SULFONAMIDES (Veterinary—Systemic)

This monograph includes information on the following:

Some commonly used brand names are:
For veterinary-labeled products—
Albon Boluses
[Sulfadimethoxine] Sulfadived 12.5% Oral
Solution [Sulfadimethoxine]
Albon 12.5% Concentrated Solution [Sulfadimethoxine]
Albon Oral Suspension 5% [Sulfadimethoxine] Sulfadine
Albon SR [Sulfadimethoxine]
Albon Tablets Sulfasal
[Sulfadimethoxine] Sulfatran
Calfspan [Sulfamethazine] Sulmet Drinking Water Solution 12.5%
[Sulfadimethoxine]
Di-Methox Injection-40% [Sulfadimethoxine] Sulmet Oblets
Di-Methox 12.5% Oral Solution [Sulfadimethoxine]
[Poultry Sulf] Sulmet Soluble Powder
[Sulfadimethoxine]
Poultry Sulf [Sulfadimethoxine, Sulflameazine, and Sulfoflaxazine] Suprasulfal III Calf Bolus
[Sulfadimethoxine]
Powder 21 [Sulfadimethoxine and Sulfaflaxazine] Sustain III
[Sulfadimethoxine] Sustain III Calf Bolus
S-125 [Sulfadimethoxine] Sustain III Calf Bolus
S-250 [Sulfadimethoxine] Sustain III Calf Bolus
[Sulfadimethoxine]
SDM Injection [Sulfadimethoxine] Triple Sulfal Bolus
[Sulfadimethoxine]
SDM Solution [Sulfadimethoxine] Vetisulid Injection
[Sulfachlorpyridazine] Vetisulid Powder
[Sulfadimethoxine and Sulfaflaxazine] Vetisulid Powder
[Sulfachlorpyridazine]
SMZ-Med 454 [Sulfadimethoxine]

Note: For a listing of dosage forms and brand names by country availability, 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; 19] They are considered ineffective against most obligate anaerobes and should not be used to treat serious anaerobic infections.[R-2; 4; 8] 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 Fuso bacterium, 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-86 to 93] 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-86]

Accepted

Coccidiosis (treatment)—Resistance to sulfonamides by coccidia has been reported in several species, including cattle, chickens.[R-12; 146] and sheep.[R-168] 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-3; 6] Calves and cattle:[R-17] Sulfadimethoxine extended-release boluses are indicated in the treatment of Eimeria bovis and Eimeria zuernii.[R-41] Sulfaquinoxaline is indicated in the control and treatment of susceptible E. bovis and E. zuernii.[R-14]

Chickens: [R-12; 146]Sulfadimethoxine oral solution and powder for oral solution are indicated in the treatment of outbreaks of coccidiosis caused by susceptible coccidia.[R-2; 4]
Sulfadimethoxine oral solution; Sulfaquinoxaline oral solution, Sulfamerazine, sulfamethazine, and sulfadimethoxine extended-release boluses are indicated in the treatment of Eimeria bovis and Eimeria zuernii.[R-14] Sulfaquinoxaline is indicated in the control of outbreaks of susceptible E. bovis and E. zuernii.[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: [R-12; 146]Sulfadimethoxine oral solution and powder for oral solution are indicated in the treatment of outbreaks of coccidiosis caused by susceptible coccidia.[R-2; 4]
Sulfadimethoxine oral solution; Sulfaquinoxaline oral solution, Sulfamerazine, sulfamethazine, and sulfadimethoxine extended-release boluses are indicated in the control of susceptible Eimeria adenoeides and Eimeria meleagritis.[R-9; 12; 108] Sulfaquinoxaline is indicated in the control of outbreaks of susceptible E. adenoeides and E. meleagritis.[R-14]

Coryza, infectious (treatment)—Chickens: [R-12; 146]Sulfadimethoxine oral solution and powder for oral solution are indicated in the treatment of outbreaks of infectious coryza caused by susceptible Haemophilus gallinarum.[R-2; 4] Sulfamethazine oral solution and Sulfaquinoxaline powder for oral solution are indicated in the control of...
infectious coryza caused by susceptible *H. gallinarum*.\textsuperscript{[R-6; 12]}

Cystitis, bacterial (treatment)—*Cats and dogs*: Sulfadimethoxine \textsuperscript{[R-2; 4]} or oral suspension\textsuperscript{[R-2; 4]} 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.\textsuperscript{[R-3; 6]}

Diphtheria (treatment)—*Cattle*: Sulfadimethoxine boluses, extended-release boluses, injection, oral solution, and powder for oral solution\textsuperscript{[R-9; 12; 14; 109]}; and sulfamethazine boluses, extended-release boluses, oral solution, and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} powder for oral solution are indicated in the treatment of diphtheria but are not recommended in advanced or serious infections.\textsuperscript{[R-6; 9; 93]} Sulfadimethoxine boluses, extended-release boluses, injection, oral solution, and powder for oral solution\textsuperscript{[R-9; 12; 14; 109]}; and sulfamethazine boluses, extended-release boluses, oral solution, and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} powder for oral solution\textsuperscript{[R-9; 12; 14; 109]} are indicated in the treatment of calf diphtheria caused by susceptible *Fusobacterium necrophorum*.\textsuperscript{[R-6; 9; 93]}

Sulfamethazine, sulfanilamide, and sulfathiazole combination is indicated as an aid in the treatment of diphtheria in calves.\textsuperscript{[R-9; 12]}

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.\textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} Calves, less than 1 month of age;\textsuperscript{[R-86; 90; 93]} Sulfachlorpyridazine injection and powder for oral solution are indicated in the treatment of diarrhea caused or complicated by *Escherichia coli*.\textsuperscript{[R-49]}

*Calves* and *cattle*: Sulfamethazine boluses, extended-release boluses, oral solution, and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} powder for oral solution\textsuperscript{[R-9; 12; 14; 109]}; and sulfamethazine and sulfathiazole combination\textsuperscript{[R-86; 90; 93]} are indicated in the treatment of enteritis (colibacillosis, scours) caused by susceptible *E. coli*.\textsuperscript{[R-7; 9; 10; 12; 13; 15]}

*Dogs*: Sulfadimethoxine boluses and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} oral suspension\textsuperscript{[R-86; 90; 93]} are indicated in the treatment of enteritis caused by susceptible *Salmonella* species.\textsuperscript{[R-3; 6]}

*Foals*: Sulfamethazine boluses are indicated in the treatment of enteritis caused by susceptible *E. coli*.\textsuperscript{[R-13]}

*Pigs*: Sulfachlorpyridazine powder for oral solution\textsuperscript{[R-3; 6]}; and sulfamethazine oral solution and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} powder for oral solution\textsuperscript{[R-9; 12; 14; 109]} are indicated in the treatment of enteritis caused by susceptible *E. coli*.\textsuperscript{[R-9; 12; 14; 109]} Sulfamethazine and sulfathiazole combination is indicated to aid in the treatment of enteritis.\textsuperscript{[R-9; 12; 14; 109]}

*Sheep*: Sulfamethazine oral solution is indicated in the treatment of enteritis caused by susceptible organisms.\textsuperscript{[R-14; 123]}

Fowl choler (treatment)—

*Chickens*: Sulfadimethoxine oral solution and powder for oral solution\textsuperscript{[R-2; 4]} are indicated in the treatment of acute fowl cholera caused by susceptible *Pasteurella multocida*.\textsuperscript{[R-2; 4]}

Sulfadimethoxine oral solution and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} powder for oral solution; sulfamerazine, sulfamethazine, and sulfadimethoxine combination powder for oral solution; and sulfadimethoxine oral solution are indicated in the control of acute fowl cholera caused by susceptible *P. multocida*.\textsuperscript{[R-9; 12; 14; 109]}

*Turkeys*: Sulfadimethoxine oral solution and powder for oral solution\textsuperscript{[R-2; 4]} are indicated in the treatment of acute fowl cholera caused by susceptible *P. multocida*.\textsuperscript{[R-2; 4]}

Sulfamerazine, sulfamethazine, and sulfadimethoxine combination powder for oral solution; and sulfadimethoxine oral solution are indicated in the control of acute fowl cholera caused by susceptible *P. multocida*.\textsuperscript{[R-14; 109]}

Fowl typhoid (treatment)—*Chickens and turkeys*: Sulfadimethoxine oral solution is indicated in the control of acute fowl typhoid cholera caused by susceptible *Salmonella gallinarum*.\textsuperscript{[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.\textsuperscript{[R-7; 11; 13]}

However, *in vitro* studies have shown high levels of resistance to sulfamethazine by *Mannheimia (Pasteurella) haemolytica* and *P. multocida*.\textsuperscript{[R-23]}

Sulfamethazine, sulfanilamide, and sulfathiazole combination is indicated as an aid in the treatment of pneumonia caused by susceptible organisms;\textsuperscript{[R-9; 12]} 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 \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} powder for oral solution\textsuperscript{[R-9; 12; 14; 109]}; sulfadimethoxine boluses, extended-release boluses, injection, oral solution, and powder for oral solution; and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} sulfamethazine and sulfathiazole combination\textsuperscript{[R-86; 90; 93]} are indicated in the treatment of bacterial pneumonia and bovine respiratory disease complex caused by susceptible organisms.\textsuperscript{[R-9; 12]}

*Sheep*: Sulfamethazine, sulfanilamide, and sulfathiazole combination is indicated as an aid in the treatment of pneumonia.\textsuperscript{[R-9; 12]} However, *in vitro* studies have shown high levels of resistance to sulfamethazine by *M. haemolytica* and *P. multocida*.\textsuperscript{[R-23]} and the sulfonamides generally have 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, but may affect aerobic organisms that create the microenvironment in which *Fusobacterium* thrive; therefore, sulfonamides may be useful in the treatment of pododermatitis but are not recommended in advanced or serious infections.\textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} Sulfamethazine and sulfathiazole combination\textsuperscript{[R-86; 90; 93]} are indicated in the treatment of pododermatitis caused by susceptible *Fusobacterium necrophorum*.\textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]}

Sulfamethazine and sulfathiazole combination and sulfanilamide, sulfaquinoxaline, and sulfathiazole combination are indicated as aids in the treatment of necrotic pododermatitis caused by susceptible *F. necrophorum*.\textsuperscript{[R-15; 96; 97]}

Pullorum disease (treatment)—*Chickens*: Sulfamethazine oral solution and \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} powder for oral solution are indicated in the control of susceptible *Salmonella pullorum*.\textsuperscript{[R-9; 12]}

Respiratory infections, bacterial (treatment)—

*Chats and dogs*: Sulfadimethoxine oral suspension and tablets are indicated in the treatment of respiratory infections, such as bronchitis, caused by susceptible organisms.\textsuperscript{[R-3; 6]}

*Pigs*: Sulfamethazine and sulfathiazole combination is indicated as an aid in the treatment of respiratory infections caused by susceptible organisms.\textsuperscript{[R-45]}

*Sheep*: Sulfamethazine oral solution is indicated in the treatment of acute respiratory infections caused by susceptible organisms.\textsuperscript{[R-44]}

Skin and soft tissue infections (treatment)—*Chats and dogs*: Sulfadimethoxine \textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} oral suspension\textsuperscript{[R-1; 5; 7; 9; 10; 12; 13; 15]} and tablets are indicated in the treatment of skin and soft tissue infections;\textsuperscript{[R-8; 4]} 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.
Sulfathiazole—Benzenesulfonamide, 4-amino-

Sulfamerazine—Benzenesulfonamide, 4-amino-

Sulfanilamide—C₆H₈N₂O₂S.

Sulfadimethoxine—C₁₂H₁₄N₄O₄S.

Sulfaquinoxaline—C₁₄H₁₂N₄O₂S.

Sulfamerazine—C₁₁H₁₂N₄O₂S.

Sulfamethazine—Benzenesulfonamide, 4-amino-

Sulfanilamide—172.20.

Sulfamerazine—264.30.

Sulfamethazine—Benzenesulfonamide, 4-amino-

Sulfanilamide—10.5.

Sulfamerazine—1-2-Quinoxalinylsulfanilamide.

Sulfadimethoxine; sulfamethazine; sulfaquinoxaline; and sulfamerazine, sulfamethazine, and sulfaquinoxaline combination; and sulfamerazine, sulfanilamide, and sulfathiazole combination. See the Dosage Forms section.

Chemical name:

Sulfachlorpyridazine—N²-(6-Chloro-3-pyridazinyl)sulfanilamide.

Sulfadimethoxine—Benzenesulfonamide, 4-amino-N-(2,6-dimethoxy-4-pyrimidinyl)-.

Sulfamerazine—Benzenesulfonamide, 4-amino-N-(4-ethyl-2-pyrimidinyl)-.

Sulfamethazine—Benzenesulfonamide, 4-amino-N-(4,6-dimethyl-2-pyrimidinyl)-.

Sulfanilamide—p-Aminobenzenesulfonamide.

Sulfaquinoxaline—N²-2-Quinoxalinylsulfanilamide.

Sulfathiazole—Benzenesulfonamide, 4-amino-N-2-thiazolyl-.

Molecular formula:

Sulfachlorpyridazine—C₁₄H₁₁C₅N₁O₁S₄.[R-36]

Sulfadimethoxine—C₁₂H₁₄N₂O₄S.[R-36]

Sulfamerazine—C₁₁H₁₂N₂O₄S.[R-36]

Sulfamethazine—C₁₂H₁₄N₄O₄S.[R-36]

Sulfanilamide—C₆H₈N₂O₂S.[R-36]

Sulfaquinoxaline—C₁₄H₁₂N₄O₂S.[R-36]

Sulfathiazole—C₁₄H₁₂N₂O₂S.[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-36]

Sulfamethazine USP—White to yellowish white powder, which may darken on exposure to light. Practically odorless.[R-36]

Sulfanilamide—White, odorless, crystalline powder.[R-36]

Sulfaquinoxaline—Yellow, odorless powder.[R-36]

Sulfathiazole USP—Fine, white or faintly yellowish white, practically odorless powder.[R-36]

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, ether, in chloroform, and in hexane; practically insoluble in water.[R-36]

Sulfamethazine USP—Very slightly soluble in water and in ether; soluble in acetone; slightly soluble in alcohol.[R-36]

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 petroluem ether.[R-36]

Sulfaquinoxaline—Practically insoluble in water; very slightly soluble in alcohol; practically insoluble in ether; freely soluble in aqueous solutions of alkalai.[R-36]

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-36]

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-19; 46]

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 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]

Sulfanilamide:

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-26] Sulfonamides may be distributed into milk; however, they vary greatly in their ability to do so. The
N-acetyl metabolites have no antimicrobial activity and
process depends on several factors, including protein binding and pKa values.

Volume of distribution—
Sulfadimethoxine:
Goats—Area: 0.49 ± 0.095 liters per kg (L/kg). [R-38]
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-46]
Sulfamethazine:
Buffalo—Area: 0.44 ± 0.17 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-67]
Lambs—Area: 0.334 ± 0.031 L/kg. [R-61]
Pigs—Area: 0.5; 0.77 ± 0.06 L/kg. [R-26]
Administered in conjunction with sulfathiazole: Area—
1.01 ± 0.12 L/kg. [R-70]
Sheep—Area: 0.4 L/kg; 0.6 L/kg. [R-98]
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-45]
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-70]
When plasma concentration is more than 50 mcg/mL—
51%, [R-70]
Goats: 86%, [R-35]
Horses: 70%, [R-37]
Sheep: 77%, [R-88]
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, glucuronidation, 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-39]
Metabolites are considered to be unable to acetylate sulfonamides to any significant degree. [R-148]
N-acetyl metabolites have no antimicrobial activity and
hydroxymetabolites have 2.5 to 39.5% of the activity of the parent compound. [R-57]
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-acetyl sulfamethazine, desaminosulfamethazine and the N-glucose conjugate of sulfamethazine. [R-72] In general, metabolites of sulfonamides are cleared more quickly than the parent drug; 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-75]
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, but there is no

**Conclusion:**
Sulfonamides are primarily metabolized in the liver but metabolism also occurs in other tissues. 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. Metabolites are considered to be unable to acetylate sulfonamides to any significant degree. N-acetyl metabolites have no antimicrobial activity and hydroxymetabolites have 2.5 to 39.5% of the activity of the parent compound. 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. In pigs, sulfamethazine is metabolized into N-acetyl sulfamethazine, desaminosulfamethazine and the N-glucose conjugate of sulfamethazine. In general, metabolites of sulfonamides are cleared more quickly than the parent drug; 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. 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, but there is no
Sulfathiazole—Total clearance:

Cattle:

Sulfadimethoxine—

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Sulfamethazine—

Sulfonamides are also distributed in relatively small amounts into milk, saliva, and into the gastrointestinal tract. {R-44}

Horses:

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-44}

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.

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-57}

Pigs: 24.5% of a sulfamethazine dose is excreted in the urine as unchanged drug and 52.1% as measured metabolite. {R-47}

Sheep: 18% of a sulfamethazine dose is excreted into the urine as parent compound and 53% as metabolites. {R-44}

Total clearance:

Buffalo—0.93 mL/min/kg. {R-85}

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-06}

Pigs—0.35 mL/min/kg. {R-45}

Ponies—0.7 mL/min/kg. {R-87}

Sheep—1.6 mL/min/kg. {R-84}

Sulfathiazole—Total clearance: Pigs—1.5 mL/min/kg. {R-78}

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-20; 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; 66}

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-61} 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; 46} Some teratogenic effects have been seen when very high doses were given to pregnant mice and rats. {R-36}

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-163; 1645} 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; 32} 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-27}

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-49}

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
The following laboratory value alterations have been reported in human, 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:

**A. 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).

### Side/adverse effects

- **Anticonvulsants, hydantoins, or oral antidiabetic agents.** (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)
- **Hemolytic anemia.** (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 Phenytoin.** (The effects of methotrexate may be potentiated during concurrent use with sulfonamides because of displacement from plasma protein binding sites; phenytoin 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)

### 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.**
- **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. It can be minimized in susceptible
Dogs

**Cutaneous drug eruption**; **hepatitis; hypothyroidism**; **idiosyncratic toxicosis**; **blood dyscrasias, including anemia, leukopenia or thrombocytopenia; fever; focal retinitis; lymphadenopathy; nonseptic polyarthritis; polymyositis; skin rash**; **keratoconjunctivitis sicca**

Note: **Iatrogenic hypothyroidism** may occur and thyroid function test values may be lowered in dogs administered sulfonamides. Although studies have looked at this reaction with potentiated sulfonamides, sulfonamides administered alone have been reported to impair thyroid function. 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. 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. 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. When sulfonamide therapy is discontinued, recovery generally occurs within 2 to 5 days.

**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. The most frequent reports have been with sulfasalazine or trimethoprim and sulfonamide combination, 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, hemoptyis, lethargy, pale mucous membranes, possibly death)

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. Sulfaquinoxaline is a vitamin K antagonist that inhibits vitamin K epoxide and vitamin K quinone reductase and causes an effect similar to that of coumarin anticoagulants. 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. Rapid discontinuation of medication and initiation of therapy with vitamin K may reverse the effects.

**Human side/adverse effects**

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**

**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.

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SULFACHLORPYRIDAZINE

Summary of Differences
Pharmacology/pharmacokinetics: Intermediate duration of action.[R-19; 24]

Oral Dosage Forms
Note: The text between [US] and [L] describes uses not included in U.S. product labeling. Text between [LCAN] and [L] describes uses that are not included in Canadian product labeling. The [US] or [L] 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: [LCAN] Enteritis (diarrhea associated with E. coli)[L] —
Calves, less than 1 month of age: Oral, 33 to 49.5 mg per kg of body weight every twelve hours.[R-87]
Withdrawal times — US: Meat — 7 days.[R-87] 
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-82]
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]

SULFADIMETHOXINE

Summary of Differences
Pharmacology/pharmacokinetics: Intermediate to long duration of action.[R-19; 24]

Oral Dosage Forms
Note: The text between [US] and [L] describes uses not included in U.S. product labeling. Text between [LCAN] and [L] describes uses that are not included in Canadian product labeling. The [US] or [L] 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: [LCAN] Calf diphtheria[L]; 
Pneumonia, bacterial[L]; or 
Pododermatitis[L] — 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-3]
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—

Parenteral Dosage Forms
Note: The text between [US] and [L] describes uses not included in U.S. product labeling. Text between [LCAN] and [L] describes uses that are not included in Canadian product labeling. The [US] or [L] 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: [LCAN] Enteritis (diarrhea associated with E. coli)[L] —
Calves, less than 1 month of age: Intravenous, 33 to 49.5 mg per kg of body weight every twelve hours.[R-47] 
Withdrawal times — US: Meat — 5 days.[R-47] 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-47]

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

USP requirements: Not in USP.[R-56]
Veterinary-labeled product(s):
Not commercially available.

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

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.

SULFADIMETHOXINE EXTENDED-RELEASE BOLUSES
Usual dose:
- Bacterial pneumonia
- Calf diphtheria
- Pododermatitis in cattle

Withdrawal times—US: Meat—21 days. 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.

Strength(s) usually available:
- Veterinary-labeled product(s):
  - 12.5 grams (Rx) [Albon SR].

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.

SULFADIMETHOXINE ORAL SUSPENSION
Usual dose:
- Bacterial pneumonia and other respiratory infections
- Cystitis
- Skin and soft tissue infections in cats and dogs
- Enteritis associated with coccidiosis or Salmonella
- Fowl cholera

Withdrawal times—US: Meat—5 days.

Strength(s) usually available:
- 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].
  - 50 mg per mL (Rx) [Albon Oral Suspension 5%].

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.

Stability: Freezing or discoloration does not affect stability. Medication should be thawed before using.

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.
±10%. Meets the requirements for Identification and pH (5.0–7.0). [R-86]

SULFADIMETHOXINE SOLUBLE POWDER USP

Usual dose:
- Bacterial pneumonia; Calf diphtheria; or
- Pododermatitis—Calves and cattle: Oral, 55 mg per kg of body weight (2.4 to 3.3 grams per kg of body weight) 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.

- Coccidiosis; or
- Fowl cholera—Chickens, broiler and replacement: Oral, 1892 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.

- Infectious coryza outbreaks—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 turkeys older than 16 weeks of age.

Strength(s) usually available: [R-92]

- 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 below 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. [R-94]

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-84]

Parenteral Dosage Forms

SULFADIMETHOXINE INJECTION

Usual dose:
- Calf diphtheria; or
- Pneumonia, bacterial; or
- Pododermatitis—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-86]

Withdrawal times—US: Meat—5 days. [R-86]

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]

- 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-86]

SULFAMERAZINE, SULFAMETHAZINE, AND SULFAQUINOXALINE

Oral Dosage Forms

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

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

Withdrawal times—Canada: Meat—12 days, Milk—96 hours.

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. 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.

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

Fowl cholera, acute—**Chicken**s 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.

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

Strength(s) usually available:
- Veterinary-labeled product(s):
  - U.S.: 400 mg sulfamerazine, 400 mg sulfamethazine, and 200 mg sulfaquinoxaline per gram (OTC) [Poultry Sulfam].
  - Canada: 15 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. Protect from moisture.

Preparation of dosage form: Medication should not be mixed or administered in galvanized containers.

Additional information: Product labeling states that litter should not be changed during treatment. Keep out of the reach of children.

USP requirements: Not in USP.

SULFAMETHAZINE EXTENDED-RELEASE 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. 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.

Withdrawal times—US: Meat—10 days. 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. Products are not labeled for use in preruminating calves or horses to be used in human food production.

Strength(s) usually available:
- Veterinary-labeled product(s):
  - U.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.

Oral Dosage Forms

Note: The text between **US** and **CAN** describes uses not included in U.S. product labeling. Text between **US** and **CAN** describes uses that are not included in Canadian product labeling. The **US** or **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:
- Oral, 330 to 350 mg per kg of body weight as a single dose.

Withdrawal times—US: Meat—8 or 12 days, depending on the product. 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 days, Milk—96 hours.
or 28 days, depending on the product. Products are not labeled for use in lactating dairy cattle.\(^{[R-9]}\)

### Strength(s) usually available:\(^{[R-92]}\)

**U.S.—**

Veterinary-labeled product(s):
- 8 grams (OTC) \[Sustain III Calf Bolus]\.
- 8.25 grams (OTC) \[Suprasulfia II Calf Bolus]\.
- 30 grams (OTC) \[Suprasulfia III Cattle Bolus]\.
- 32.1 grams (OTC) \[Sustain III Cattle Bolus]\.

**Canada—**

Veterinary-labeled product(s):
- 8 grams (OTC) \[Calspan]\.
- 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.\(^{[R-84]}\)

### 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.

*Sheep*: 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.\(^{[R-14]}\)

**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—\(^{[R-12]}\)*Sheep*: 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.\(^{[R-12]}\)

**Withdrawal times**—Canada: Meat—10 days, depending on the product.\(^{[R-14]}\)

### 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.\(^{[R-84]}\)

### SULFAMETHAZINE POWDER FOR ORAL SOLUTION

#### Usual dose:
*Calf diphtheria*; or
Pododermatitis—*Calves and 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.
Oral Dosage Forms

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE BOLUSES

Usual dose:
- Bacterial pneumonia
- Calf diphtheria; or
- Pododermatitis

Veterinary-labeled product(s):
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:

SULFAMETHAZINE AND SULFATHIAZOLE

Usual dose:
- Oral, 128 to 187 mg per kg of body weight daily.

Withdrawal times:
- US: Meat—10 days.

Strength(s) usually available:

SULFAMETHAZINE, SULFANILAMIDE, AND SULFATHIAZOLE

Usual dose:
- 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 every 24 hours. (R-97)

Withdrawal times:
- Canada: Meat—10 days, Milk—96 hours. (R-97)

Strength(s) usually available:
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.\[^{[R-15]}\]

iel^17^i Respiratory infections, bacterial^13^—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.\[^{[R-86]}\]

**SULFAQUINOXALINE**

**Summary of Differences**

Pharmacology/pharmacokinetics: Sulfadimethoxine 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.\[^{[R-40-80]}\]

**Oral Dosage Forms**

Note: The text between \[^{[el]}\] and \[^{[el]}\] describes uses not included in U.S. product labeling. Text between \[^{[el; el]}\] and \[^{[el]}\] describes uses that are not included in Canadian product labeling. The \[^{[el; el]}\] or \[^{[el]}\] 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—**

iel^17^i Calves and cattle^17^: 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 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 sulfadimethoxine 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 sulfadimethoxine, within ±10%. Meets the requirements for Identification, Deliverable volume and pH (not less than 12).\[^{[R-86]}\]

Developed: 07/01/97

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

**References**
2. Sulfadimethoxine product information (Albon 12.5% Concentrated


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