pneumonia, bacterial [EL]—*Cattle* and *pigs:* Oral, 237.6 mg per kg of body weight as an initial dose, followed by 118.8 mg per kg of body weight every twenty-four hours for three days, administered as an individual animal drench or in the only source of drinking water.{R-9}
Withdrawal times—US: *Cattle*—Meat: 10 days. *Pigs*—Meat: 15 days.{R-9} These withdrawal times apply when the medication is administered for a maximum of five days. Products are not labeled for use in lactating dairy cows or preruminating calves to be used in the production of human food.
[EL CAN] Fowl cholera, acute [EL]; or
[EL CAN] Pullorum disease [EL]—*Chickens:* Oral, 128 to 187 mg per kg of body weight a day for six days, administered in the only source of drinking water.{R-9}
Withdrawal times—US: Meat—10 days.{R-9} Products are not labeled for use in chickens laying eggs for human consumption.
[EL CAN] Infectious coryza [EL]—*Chickens:* Oral, 128 to 187 mg per kg of body weight a day for two days, administered in the only source of drinking water.{R-9}
Withdrawal times—US: Meat—10 days.{R-9} Products are not labeled for use in chickens laying eggs for human consumption.

Strength(s) usually available:{R-92}
U.S.—
Veterinary-labeled product(s):
453.5 grams of sulfamethazine powder per packet (OTC) [*SMZ-Med 454; Sulmet Soluble Powder*].{R-9}
Canada—
Veterinary-labeled product(s):
Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

Preparation of dosage form: Fresh solutions should be prepared daily.{R-12}

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Oral Dosage Forms

Note: The text between [EL US] and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN] and [EL] describes uses that are not included in Canadian product labeling.
The [EL US] or [EL CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE BOLUSES

Usual dose:
[EL US] Bacterial pneumonia [EL];
[EL US] Calf diphtheria [EL]; or
[EL US] Pododermatitis [EL]—*Cattle:* Oral, 48.8 mg sulfamethazine, 73 mg sulfanilamide, and 73 mg sulfathiazole per kg of body weight as an initial dose, followed by 24.4 mg sulfamethazine, 36.5 mg sulfanilamide, and 36.5 mg sulfathiazole per kg of body weight, administered twelve hours later.{R-97}
Withdrawal times—Canada: Meat—10 days, Milk—96 hours.{R-97}

Strength(s) usually available:{R-92}
U.S.—
Veterinary-labeled product(s):
Not commercially available.
Canada—
Veterinary-labeled product(s):
3.9 grams sulfamethazine, 5.85 grams sulfanilamide, and 5.85 grams sulfathiazole (OTC) [*Triple Sulfa Bolus*].{R-97}

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from moisture.

Additional information: Animals should maintain an adequate water intake during the treatment period.

USP requirements: Not in USP.{R-56}

SULFAMETHAZINE AND SULFATHIAZOLE

Oral Dosage Forms

Note: The text between [EL US] and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN] and [EL] describes uses that are not included in Canadian product labeling.
The [EL US] or [EL CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFAMETHAZINE AND SULFATHIAZOLE POWDER FOR ORAL SOLUTION

Usual dose:
[EL US] Enteritis [EL]—*Cattle* and *pigs:* Oral, 144 mg of sulfamethazine and 72 mg of sulfathiazole per kg of body weight as an initial dose, followed by 72 mg of sulfamethazine and 36 mg of sulfathiazole per kg of body weight a day for three days, administered as an individual animal drench or in the only source of drinking water.{R-15}
Withdrawal times—Canada: *Cattle*—Meat: 10 days, Milk: 96 hours. *Pigs*—Meat: 10 days.{R-15}
[EL US] Pneumonia, bacterial [EL]; or
[EL US] Pododermatitis [EL]—*Cattle:* Oral, 144 mg of sulfamethazine and 72 mg of sulfathiazole per kg of body weight as an initial dose, followed by 72 mg of sulfamethazine and 36 mg of sulfathiazole per kg of body weight a day for three days,

administered as an individual animal drench or in the only source of drinking water.{R-15}
Withdrawal times—Canada: *Cattle*—Meat: 10 days, Milk: 96 hours.{R-15}

[EL US]Respiratory infections, bacterial[EL]—*Pigs:* Oral, 144 mg of sulfamethazine and 72 mg of sulfathiazole per kg of body weight as an initial dose, followed by 72 mg of sulfamethazine and 36 mg of sulfathiazole per kg of body weight a day for three days, administered as an individual animal drench or in the only source of drinking water.{R-15}
Withdrawal times—Canada: *Cattle*—Meat: 10 days, Milk: 96 hours.{R-15}

Strength(s) usually available:{R-92}
U.S.—
Veterinary-labeled product(s):
Not commercially available.
Canada—
Veterinary-labeled product(s):
630 mg sulfamethazine and 315 mg of sulfathiazole per gram of powder (OTC) [*S-M-T; Sulfa-MT*].
667 mg of sulfamethazine and 333 mg of sulfathiazole per gram of powder (OTC) [*Powder 21*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from moisture.{R-15}

Additional information: Animals should maintain an adequate water intake during the treatment period. These products should not be administered in animal feeds.

USP requirements: Not in USP.{R-56}

SULFAQUINOXALINE

Summary of Differences

Pharmacology/pharmacokinetics: Sulfaquinoxaline is minimally absorbed systemically and is referred to as an enteric sulfonamide.{R-19; 24}

Side/adverse effects: Clotting disorders similar to those resulting from coumarin anticoagulants have been reported in chickens and dogs.{R-46-50}

Oral Dosage Forms

Note: The text between [EL US] and [EL] describes uses not included in U.S. product labeling. Text between [EL CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL US] or [EL CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

SULFAQUINOXALINE ORAL SOLUTION USP

Usual dose:

Acute fowl cholera; or

Acute fowl typhoid—*Chickens* and *turkeys:* Oral, a 0.04% solution, administered as the only source of drinking water for two to three days.{R-14}
Withdrawal times—Products are not labeled for use in chickens or turkeys laying eggs for human consumption. US: Meat—10 days.{R-14} Canada: Meat—12 days.{R-95}

Coccidiosis—

[EL CAN]*Calves* and *cattle*[EL]: Oral, 13.2 mg per kg of body weight a day, administered as the only source of drinking water (a 0.015% solution) for three to five days.{R-14}
Withdrawal times—US: Meat—10 days.{R-14} Products are not labeled for use in preruminating calves or lactating dairy cattle.

Chickens: Oral, a 0.04% solution, administered as the only source of drinking water for two to three days.{R-14} Treatment should be stopped for three days, then the medication readministered as a 0.025% solution for two to four more days. The schedule may be repeated, if necessary.{R-14}
Withdrawal times—Products are not labeled for use in chickens laying eggs for human consumption. US: Meat—10 days.{R-14} Canada: Meat—12 days.{R-95}

Turkeys: Oral, a 0.025% solution of sulfaquinoxaline, administered as the only source of drinking water for two days. Treatment should be stopped for three days, then the medication readministered as a 0.025% solution for two days; treatment is then stopped for three days, then medication is readministered as the 0.025% solution for two final days. The complete schedule may be repeated, if necessary.{R-14}
Withdrawal times—Products are not labeled for use in turkeys laying eggs for human consumption. US: Meat—10 days.{R-14} Canada: Meat—12 days.{R-95}

Note: For treatment of coccidiosis in chickens and turkeys, it is recommended that litter not be changed until absolutely necessary.

Strength(s) usually available:{R-92}
U.S.—
Veterinary-labeled product(s):
200 mg per mL (OTC) [GENERIC].{R-14}
Canada—
Veterinary-labeled product(s):
192 mg per mL (OTC) [GENERIC].{R-95}

Preparation of dosage form: Fresh solutions should be prepared daily. To help avoid toxic reactions, the medication should be evenly mixed in drinking water.

Caution: People who handle this medication should avoid contact with eyes, skin, or clothing to prevent eye and skin burns. In case of contact, the areas affected should be flushed for at least fifteen minutes; medical attention should be sought for eye exposure.{R-14} Keep out of the reach of children.{R-14}

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from moisture.{R-15}

Additional information: Animals should maintain an adequate water intake during the treatment period.

Chickens: Prolonged administration of sulfaquinoxaline may result in depressed feed intake, deposition of crystals in the kidney, or interference with normal blood clotting.{R-14}

USP requirements: Preserve in tight, light-resistant containers. Label it to indicate that it is for veterinary use only. Contains the equivalent of the labeled concentration of sulfaquinoxaline, within ±10%. Meets the requirements for Identification, Deliverable volume and pH (not less than 12).{R-56}

Developed: 07/01/97
Interim revision: 07/10/98; 11/10/99; 06/30/02; 04/05/03; 06/30/07

References

1. Sulfadimethoxine product information (Albon Boluses, Pfizer—US), Rev 12/00. Available at www.pfizerah.com. Accessed on February 23, 2007.
2. Sulfadimethoxine product information (Albon 12.5% Concentrated

Solution, Pfizer—US). In: Arrioja-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2007.
3. Sulfadimethoxine product information (Albon Oral Suspension, Pfizer—US), Rev 3/03. Available at www.pfizerah.com. Accessed on February 23, 2007.
4. Sulfadimethoxine product information (Di-Methox Soluble Powder, Agri Laboratories—US). Available at www.agrilabs.com. Accessed on February 26, 2007.
5. Sulfadimethoxine product information (Albon SR, Pfizer—US), Rev 12/00. Available at www.pfizerah.com. Accessed on February 23, 2007.
6. Sulfadimethoxine product information (Albon Tablets, Pfizer—US), Rev 3/03. Available at www.pfizerah.com. Accessed on February 23, 2007.
7. Sulfamethazine package insert (Calfspan, Pfizer—Canada). Available at www.pfizer.ca. Accessed on February 28, 2007.
8. Sulfamethazine product information (Sulfamethazine bolus, PVL—Canada) In: Arrioja-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2007.
9. Sulfamethazine product information (Sulmet Soluble Powder, Fort Dodge—US). Available at www.fortdodgelivestock.com. Accessed on February 23, 2007.
10. Sulfamethazine product information (Sustain III, Durvet—US), Rev 10/03. Available at www.durvet.com. Accessed on March 1, 2007.
11. Sulfamethazine product information (Suprasulfa III Calf Bolus, Agripharm—US). In: Arrioja-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2007.
12. Sulfamethazine product information (Sulmet Drinking Water Solution 12.5%, Fort Dodge—US). Available at www.fortdodgelivestock.com. Accessed on February 23, 2007.
13. Sulfamethazine product information (Sulmet Oblets, Fort Dodge—US). Available at www.fortdodgelivestock.com. Accessed on February 23, 2007.
14. Sulfaquinoxaline product information (20% Sulfaquinoxaline Sodium Solution, IVX—US). In: Arrioja-Dechert A, editor. Compendium of veterinary products, CD ed. Port Huron, MI: North American Compendiums, Inc., 2007.
15. Sulfamethazine and sulfathiazole product information (S-M-T, Vetoquinol—Canada). Available at www.vetoquinol.ca. Accessed on February 28, 2007.
16. Sulfamethazine product information (Sulfa 25% Solution, Vetoquinol—Canada). Available at www.vetoquinol.ca. Accessed on February 28, 2007.
17. Prescott JF, Baggott, JD, editors. Antimicrobial therapy in veterinary medicine, 2nd ed. Ames, IA: Iowa State University Press, 1993. p. 119-26.
18. Appelgate J. Clinical pharmacology of sulfonamides. Mod Vet Pract 1983: 667-9.
19. Riviere J, Craigmill AL, Sundlof SF. Handbook of comparative pharmacokinetics and residues of veterinary antimicrobials. Boca Raton, FL: CRC Press, Inc., 1991. p. 339-407.
20. Plumb DC. Veterinary drug handbook. White Bear Lake, MN: PharmaVet Publishing, 1991. p. 520-9.
21. Vree TB, Reekers-Ketting JJ, Hekster CA, et al. Acetylation and deacetylation of sulphonamides in dogs. J Vet Pharmacol Ther 1983; 6: 153-6.
22. Mathis GF, McDougald LR. Drug responsiveness of field isolates of chicken coccidia. Poultry Sci 1982; 61: 38-45.
23. Watts JL, Yancey RJ, Salmon SA, et al. A 4-year survey of antimicrobial susceptibility trends for isolates from cattle with bovine respiratory disease in North America. J Clin Microbiol 1994 Mar; 32(3): 725-31.
24. Spoo JW, Riviere JE. Sulfonamides. In: Adams HR, editor. Veterinary pharmacology and therapeutics, 8th ed. Ames, Iowa: Blackwell Publishing. 2001. p. 796.
25. Charm SE, Zoner E, Salter R. Confirmation of widespread sulfonamide contamination in Northeast United States market milk. J Food Prod 1988 Dec; 51(12): 920-4.
26. Cribb AE, Spielberg SP. An in vitro investigation of predisposition to sulphonamide idiosyncratic toxicity in dogs. Vet Res Comm 1990; 14: 241-52.
27. Cribb AE. Idiosyncratic reactions to sulfonamides in dogs. J Am Vet Med Assoc 1989 Dec; 195(11): 1615.
28. Collins BK, Moore CP, Hagee JH. Sulfonamide-associated keratoconjunctivitis sicca and corneal ulceration in a dysuric dog. J Am Vet Med Assoc 1986 Oct; 189(8): 924-6.
29. Sansom J, Barnett KC, Long RD. Keratoconjunctivitis sicca in the dog associated with the administration of salicylazosulphapyridine (sulphasalazine). Vet Rec 1985; 116: 391-3.
30. Morgan RV, Bachrach A. Keratoconjunctivitis sicca associated with sulfonamide therapy in dogs. J Am Vet Med Assoc 1982; 180: 432-4.
31. Roudaut B, Moretain JP. Sulphonamide residues in milk of dairy cows following intravenous injection. Food Addit Contam 1990; 7(4): 527-33.
32. Paulson GD, Feil VJ, Giddings JM, et al. Lactose conjugation of sulphonamide drugs in the lactating dairy cow. Xenobiotica 1992; 22(8): 925-39.
33. Van Gogh H, Van Deurzen JM, Van Duin CTM, et al. Influence of gestation on the pharmacokinetics of four sulphonamides in goats. Res Vet Sci 1990; 48: 152-7.
34. Nielsen P, Rasmussen F. Half-life, apparent volume of distribution, and protein-binding for some sulphonamides in cows. Res Vet Sci 1977; 22: 205-8.
35. Van Gogh H. Pharmacokinetics of nine sulphonamides in goats. J Vet Pharmacol Ther 1980; 3: 69-81.
36. USP dictionary of USAN and international drug names, 2007 ed. Rockville, MD: The United States Pharmacopeial Convention, Inc., 2007.
37. Nouws JFM, Firth EC, Vree TB, et al. Pharmacokinetics and renal clearance of sulfamethazine, sulfamerazine, and sulfadiazine and their N4-acetyl and hydroxy metabolites in horses. Am J Vet Res 1987 Mar; 48(3): 392-402.
38. Boxenbaum HG, Fellig J, Hansen LJ, et al. Pharmacokinetics of sulphadimethoxine in cattle. Res Vet Sci 1977; 23: 24-8.
39. Baggot JD, Ludden TM, Powers TE. The bioavailability, disposition kinetics and dosage of sulphadimethoxine in dogs. Can J Comp Med 1976 Jul; 40: 310-7.
40. Ladefoged O, Christiansen SE. A computer method for the calculation of pharmacokinetic parameters after repetitive drug administration, and its use in calculations of kinetic parameters of sulphadimethoxine in pigs and rabbits. J Vet Pharmacol Ther 1979; 2: 95-9
41. Sams RA, Baggot JD. Bioavailability, disposition kinetics, and dosage of sulfadimethoxine in dogs—a correction. Can J Comp Med 1977 Oct; 41(4): 479-80.
42. Baggot JD. Pharmacokinetics of sulfadimethoxine in cats. Aust J Exp Biol Med Sci 1977; 55(6): 663-70.
43. Bajwa RS, Singh J. Studies on the levels of sulphadimethoxine and sulphamethoxypyridazine in blood of poultry. Indian J Anim Sci 1977 Sep; 47(9): 549-53.
44. Bourne DWA, Bialer M, Dittert LW, et al. Disposition of sulfadimethoxine in cattle: inclusion of protein binding factors in a pharmacokinetic model. J Pharm Sci 1981 Sep; 79(9): 1068-72.
45. Righter JF, Showalter DH, Teske RH. Pharmacokinetic study of sulfadimethoxine depletion in suckling and growing pigs. Am J Vet Res 1979; 40(5): 713-5.
46. Preusch PC, Hazelett SE, Lemasters KK. Sulfaquinoxaline inhibition of vitamin K epoxide and quinone reductase. Arch Biochem Biophys 1989 Feb 15; 269(1): 18-24.
47. Daft BM, Bickford AA, Hammarlund MA. Experimental and field sulfaquinoxaline toxicosis in leghorn chickens. Avian Dis 1989; 33: 30-4.
48. Brown MJ. Adverse reactions to sulfaquinoxaline in coyote pups. J Am Vet Med Assoc 1982; 181(11): 1419-20.
49. Osweiler GD, Green RA. Canine hypoprothrombinemia resulting

from sulfaquinoxaline administration. Vet Hum Tox 1978 Jun; 20(3): 190-2.
50. Neer TM, Savant RL. Hypoprothrombinemia secondary to administration of sulfaquinoxaline to dogs in a kennel setting. J Am Vet Med Assoc 1992 May; 200(9): 1344-5.
51. Littlefield NA, Gaylor DW, Blackwell BN, et al. Chronic toxicity/carcinogenicity studies of sulphamethazine in B6C3F1 mice. Food Chem Toxicol 1989; 27(7): 455-63.
52. Paulson G, Struble C, Mitchell A. Comparative metabolism of sulfamethazine [4-Amino-N-(4,6 dimethyl-2-pyrimidinyl)benzenesulfonamide] in the rat, chicken, pig, and sheep. 5th International Congress of Pesticide Chemistry 1983: 375-80.
53. Witkamp RF, Yun HI, van't Klooster GA, et al. Comparative aspects and sex differentiation of plasma sulfamethazine elimination and metabolite formation in rats, rabbits, dwarf goats, and cattle. Am J Vet Res 1992 Oct; 53(10): 1830-5.
54. Paulson GD. The effect of dietary nitrite and nitrate on the metabolism of sulphamethazine in the rat. Xenobiotica 1986; 16(1): 53-61.
55. Khan FH, Nawaz M, Anwar-Ul-Hasson S. Pharmacokinetics of sulfamethazine in buffaloes. Ann Rech Vet 1980; 11(1): 9-12.
56. The United States pharmacopeia. The national formulary. USP 30th revision (May 1, 2007). NF 25th ed (May 1, 2007). Rockville, MD: The United States Pharmacopeial Convention, Inc., 2006.
57. Wilson RC, Hammond LS, Clark CH, et al. Bioavailability and pharmacokinetics of sulfamethazine in the pony. J Vet Pharmacol Ther 1989; 12: 99-102.
58. Srivastava AK, Rampal S. Disposition kinetics and dosage regimen of sulphamethazine in sheep (ovis aries). Br Vet J 1990; 146: 239-42.
59. Siddique AB, Simunek J. Blood-brain barrier to sulfamethazine in rat and sheep fetus. Acta Vet Brno 1977; 46: 101-9.
60. Siddique AB, Simunek J. Placental transfer of sulfamethazine in sheep at different stages of gestation. Acta Vet Brno 1977; 46: 95-100.
61. Bourne DWA, Bevill RG, Sharma RM, et al. Disposition of sulfonamides in food-producing animals: pharmacokinetics of sulfamethazine in lambs. Am J Vet Res 1977; 38(7): 967-72.
62. Bulgin MS, Lane VM, Archer TE, et al. Pharmacokinetics, safety, and tissue residues of sustained-release sulfamethazine in sheep. J Vet Pharmacol Ther 1991; 14: 36-45.
63. Abdel Hamid Youssef S, El-Gendi AYI, El-Sayed MGA, et al. Some pharmacokinetic and biochemical aspects of sulphadiazine and sulphadimidine in ewes. J Vet Pharmacol Ther 1981; 4: 173-82.
64. Bevill RF, Rajinder MS, Meachum SH, et al. Disposition of sulfonamides in food-producing animals: concentrations of sulfamethazine and its metabolites in plasma, urine, and tissues of lambs following intravenous administration. Am J Vet Res 1977 Jul; 30(7): 873-7.
65. Righter HF, Showalter DH, Teske RH. Comparative plasma kinetics of orally administered sulfamethazine in clinically parasitized and parasitism-treated lambs. J Vet Pharmacol Ther 1979; 2: 203-8.
66. Sweeney RW, Bordalaye PC, Smith CM, et al. Pharmacokinetic model for predicting sulfamethazine disposition in pigs. Am J Vet Res 1993 May; 54(5): 750-4.
67. Duffee NE, Bevill RF, Thurman JC, et al. Pharmacokinetics of sulfamethazine in male, female, and castrated male swine. J Vet Pharmacol Ther 1984; 7: 203-11.
68. Ashworth RB, Epstein RL, Thomas MH, et al. Sulfamethazine blood/tissue correlation study in swine. Am J Vet Res 1986 Dec; 47(12): 2596-603.
69. Klasco RK, editor. USP DI Drug information for the healthcare professional. Volume I. Greenwood Village, CO: MICROMEDEX, Inc.; 2006.
70. Van Poucke LSG, Van Peteghem CH. Pharmacokinetic and tissue residues of sulfathiazole and sulfamethazine in pigs. J Food Protect 1994 Sep; 57(9): 796-801.
71. Struble LB, Paulson GD. The metabolism and deamination of [^{14}C]-sulphamethazine in a germ-free pig: the influence of nitrate and nitrite. Food Chem Toxicol 1988 May; 260: 797-801.
72. Mitchell AD, Paulson GD, Saylskie RG. Steady state kinetics of ^{14}C-sulfamethazine {4-amino-N-(4,6-dimethyl-2-pyrimidinyl)benzene[U-^{14}C]sulfonamide} metabolism in swine. Drug Metab Dispos 1986; 14(2): 155-60.
73. Mitchell AD, Paulson GD. Depletion kinetics of ^{14}C-sulfamethazine in swine. Drug Metab Dispos 1986; 14(2): 161-7.
74. Whipple DM, Samuelson G, Heath GE, et al. Tissue residue depletion and recycling of sulfamethazine in swine. J Am Vet Med Assoc 1980; 176(12): 1348-52.
75. Kuiper HA, Aerts RMC, Haagsma N, et al. Case study of the depletion of sulfamethazine from plasma and tissues upon oral administration to piglets affected with atrophic rhinitis. J Agric Food Chem 1988; 36: 822-5.
76. Church TL, Janzen ED, Sisodia CS, et al. Blood levels of sulfamethazine achieved in beef calves on medicated drinking water. Can Vet J 1979; 20: 41-4.
77. Paulson GD, Feil VJ, Zaylskie RG, et al. Depletion of residues from milk and blood of cows dosed orally and intravenously with sulfamethazine. J Assoc Off Anal Chem 1994; 77(4): 895-900.
78. Nouws JFM, Mevius D, Vree TB, et al. Pharmacokinetics, metabolism, and renal clearance of sulfadiazine, sulfamerazine, and sulfamethazine and of their N_4-acetyl and hydroxy metabolites in calves and cows. Am J Vet Res 1988 Jul; 49(7): 1059-65.
79. Nouws JFM, Vree TB, Baakman M, et al. Age and dosage dependency in the plasma disposition and the renal clearance of sulfamethazine and its N_4-acetyl and hydroxy metabolites in calves and cows. Am J Vet Res 1986 Mar; 47(3): 642-9.
80. Murphy J, Wong M, Ray WH. The advantages of a timed-release sulfamethazine bolette for calves. Vet Med 1986 Sep; 8(9): 882-5.
81. Miller GE, Stowe CM, Jegers A, et al. Blood concentration studies of a sustained release form of sulfamethazine in cattle. J Am Vet Med Assoc 1969; 154: 773-8.
82. Bevill RF, Dittert LW, Bourne DWA. Disposition of sulfonamides in food-producing animals IV: pharmacokinetics of sulfamethazine in cattle following administration of an intravenous dose and 3 oral dosage forms. J Pharm Sci 1977 May; 66(5): 619-23.
83. Bajwa RS, Singh J. Studies on the effect of prolonged administration of sulphadimethoxine and sulphamethoxypyridazine on the growth rate and hematology of chicks. Indian J Anim Sci 1977 Oct; 47(10): 692-3.
84. Koritz D, Bourne DWA, Dittert LW, et al. Disposition of sulfonamides in food-producing animals: pharmacokinetics of sulfathiazole in sheep. Am J Vet Res 1977; 38(7): 979-82.
85. Panel comment, Rec 6/20/96.
86. National Committee for Clinical Laboratory Standards publication. Villanova, PA: NCCLS, 1983; 3(14): M2-T3.
87. Sulfachlorpyridazine product information (Vetisulid Injection, Fort Dodge—US). Available at www.fortdodgelivestock.com. Accessed on February 23, 2007.
88. Sulfadimethoxine product information (Sulfadimethoxine Injection-40%, Vedco—US). Available at www.vedco.com. Accessed on February 26, 2007.
89. Sulfachlorpyridazine product information (Vetisulid Powder, Fort Dodge—US), Rev 9/98. Available at www.fortdodgelivestock.com. Accessed on February 23, 2007.
90. Duran SP, Valera RC, Manzano JV, et al. Comparative in-vitro susceptibility of Bacteroides and Fusobacterium isolated from footrot in sheep to 28 antimicrobial agents. J Vet Pharmacol Ther 1991; 14: 185-92.
91. Sulfadimethoxine product information (S-125, Vetoquinol—Canada). Available at www.vetoquinol.ca. Accessed on February 23, 2007.
92. Arrioja-Dechert A, editor. Compendium of veterinary products, CD ed. Port Huron, MI: North American Compendiums, Inc.,

2007.
93. Stowe CM, Sisodia CS. The pharmacologic properties of sulfadimethoxine in dairy cattle. Am J Vet Res 1963; 24: 525-35.
94. Reynolds JEF, editor. Martindale, the extra pharmacopeia. 29th ed. London: The Pharmaceutical Press, 1989. p. 301.
95. Sulfaquinoxaline product information (Sulfaquinoxaline 19.2% Liquid Concentrate, Dominion Veterinary—Canada). Available at www.domvet.com. Accessed on February 28, 2007.
96. Sulfamethazine and sulfathiazole combination product information (Powder 21, PVL—Canada). In: Arrioja-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2007.
97. Sulfamethazine, sulfanilamide, and sulfathiazole product information (Triple Sulfa Bolus, PVL—Canada) In: Arrioja-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2007.
98. AVC (Marion Merrell Dow), Rev 4/91. In: PDR Physicians' desk reference. 49th ed. 1995. Montvale, NJ: Medical Economics Data Production Company, 1995. p. 1394-5.
99. Reece RL, Barr DA, Gould JA. Poisoning in a chicken flock caused by sulphachloropyrazine. Vet Rec 1986; 119: 324-5.
100. Hall IA, Campbell KL, Chambers MD, et al. Effect of trimethoprim/sulfamethoxazole on thyroid function in dogs with pyoderma. J Am Vet Med Assoc 1993 Jun 15; 202(12): 1959-62.
101. Panciera DL, Post K. Effect of oral administration of sulfadiazine and trimethoprim in combination on thyroid function in dogs. Can J Vet Res 1992; 56: 349-52.
102. Rasmussen F. Mammary excretion of sulphonamides. Acta Pharmacol Toxicol 1958; 15: 139-48.
103. Panel comment, 5/8/96.
104. Drugs prohibited for extra-label use in animals. In: Code of Federal Regulations. Washington, D.C.: US Government Printing Office. April 1, 2002. 21 CFR 530.41. Available at www.gpoaccess.gov/cfr/index.html. Accessed on March 5, 2007.
105. Langston VC, Davis LE. Factors to consider in the selection of antimicrobial drugs for therapy. Compend Contin Educ Pract Vet 1989 Mar; 11(3): 355-63.
106. Panel comment, 5/21/96.
107. Panel comment, 5/23/96.
108. Panel comment, 5/21/96.
109. Sulfamethazine, sulfamerazine, and sulfaquinoxaline product information (PoultrySulfa, Alpharma—US). In: Arrioja-Dechert A, editor. Compendium of veterinary products, CD edition. Port Huron, MI: North American Compendiums, Inc., 2007.

