PRODUCT FEATURES

- EQUISUL-SDT is proven effective in horses for the treatment of lower respiratory tract infections caused by susceptible strains of Streptococcus equi subsp. zooepidemicus in controlled field trials.
- EQUISUL-SDT safety was demonstrated in a controlled study in horses at 1X, 3X and 5X the recommended dose for 30 days.
- Easy-to-use liquid formulation.
- Significantly higher bioavailability on a mg-to-mg basis compared to an existing approved paste product, based on a pharmacokinetic crossover study.
- Low incidence of side effects in our controlled safety studies.

135 mL BOTTLE — REORDER NO: 28000
900 mL BOTTLE — REORDER NO: 28001

NDC 51072-020-01
NDC 51072-020-00

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Manufactured in the USA

FDA approved product (NADA 141-360)

EQUISUL-SDT®
(Sulfadiazine/Trimethoprim)
Contains 400 mg combined active ingredient (333 mg sulfadiazine and 67 mg of trimethoprim)

Federal law (USA) restricts this drug to use by or on the order of a licensed veterinarian.
EQUISUL-SDT is produced using Aurora Pharmaceutical’s patented drug product formulation. The product demonstrated 20% increased bioavailability over an existing paste product in a pharmacokinetic crossover study.

Administer EQUISUL-SDT orally at the dosage of 24 mg combined active ingredients per kilogram body weight (10.9 mg/lb.) twice daily for 10 days. EQUISUL-SDT can be administered by volume at 2.7 mL per 45.4 kg (2.7 mL/100 lb.) body weight. The product is available in 900 mL and 135 mL bottles.

**Efficacy**

In a controlled field efficacy study of EQUISUL-SDT in horses with lower respiratory tract infections caused by *Streptococcus equi* subsp. *zoopidemicus*, 59% (66/112) of the horses receiving EQUISUL-SDT were successfully treated, showing complete resolution of clinical symptoms within seven days after completion of treatment. In contrast, only 15% of the negative control horses demonstrated improvement during the same period. Additionally, transtracheal wash samples taken before and after treatment demonstrated that EQUISUL-SDT further indicated complete bacterial clearance of *Streptococcus equi* subsp. *zoopidemicus* in 66% of the treated animals. The incidences of adverse events associated with EQUISUL-SDT treatment during this study were comparable to those seen in the saline control group and were largely self-limiting. Diarrhea was seen in only 1.1% of the animals treated and resolved without treatment.

**Take Home Message From Efficacy Study**

Horses with lower respiratory tract infections caused by *Streptococcus equi* subsp. *zoopidemicus* were treated with EQUISUL-SDT at a dosage of 24 mg/kg twice daily for 10 days. Improved bioavailability allows a 20% lower dose than previously published.1 EQUISUL-SDT effectively treated the clinical signs of respiratory infection and eliminated the infection from the respiratory tract.


**Safety**

In a controlled safety study, horses were administered up to five times the recommended dose of EQUISUL-SDT twice daily for 30 consecutive days. While a higher incidence of loose stool was seen in animals treated with the higher dose of EQUISUL-SDT, in all cases, the incidents were self-limiting and resolved without treatment. EQUISUL-SDT is the only sulfadiazine/trimethoprim product for horses to be tested according to modern FDA requirements.

**Take Home Message From Safety Study**

EQUISUL-SDT had no serious adverse effects on clinical or laboratory parameters and no significant changes were seen in the representative tissues of mature horses when administered at up to five times the intended combined dosage of 24 mg/kg twice daily for 30 consecutive days.

Clinical Pathology
There were no significant clinical changes in clinical pathology parameters related to the administration of EQUISUL-SDT.
Sulfadiazine and trimethoprim have been used to treat infection in horses for many years. The suspension used in this study is a novel formulation with high bioavailability. When given twice daily at a dose of 24 mg/kg body weight over a 10-day dosing period, blood plasma levels remain above the MIC90 for *Streptococcus equi* subsp. *zooepidemicus* greater than 98% of the time. As with all antibiotics, it is important to follow label directions including the full 10-day dose be administered to optimize the antimicrobial value, limit the potential development of resistance, and to follow the AVMA policy on judicious use of antimicrobials.

In *Streptococcus equi* subsp. *zooepidemicus* samples isolated from lower respiratory tract infections in horses from 1989 to 2008, the MIC90 of potentiated sulfonamides has not increased, indicating that they remain valuable antimicrobials in the treatment of lower respiratory disease in horses.2 In our study, the suspension was shown to be safe, with very few adverse events noted over the 10-day treatment period.


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**Pilot Dose Study**

As a class, the effectiveness of potentiated sulfonamides is most closely related to the time the drug concentration remains above MIC90. The results of our pilot study administering a dose of 24 mg/kg of combined active ingredients resulted in a positive clinical outcome and provided drug concentrations above the MIC90 for at least 98% of the dosing interval.

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Aurora Pharmaceutical is an FDA-inspected facility and manufactures under cGMP standards. All USP grade materials are tested according to compendial standards, including tests for potency and impurities of active ingredients. Aurora products are required to pass testing prior to release for sale, thus guaranteeing batch consistency. Aurora products are tested on stability to assure quality through labeled expiration.

Aurora Pharmaceutical, LLC
www.aurorapharmaceutical.com
EQUISUL-SDT®
(Sulfadiazine/Trimethoprim)
Oral Suspension

For use in horses only.

NADA 141-360

CAUTION

Federal law (USA) restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION

EQUISUL-SDT® is a broad-spectrum antimicrobial from the potentiaded sulfonamide class of chemotherapeutic agents. These two drugs block different sequential steps in the biosynthesis of nucleic acids. Sulfadiazine inhibits bacterial synthesis of dihydrofolic acid by competing with para-aminobenzoic acid. Trimethoprim blocks the production of tetrahydrofolic acid from dihydrofolic acid, reversibly inhibiting dihydrofolate reductase. The effect of the dual action is to reduce the minimum inhibitory concentration of each agent (synergism) and to convert a bacteriostatic action to a bactericidal action. Sulfadiazine is the non-proprietary name for 4-amino-N-2-pyrimidyl-nitrobenzenesulfonamide. Trimethoprim is the non-proprietary name for (3,4,5-trimethoxyphenyl)methyl-2,4-pyrimidinediamine.

Figure 1. Structure of sulfadiazine

Figure 2. Structure of trimethoprim

EQUISUL-SDT® is indicated for the treatment of lower respiratory and other soft tissue infections in horses caused by susceptible strains of Streptococcus equi subsp. zooepidemicus.

DOSEAGE AND ADMINISTRATION

Shake well before use.

Administer EQUISUL-SDT orally at the dosage of 42 mg combined active ingredients per kilogram body weight (10.9 mgb/kg) twice daily for 10 days. EQUISUL-SDT can be administered by stomach tube at a volume of 2.7 mL per 4.5 kg (2.7 mL/100 lb) body weight.

CONTRAINDICATIONS

EQUISUL-SDT is contraindicated in horses with a known allergy to sulfadiazine, sulfonamide class antimicrobials, or trimethoprim.

WARNING

Do not use in horses intended for human consumption.

HUMAN WARNINGS

Not for use in humans. For use in animals only. Keep this and all drugs out of the reach of children. Consult a physician in the case of accidental human exposure.

Antimicrobial drugs, including sulfonamides, can cause mild to severe allergic reactions in some individuals. Avoid direct contact of the product with the skin, eyes, mouth, and clothing. Persons with a known sensitivity to sulfonamides or trimethoprim should avoid exposure to this product. If an allergic reaction occurs (e.g., skin rash, hives, difficulty breathing, facial swelling), seek medical attention.

PRECAUTIONS

Prescribing antibacterial drugs in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to treated animals and may increase the risk of development of drug-resistant animal pathogens.

The administration of antimicrobials, including sulfadiazine and trimethoprim, to horses under conditions of stress may be associated with an increased risk of diarrheic diarrhea that can be fatal. If acute diarrheic diarrhea or changes in fecal consistency are observed, additional doses of EQUISUL-SDT should not be administered and appropriate therapy should be initiated.

The safe use of EQUISUL-SDT® has not been evaluated in breeding, pregnant, or lactating horses. Potentially sulfonamides should only be used in pregnant or lactating mares when the benefits to the mare justify the risks to the fetus. Use of potentiated sulfonamides during pregnancy has been associated with an increased risk of congenital abnormalities that may be related to folate deficiency. In humans, sulfonamides pass through the placenta, are excreted in milk, and may cause hyperbilirubinemia-induced neurotoxicity in nursing neonates.

Caution: For use in horses only.

Oral Suspension

Equisul-sDT

For the 5-[(3,4,5-trimethoxyphenyl)methyl]-2,4-pyrimidinediamine.

Figure 1. Structure of trimethoprim

Decreased hematopoietic activity and blood dyscrasias have been associated with the use of elevated doses and/or prolonged administration of potentiated sulfonamides. EQUISUL-SDT® should be discontinued if prolonged clotting times, or decreased platelet, white blood cell or red blood cell counts are observed.

Sulfonamides should be used with caution in horses with impaired hepatic function. Although rare, sulfonamide use has been associated with fulminant hepatic necrosis in humans.

Neurologic abnormalities have been reported in several species following administration of potentiated sulfonamides. In horses, potentiated sulfonamides have been associated with gait alterations and behavioral changes that resolved after discontinuance of the drug.

The safe use of EQUISUL-SDT® has not been evaluated in horses less than 1 year of age.

ADVERSE REACTIONS

Reactions reported during a field study of 270 horses of various breeds, ranging from 1 to 25 years of age, which had been treated with EQUISUL-SDT® for 10 days are summarized in Table 1. At least one episode of loose stool of varying severity was observed in 98 of 382 (30%) of horses treated with EQUISUL-SDT® (n = 182), and 74 of 88 (83%) saline control horses. Of those animals experiencing loose stool, 2 out of 182 (1.1%) of the EQUISUL-SDT-treated horses and 0 out of 88 (0%) placebo-treated horses were removed from the study due to diarrhea (defined as at least one episode of watery stool). Both cases of diarrhea in this study were self-limiting and were observed several days after discontinuation of EQUISUL-SDT®.

Table 1. Number of Horses with Adverse Reactions During the Field Study with EQUISUL-SDT®

To report suspected adverse events, for technical assistance or for a copy of the MSDS, contact Aurora Pharmaceutical LLC at 1-888-215-1256 or visit our web site at www.aurora-pharm.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or visit the following web site: http://www.fda.gov/cvm/AnimalSafetyHealth.

CLINICAL PHARMACOLOGY

Following oral administration, EQUISUL-SDT® is rapidly absorbed and widely distributed throughout body tissues. Sulfadiazine levels are usually highest in the liver, while the tissue concentration to other tissues is only slightly lower than plasma concentrations. Concentrations of trimethoprim are usually higher in the lungs, kidney, and liver than in the blood. Sulfadiazine and trimethoprim are both eliminated primarily by renal excretion, both by glomerular filtration and tubular secretion. Urine concentrations of both trimethoprim and sulfadiazine in horses are several-fold higher than blood concentrations.

Based upon blood concentrations obtained during the study, it was noted that the sulfadiazine and trimethoprim plasma concentrations did not increase in proportion to dose. For sulfadiazine, the 3X dose resulted in an average exposure of 2.0X and 2.6X the corresponding MIC values for EQUISUL-SDT® against indicated pathogens isolated from lower respiratory tract infections in horses enrolled in a 2010-2011 effectiveness field study as presented in Table 3. All MICs were determined in accordance with the Clinical and Laboratory Standards Institute (CLSI) Approved Standard M31-A3 using a broth microdilution method and 3% lysed horse blood.

Table 2. Median (range) of sulfadiazine and trimethoprim pharmacokinetics parameters following repeat dosing of 24 mg/kg bid EQUISUL-SDT for 7 days to six horses in fed condition

Concentrations of sulfadiazine and trimethoprim with T+MIC(90) (%) values are shown in Table 3. The minimum inhibitory concentration (MIC) values for EQUISUL-SDT® against indicated pathogens isolated from lower respiratory tract infections in horses enrolled in a 2010-2011 effectiveness field study are presented in Table 3. All MICs were determined in accordance with the Clinical and Laboratory Standards Institute (CLSI) Approved Standard M31-A3 using a broth microdilution method and 3% lysed horse blood.

Table 3. Trimethoprim/sulfadiazine minimum inhibitory concentration (MIC) values of isolates recovered from horses with lower respiratory infection caused by Streptococcus equi subsp. zooepidemicus treated with EQUISUL-SDT® in the U.S. 2010-2011

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ANIMAL SAFETY

In a target animal safety study, EQUISUL-SDT® was administered orally to 32 healthy adult horses at 0 (0X), 24 (1X), 72 (3X), or 120 (5X) mg/kg bid daily for 30 days. Local tissue was the most common abnormal observation. Observations of loose stool (pellets with liquid or unformed/couple stool) occurred more often in horses treated with EQUISUL-SDT® than in those treated with a dose of loose stool increasing in a dose related manner. All incidents of loose stool were self-limiting and resolved without treatment.

Horses in all EQUISUL-SDT® groups demonstrated statistically significantly higher mean serum creatinine concentrations, and those in the 3X and 5X groups demonstrated statistically significantly higher mean serum albumin concentrations. Statistically significantly higher mean neutrophil counts and serum gamma glutamyl transferase (GGT) activity were seen in the 1X and 5X groups. Individual animal creatinine, GGT, and albumin concentrations remained within the reference range. Individual animal elevations in absolute neutrophil counts ranged up to 7.08 x 10⁹/mL (reference range: 1.96-5.31 x 10³/mL).

Based upon blood concentrations obtained during the study, it was noted that the sulfadiazine and trimethoprim plasma concentrations did not increase in proportion to dose. For sulfadiazine, the 3X and 5X dose resulted in an average exposure of 2.0X and 2.6X the corresponding concentrations observed following a 1X dose. For trimethoprim, the corresponding values were 2.5X and 3.5X as compared to the 1X dose. Furthermore, marked interspecies variation, particularly with sulfadiazine, resulted in substantial overlap of individual subject blood levels across the three dosing groups.

STORAGE CONDITIONS

Store at 59°F to 86°F (15° to 30°C). Brief periods up to 104°F (40°C) are permitted. Protect from freezing.

HOW SUPPLIED

EQUISUL-SDT® is available in the following package sizes:

150 mL amber glass bottle containing 155 mL
950 mL amber glass bottle containing 900 mL

[Footnote]

MANUFACTURED BY: Aurora Pharmaceutical, LLC
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