Monitoring a mare's health throughout gestation provides a foundation for a safe foaling

SKIP DICKSTEIN

Some Unknowns *in* Broodmare Treatments

RESEARCHERS CALL FOR **MORE STUDY** OF MEDICATION SIDE EFFECTS IN **PREGNANT BROODMARES**

By **AMANDA DUCKWORTH**

IT IS LOGICAL that a happy, healthy broodmare is more likely to have an easier time with her pregnancy than a mare struggling on the health front. Monitoring the mare's well-being throughout gestation is important in order for her to have the best chance for a safe foaling.

Understanding that concept is a simpler process than the actual realities of animal husbandry, but it remains a basic cornerstone of broodmare care. For those in need of a primer on the topic, Dr. Ben Espy wrote "Expectant Mare: Assuring the Health and Well-Being of the Pregnant Mare" for the American Association of Equine Practitioners.

"We often think of pregnancy as a delicate and fragile condition," Espy said. "When it comes to horses, this perception is perhaps due to the mare's relatively poor reproductive performance in comparison to other domestic animals. However, in a natural setting, the mare does comparatively well reproductively. Therefore, this seemingly poor performance is due as much to improper management as to any reproductive deficiency. Fortunately, management is something we can control."

Proper management is crucial, and Thoroughbred broodmares usually are well monitored for signs of issues, but as anyone who works with horses knows, unexpected things still happen. Researchers examined that in "Descriptive Study of Medication Usage and Occurrence of Disease and Injury During Gestation in Thoroughbred Broodmares," published in the November 2022 issue of the *Journal of Equine Veterinary Science*.

"Over the last decade there has been a trend for increasing use of reproductive therapeutics in Thoroughbred broodmares, despite per-cycle pregnancy rates, incidence of pregnancy loss, live foal rates, and the prevalence of conditions such as postcovering endometritis remaining largely unchanged," researchers noted. "Antibiotic preparations appear to be commonly included in such treatment regimens, raising concerns over whether current practices align with industry guidelines for antimicrobial stewardship.

"There is currently a lack of information on the use of non-reproductive medications in Thoroughbred broodmares during the gestation period. Moreover, little is known about the incidence of many important diseases occurring during pregnancy, including placentitis, which has been associated with pregnancy loss, intrauterine fetal growth retardation, prematurity, and congenital sepsis."

In the study, researchers looked to describe the use of reproductive therapeutics, estimate the incidence of disease and injury, and describe non-reproductive medications administered to Thoroughbreds during their pregnancies. Seven farms in the United Kingdom and Ireland participated in the study, and retrospective information for 275 pregnancies of 235 mares over

COURTESY OF AIRDRIE STUD

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the course of two breeding seasons from 2019-2020 was gathered.

Details included a mare's signalment, breeding history, reproductive management during the breeding seasons, veterinary-attended episodes of illness or injury, and medication usage during gestation.

According to researchers, pre-estrous medications or ovulatory agents were administered to 55% of the mares and post-covering treatments were administered 73% while antibiotics were used in 69% of post-covering treatments. Of mares with no visible fluid on post-covering ultrasound, 37% still received treatment. They also found that 34% of mares suffered at least one veterinary-attended episode of disease or injury, with conditions affecting the musculoskeletal system (23%) and placentitis (5%) being the most prevalent. In total, 47% of mares received at least one non-reproductive medication during gestation, with antibiotics (25%) and non-steroidal anti-inflammatory drugs (23%) being most frequently prescribed.

"Findings have updated knowledge by providing up-to-date estimates of the use of reproductive therapeutics in Thoroughbred broodmares," concluded researchers. "Post-covering treatments were administered to the major-

Studies have found a high incidence of medication during pregnancy

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ity of mares and frequently included antibiotic preparations. Novel estimates were produced, which demonstrated a high incidence of disease and medication usage during pregnancy in Thoroughbreds, with over two thirds of mares requiring veterinary intervention at least once for disease or injury during gestation and almost half of mares receiving at least one medication (excluding post-covering therapeutics and/or those administered at the time of twin manual reduction) during gestation.

"There is a continuing trend for the use of reproductive therapeutics, particularly post-covering treatments containing antimicrobials in the majority of Thoroughbred broodmares, including in the absence of intrauterine fluid, highlighting important knowledge gaps around decision making and cost-benefits of current strategies. Occurrence of disease and medication usage during gestation are high, warranting additional investigation, particularly in the context of associations with offspring health outcomes."

As referenced in the previous study, one area where early detection and management have played an important part in reducing issues for broodmares involves multiple simultaneous pregnancies. If left undiagnosed, multiple pregnancies often end in abortion, stillbirth, or birth of foals that have reduced chances of survival.

> "PROGNOSIS FOR LIFE AND FUTURE FERTILITY IN BROODMARES FOLLOWING HYDROPS IS REPORTEDLY GOOD, BUT EVIDENCE TO SUPPORT THESE REPORTS IS LIMITED."
>
> —JOURNAL OF EQUINE VETERINARY SCIENCE

To mitigate these issues, veterinarians usually reduce the multiple pregnancies to a single pregnancy for the safety of the mare and the remaining foal. The earlier this is done, the better the outcome tends to be. Understanding why a mare might be at-risk could be helpful throughout her broodmare career. In July 2022, *Animals (Basel)* published "Mixed-Effects Modelling of the Risk Factors Associated with Multiple Pregnancies in Thoroughbred Mares."

"Knowledge of the factors associated with increased risk of multiple pregnancies can assist with identifying mares at risk," explained researchers. "Furthermore, the incidence of multiple pregnancies could be reduced if modifiable risk factors are identified and used to inform preventive measures.

"The prevalence of multiple pregnancies reported in Thoroughbreds between 1993 and 2018 has shown a gradual increase over time. Whether this is due to genetic reasons, notable changes in the use of reproductive hormones in stud medicine, or other as yet unidentified reasons is not known."

Researchers noted that while some other studies have identified risk factors associated with an increased risk of multiple pregnancies, they all looked at the factors individually and not the effect of when they occur simultaneously. For this study, they used statistical modeling to identify risk factors.

Reproductive information was gathered from 32 different farms in the United Kingdom. Of 2,241 pregnancies in the data set, 360 of them involved multiples. Of those, 344 were twins and 16 were triplets. The multiple pregnancies were manually reduced at a median of 16 days into the gestation period. Researchers examined 27 factors along with the contribution of the mare, stallion, farm, and veterinarian.

"We found that multiple ovulations and the use of a drug that mimics prostaglandin F2α to induce estrus both increased the risk of a mare having a multiple pregnancy," researchers concluded. "Mares that had a foal that same year, had a uterine cyst, or who did not get pregnant on the first cycle they were bred on were at a decreased risk of having a multiple pregnancy. Factors that impact the early embryonic environ-

ment are more important influences of multiple pregnancies when compared to the genetics of the mare. The increased incidence of multiple pregnancies but not multiple ovulations over the previous decades might well reflect improved management of the endometrium as opposed to selection of mares with increased risk for multiple pregnancies.

"Contrary to some previous studies, no significant variance in multiple pregnancies risk was identified for mare age and hCG or through inclusion of the mare, stallion, stud, nor veterinarian in either the empty or final models."

The fact that the mares themselves were not contributing to the likelihood of multiple pregnancies was an unexpected result for the researchers.

"Previously, it has been speculated that the increase in multiple pregnancies is driven by selection of mares with a genetic predisposition to multiple ovulations, but here we did not find any evidence to support this," researchers said. "An alternative explanation for an increase in multiple pregnancies is the increased use of PGF2 α analogues in practice, found here to increase the risk of multiple pregnancies. Further, the decreased risk associated with multiple covers and uterine cysts supports the important role for the early embryonic environment in supporting progressing of embryos to at least 15 days of gestation. Given the significant efforts over the last decade to prepare the endometrium for conception, it is also plausible that the increase in multiple pregnancies can be attributed to improved conception rates irrespectively of one or multiple embryos being present."

Another of the more unusual but quite serious conditions a broodmare can develop during her pregnancy is hydrops, which occurs when an overaccumulation of placental fluid takes place during the last months of pregnancy. Hydrops can happen in one of two ways. Hydrallantois, which is when there is excessive allantoic fluid, is the more common, but hydramnion, which is excessive amniotic fluid, can also occur.

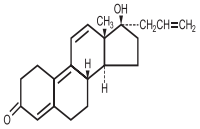
The *Journal of Equine Veterinary Science* published "Treatment of Hydropsical Conditions Using Transcervical Gradual Fetal Fluid Drainage in Mares With or Without Concurrent Abdominal Wall Disease" in May 2018.

"When they occur, they are true emergencies due to the severe enlargement of the pregnant uterus, which can result in clinical signs, such as an enlarged round

Altren®
(altrenogest)
SOLUTION 0.22% (2.2 mg/mL)

CAUTION:
Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:
Altren® (altrenogest) Solution 0.22% contains the active synthetic progestin, altrenogest. The chemical name is 17α-allyl-17β-hydroxyestra-4,9,11-trien-3-one. The CAS Registry Number is 850-52-2. The chemical structure is:



Each mL of Altren® (altrenogest) Solution 0.22% contains 2.2 mg of altrenogest in an oil solution.

ACTIONS:
Altren® (altrenogest) Solution 0.22% produces a progestational effect in mares.

INDICATIONS:
Altren® (altrenogest) Solution 0.22% is indicated to suppress estrus in mares. Suppression of estrus allows for a predictable occurrence of estrus following drug withdrawal. This facilitates the attainment of regular cyclicity during the transition from winter anestrus to the physiological breeding season. Suppression of estrus will also facilitate management of prolonged estrus conditions. Suppression of estrus may be used to facilitate scheduled breeding during the physiological breeding season.

CONTRAINDICATIONS:
Altren® (altrenogest) Solution 0.22% is contraindicated for use in mares having a previous or current history of uterine inflammation (i.e., acute, subacute, or chronic endometritis). Natural or synthetic gestagen therapy may exacerbate existing low-grade or "smoldering" uterine inflammation into a fulminating uterine infection in some instances.

PRECAUTIONS:
Various synthetic progestins, including altrenogest, when administered to rats during the embryogenic stage of pregnancy at doses manyfold greater than the recommended equine dose caused fetal anomalies, specifically masculinization of the female genitalia.

DOSAGE AND DIRECTIONS:
While wearing protective gloves, remove shipping cap and seal; replace with enclosed plastic dispensing cap. Remove cover from bottle dispensing tip and connect luer lock syringe (without needle). Draw out appropriate volume of Altren® solution. (Note: Do not remove syringe while bottle is inverted as spillage may result.) Detach syringe and administer solution orally at the rate of 1 mL per 110 pounds of body weight (0.044 mg/kg) once daily for 15 consecutive days. Administer solution directly on the base of the mare's tongue or on the mare's usual grain ration. Replace cover on bottle dispensing tip to prevent leakage. Excessive use of a syringe may cause the syringe to stick; therefore, replace syringe as necessary.

DOSAGE CHART:

Approximate Weight in Pounds	Dose in mL
770	7
880	8
990	9
1100	10
1210	11
1320	12

WHICH MARES WILL RESPOND TO ALTREN® (altrenogest) SOLUTION 0.22%:
Extensive clinical trials have demonstrated that estrus will be suppressed in approximately 95% of the mares within three days; however, the post-treatment response depended on the level of ovarian activity when treatment was initiated. Estrus in mares exhibiting regular estrus cycles during the breeding season will be suppressed during treatment; these mares return to estrus four to five days following treatment and continue to cycle normally. Mares in winter anestrus with small follicles continued in anestrus and failed to exhibit normal estrus following withdrawal.

Response in mares in the transition phase between winter anestrus and the summer breeding season depended on the degree of follicular activity. Mares with inactive ovaries and small follicles failed to respond with normal cycles post-treatment, whereas a higher proportion of mares with ovarian follicles 20 mm or greater in diameter exhibited normal estrus cycles post-treatment. Altrenogest Solution 0.22% was very effective for suppressing the prolonged estrus behavior frequently observed in mares during the transition period (February, March and April). In addition, a high proportion of these mares responded with regular estrus cycles post-treatment.

SPECIFIC USES FOR ALTREN® (altrenogest) SOLUTION 0.22%:

SUPPRESSION OF ESTRUS TO:
1. Facilitate attainment of regular cycles during the transition period from winter anestrus to the physiological breeding season. To facilitate attainment of regular cycles during the transition phase, mares should be examined to determine the degree of ovarian activity. Estrus in mares with inactive ovaries (no follicles greater than 20 mm in diameter) will be suppressed but these mares may not begin regular cycles following treatment. However, mares with active ovaries (follicles greater than 20 mm in diameter) frequently respond with regular post-treatment estrus cycles.
2. Facilitate management of the mare exhibiting prolonged estrus during the transition period. Estrus will be suppressed in mares exhibiting prolonged behavioral estrus either early or late during the transition period. Again, the post-treatment response depends on the level of ovarian activity. The mares with greater ovarian activity initiate regular cycles and conceive sooner than the inactive mares. Altren® (altrenogest) Solution 0.22% may be administered early in the transition period to suppress estrus in mares with inactive ovaries to aid in the management of these mares or to mares later in the transition period with active ovaries to prepare and schedule the mare for breeding.
3. Permit scheduled breeding of mares during the physiological breeding season. To permit scheduled breeding, mares which are regularly cycling or which have active ovarian function should be given Altren® (altrenogest) Solution 0.22% daily for 15 consecutive days beginning 20 days before the date of the planned estrus. Ovulation will occur 5 to 7 days following the onset of estrus as expected for non-treated mares. Breeding should follow usual procedures for mares in estrus. Mares may be regulated and scheduled either individually or in groups.

ADDITIONAL INFORMATION:
A 3-year well controlled reproductive safety study was conducted in 27 pregnant mares, and compared with 24 untreated control mares. Treated mares received 2 mL altrenogest solution 0.22%/110 lb body weight (2x dosage recommended for estrus suppression) from day 20 to day 325 of gestation. This study provided the following data:

1. In filly offspring (all ages) of treated mares, clitoral size was increased.
2. Filly offspring from treated mares had shorter interval from Feb. 1 to first ovulation than fillies from their untreated mare counterparts.
3. There were no significant differences in reproductive performance between treated and untreated animals (mares & their respective offspring) measuring the following parameters:
   - interval from Feb. 1 to first ovulation, in mares only.
   - mean interovulatory interval from first to second cycle and second to third cycle, mares only.
   - follicle size, mares only.
   - at 50 days gestation, pregnancy rate in treated mares was 81.8% (9/11) and untreated mares was 100% (4/4).
   - after 3 cycles, 11/12 treated mares were pregnant (91.7%) and 4/4 untreated mares were pregnant (100%).
   - colt offspring of treated and control mares reached puberty at approximately the same age (82 & 84 weeks respectively).
   - stallion offspring from treated and control mares showed no differences in seminal volume, spermatozoal concentration, spermatozoal motility, and total sperm per ejaculate.
   - stallion offspring from treated and control mares showed no difference in sexual behavior.
   - testicular characteristics (scrotal width, testis weight, parenchymal weight, epididymal weight and height, testicular height, width & length) were the same between stallion offspring of treated and control mares.

REFERENCES:
Shoemaker, C.F., E.L. Squires, and R.K. Shideler, 1989.

Safety of Altrenogest in Pregnant Mares and on Health and Development of Offspring. Eq. Vet. Sci. (9); No. 2: 69–72.

Squires, E.L., R.K. Shideler, and A.O. McKinnon. 1989.

Reproductive Performance of Offspring from Mares Administered Altrenogest During Gestation. Eq. Vet. Sci. (9); No. 2: 73–76.

WARNING:
For oral use in horses only. Keep this and all other medications out of the reach of children. Do not use in horses intended for human consumption.

HUMAN WARNINGS:
Skin contact must be avoided as Altren® (altrenogest) Solution 0.22% is readily absorbed through unbroken skin. Protective gloves must be worn by all persons handling this product. Pregnant women or women who suspect they are pregnant should not handle Altren® (altrenogest) Solution 0.22%. Women of child bearing age should exercise extreme caution when handling this product. Accidental absorption could lead to a disruption of the menstrual cycle or prolongation of pregnancy. Direct contact with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

INFORMATION FOR HANDLERS:
WARNING: Altren® (altrenogest) Solution 0.22% is readily absorbed by the skin. Skin contact must be avoided; protective gloves must be worn when handling this product.

Effects of Overexposure
There has been no human use of this specific product. The information contained in this section is extrapolated from data available on other products of the same pharmacological class that have been used in humans. Effects anticipated are due to the progestational activity of altrenogest.

Acute effects after a single exposure are possible; however, continued daily exposure has the potential for more untoward effects such as disruption of the menstrual cycle, uterine or abdominal cramping, increased or decreased uterine bleeding, prolongation of pregnancy and headaches. The oil base may also cause complications if swallowed.

In addition, the list of people who should not handle this product (see below) is based upon the known effects of progestins used in humans on a chronic basis.

PEOPLE WHO SHOULD NOT HANDLE THIS PRODUCT:
1. Women who are or suspect they are pregnant.
2. Anyone with thrombophlebitis or thromboembolic disorders or with a history of these events.
3. Anyone with cerebral-vascular or coronary-artery disease.
4. Women with known or suspected carcinoma of the breast.
5. People with known or suspected estrogen-dependent neoplasia.
6. Women with undiagnosed vaginal bleeding.
7. People with benign or malignant tumors which developed during the use of oral contraceptives or other estrogen-containing products.
8. Anyone with liver dysfunction or disease.

Accidental Exposure
Altrenogest is readily absorbed from contact with the skin. In addition, this oil based product can penetrate porous gloves. Altrenogest should not penetrate intact rubber or impervious gloves; however, if there is leakage (i.e., pinhole, spillage, etc.), the contaminated area covered by such occlusive materials may have increased absorption. The following measures are recommended in case of accidental exposure.

Skin Exposure: Wash immediately with soap and water.

Eye Exposure: Immediately flush with plenty of water for 15 minutes. Get medical attention.

If Swallowed: Do not induce vomiting. Altren® (altrenogest) Solution 0.22% contains an oil. Call a physician. Vomiting should be supervised by a physician because of possible pulmonary damage via aspiration of the oil base. If possible, bring the container and labeling to the physician.

Store upright at or below 25° C (77° F). Reclose tightly.

HOW SUPPLIED:
Altren® (altrenogest) Solution 0.22% (2.2 mg/mL). Each mL contains 2.2 mg altrenogest in an oil solution. Available in 150 mL and 1000 mL plastic bottles.

Manufactured by:
Aurora Pharmaceutical, Inc.
Northfield, Minnesota 55057

Approved by FDA under ANADA # 200-620

aurora PHARMACEUTICAL®

07/2021

EQUISUL-SDT®
(Sulfadiazine/Trimethoprim) Oral Suspension

For use in horses only.

Approved by FDA under 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 potentiated 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 by 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-pyrimidinylbenzenesulfonamide. Trimethoprim is the non-proprietary name for 5-[(3,4,5-trimethoxyphenyl) methyl]-2,4-pyrimidinediamine.

Figure 1. Structure of sulfadiazine

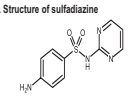
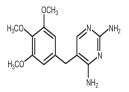


Figure 2. Structure of trimethoprim



Each mL of EQUISUL-SDT contains 400 mg combined active ingredients (333 mg sulfadiazine and 67 mg trimethoprim) in an aqueous suspension.

INDICATION
EQUISUL-SDT is indicated for the treatment of lower respiratory tract infections in horses caused by susceptible strains of *Streptococcus equi* subsp. *zooepidemicus*.

DOSAGE AND ADMINISTRATION

Shake well before use.

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.

EQUISUL-SDT in containers of 280 mL and 560 mL with draw-off caps: Remove cap. Peel off white foil backed bottle seal and replace cap. Peel off outer cap seal exposing (hole) opening. Push an oral tip syringe into the cap opening. Invert and draw out appropriate volume of EQUISUL-SDT solution. (Note: Do not remove syringe while the bottle is inverted as possible spillage may result.) Detach syringe and administer 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.

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 acute diarrhea that can be fatal. If acute diarrhea or persistent 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. Potentiated 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.

Decreased hematopoetic 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 behavior changes that resolved after discontinuation of the drug.

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

ADVERSE REACTIONS
Adverse 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 either EQUISUL-SDT (n = 182) or with a saline control (n = 88) are summarized in Table 1. At least one episode of loose stool of varying severity was observed in 69 of 182 (38%) of the EQUISUL-SDT-treated horses, and 29 of 88 (33%) saline control horses. Of those animals experiencing loose stool, 2 of 182 (1.1%) of the EQUISUL-SDT-treated horses and 0 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 resolved without treatment within 5–10 days after discontinuation of EQUISUL-SDT.

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

Adverse Reactions	Equisul-SDT (n=182)	Saline control (n=88)
Loose stool (including diarrhea)	69 (38%)	29 (33%)
Colic	3 (1.6%)	2 (2.2%)
Diarrhea	2 (1.1%)	0 (0%)

To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Aurora Pharmaceutical, Inc. at 1-888-215-1256 or www.auroraparmaceutical.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY
Following oral administration, EQUISUL-SDT is rapidly absorbed and widely distributed throughout body tissues. Sulfadiazine levels are usually highest in the kidney, while the tissue concentration in 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 sulfadiazine and trimethoprim are several-fold higher than blood concentrations.[1] Sulfadiazine and trimethoprim are 20% and 35% bound to plasma protein, respectively. Administration of sulfadiazine and trimethoprim with food has no apparent effect on the absorption of sulfadiazine but the absorption of trimethoprim is decreased.

Based on a study in fed horses, trimethoprim concentrations following repeat oral administration of 24 mg/kg EQUISUL-SDT to 6 horses reached peak concentration in 0.5 to 12.0 hours. The median plasma elimination half-life was 3 hours, with a range of 2.31 to 4.96 hours. Peak sulfadiazine concentrations were reached within 1.0 to 12.0 hours in the same study. The median plasma elimination half-life for sulfadiazine was approximately 7.80 hours, with a range of 6.78 to 10.39 hours. Only minor accumulation of both drugs was observed following repeat oral administration of EQUISUL-SDT and both drugs reached steady state by day 3. Sulfadiazine and trimethoprim key steady state parameters associated with administration in 6 fed horses over a period of 7 days are found in Table 2.

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

Drug	Sulfadiazine	Trimethoprim
Tmax (hr)	4.75 (1.00–12.00)	8.50 (0.50–12.00)
Cmax (µg/mL)	17.63 (10.10–31.15)	0.78 (0.60–1.14)
AUC 0–12 (last dose) (hr*µg/mL)	159.35 (73.90–282.54)	5.47 (3.31–10.91)
T 1/2 (hr)	7.80 (6.78–10.39)	3.00 (2.31–4.96)

MICROBIOLOGY
EQUISUL-SDT is the combination of the sulfonamide sulfadiazine and trimethoprim. These two drugs block sequential steps in nucleic acids biosynthesis. Sulfadiazine inhibits bacterial synthesis of dihydrofolic acid by competing with para-aminobenzoic acid. Trimethoprim blocks the production of tetrahydrofolic acid from dihydrofolic acid by reversibly inhibiting dihydrofolate reductase. The two drugs act synergistically, reducing the minimum inhibitory concentration of each, while enhancing the bacteriostatic action of each separately to a bactericidal action when combined.

EQUISUL-SDT administered as a combined sulfadiazine-trimethoprim dose of 24 mg/kg body weight twice daily for 7 days provided concentrations of sulfadiazine and trimethoprim with T>MIC90 (%T) values of 100% and 98% respectively. 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 system and 3% lysed horse blood.

Table 3. Trimethoprim/sulfadiazine minimum inhibitory concentration (MIC) values[a] 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)

Treatment Outcome	Success	Failure
Number of Isolates	65[c]	46
Time of Sample Collection	Pre-Treatment	Pre-Treatment
MIC 50[b] (µg/mL)	0.25/4.75	0.25/4.75
MIC 90[b] (µg/mL)	0.25/4.75	0.25/4.75
MIC Range (µg/mL)	0.12/2.4 to 0.5/9.5	0.12/2.4 to 0.5/9.5

[a] The correlation between *in vitro* susceptibility data and clinical effectiveness is unknown.
[b] The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.
[c] One isolate of *S. equi* subsp. *zooepidemicus* was not tested.

EFFECTIVENESS
A negative control, randomized, masked, field study evaluated the effectiveness of EQUISUL-SDT administered at 24 mg/kg body weight, orally, twice daily for 10 days for the treatment of lower respiratory tract infections in horses caused by *Streptococcus equi* subsp. *zooepidemicus*. In this study, a total of 182 horses were treated with EQUISUL-SDT, and 88 horses were treated with saline. One hundred seventy-three horses (112 EQUISUL-SDT and 61 saline) were included in the statistical analysis. Therapeutic success was characterized by absence of fever and no worsening of clinical signs at Day 5 and Day 10, and significant clinical improvement or resolution of clinical signs of lower respiratory tract infection by Day 17. The observed success rates are 58.9% (66/112) and 14.8% (9/61) for the EQUISUL-SDT and saline-treated groups, respectively.

Table 4 summarizes the statistical analysis results on the overall success rate.

Table 4. Overall Clinical Effectiveness Results

	Equisul-SDT	Saline	P-value*
Least Square Means	61%	13.1%	0.0123

* P-value and estimated success rates are based on back-transformed mean estimates from the statistical analysis.

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 twice daily for 30 days. Loose stool was the most common abnormal observation. Observations of loose stool (pellets with liquid or unformed/cowpile stool) occurred more often in horses treated with EQUISUL-SDT with the incidence 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 higher mean neutrophil counts and mean 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 7.09 x 10^3/mcL (reference range: 1.96-5.31 x 10^3/mcL).

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, a 3X and 5X dose resulted in an average exposure of 2.0X and 2.6X the 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 intersubject variability, particularly with sulfadiazine, resulted in substantial overlap of individual subject blood levels across the three dosing groups.

STORAGE CONDITIONS
Store upright at 59°– 86° F (15°– 30° C).
Brief periods up to 104° F (40° C) are permitted. Protect from freezing. EQUISUL-SDT in containers of 280 mL and 560 mL — discard 60 days after removing bottle seal.

HOW SUPPLIED
EQUISUL-SDT is available in the following package sizes:
135 mL
280 mL
560 mL
900 mL

[footnote]

[1] Kahn CM, Line S, eds. The Merck Veterinary Manual. 10th Ed. Merck & Co. 2010.

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ALTREN®
(altrenogest)

Throughout the mare breeding season, **Altren® (altrenogest)** is quickly becoming the product of choice in handling estrus issues in horses.

Containing the same formulation and active ingredient as Regu-Mate®(altrenogest) and backed by Aurora's *Best-Price-Always* commitment, Altren is becoming the industry's most requested altrenogest product line, enhanced by Altren's proprietary 150 mL dose and FDA-approved vented cap.

Spending more no longer makes sense when it comes to effective estrus management.

Wade Shoemaker, DVM
Countryside Large Animal Veterinary Clinic
Greeley, CO

"Altren® (altrenogest) is a product our practice relies on to provide the same active ingredient as Regu-Mate® (altrenogest), but at a much better price point.

My clients appreciate the cost savings I can pass on to them. Altren has quickly become the #1 altrenogest in our practice due to the cost savings and specialized packaging.

We routinely send the Altren 150 mL home with clients, especially if we have a problem mare that needs to be on altrenogest after breeding.

That will allow us to get out to the ranch at 15 days for the first preg-check and then decide if the mare stays on the Altren or not.

It's been a great deal for us and for the client."

TOOLS OF THE TRADE

Andy Roberts, DVM
Lexington, KY

"EQUISUL-SDT® is my first course broad spectrum antibiotic. Because the combination of Sulfadiazine/ Trimethoprim is so broad spectrum, I can treat problematic respiratory bacteria before they become a major problem.

EQUISUL-SDT is mainly used for respiratory issues, i.e., a febrile horse, elevated SAA, no cough and making a presumptive diagnosis that they have an early respiratory issue. I want a horse on this product a minimum of 10 days.

With the convenient 560 mL bottles, I can script it out to a trainer/owner for 10 days."

EQUISUL-SDT®
(Sulfadiazine/Trimethoprim)

Equisul-SDT® (Sulfadiazine/Trimethoprim) is ready to handle those pneumonia-prone signs of respiratory infections following foaling and pre-breeding.

Containing a higher bioavailability compared to approved paste products, Equisul-SDT is the equine veterinarian's go-to antibiotic of choice, especially when the treatment of lower respiratory tract infections caused by susceptible strain of *Streptococcus equi* subsp. *Zooepidemicus* are indicated.

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Researchers say it's important to know the factors associated with increased risk of multiple pregnancies in order to identify mares at risk

abdomen, dyspnea, reluctance to walk, and colic, and may lead to the development of abdominal wall disease," said researchers. "The pathogenesis of hydropsical conditions is not fully elucidated, but they have been associated with placentitis and fetal abnormalities."

Researchers went on to explain that the study involved six cases involving hydrops, five of which featured hydrallantois. In order to treat the mares, the pregnancies could not continue.

"All mares were treated by termination of the pregnancy through gradual fluid drainage transcervically over a number of hours, and their fetuses were delivered vaginally," researchers said. "All fetuses were euthanized immediately after vaginal delivery. Of the six mares, two had signs of placentitis, two were confirmed seropositive for leptospirosis, and two were euthanized (one because of a vaginal tear that communicated through the peritoneum and one mare that developed abdominal wall rupture and laminitis). The remaining four mares were available for follow-up; three mares were not rebred, and one mare became an embryo donor, with a successful embryo recovery."

The future for mares that have been afflicted with hydrops was then examined more in depth in the study "Factors Affecting Survival and Future Foaling Rates in Thoroughbred Mares with Hydrops," in the June 2022 issue of the *Journal of Equine Veterinary Science*.

"Prognosis for life and future fertility in broodmares following hydrops is reportedly good, but evidence to support these reports is limited," said researchers. "The objective of this case series was to describe the prognosis for survival and fertility in mares presented to a referral hospital following diagnosis of hydrops."

For the study, researchers reviewed medical records of 39 mares that presented with hydrops. They examined the history (gestation, sire of the foal), clinical findings at presentation and throughout hospitalization (complications, treatments, survival to discharge), and future foaling rates of the broodmares. They found that 90% of mares survived hydrallantois and 75% survived hydramnios. Of the mares that were bred again, 95% of them successfully had a foal, and of those, 75% were able to do so the year following hydrops. The condition did not reoccur in any of the mares.

Researchers also concluded that those mares managed with transcervical gradual fluid drainage survived 100% of the time. Those treated in a different manner survived 78.6% of the time. Causes for death include hypovolemic shock, hemorrhage, and laminitis.

"Complications observed in mares not returning to breeding included hypovolemic shock and hemorrhage," explained researchers. "Causes of non-survival included peritonitis secondary to abdominal wall rupture or uterine tear, and tibial fracture. These results suggest that prognosis for survival and future fertility following a diagnosis of hydrops is good, provided the hydrops is diagnosed and treated appropriately with no damage to the reproductive tract or abdominal wall."

Even under the best management programs, the unexpected can occur, and working with a veterinarian can help broodmares get back on track when it comes to healthy pregnancies. BH

PHOTOS BY Z

OBS Offers Quality Local Feed

Ocala Breeders Feed and Supply is located in the heart of horse country, Ocala, Florida. With a dedicated horse feed production plant and two retail locations, we guarantee locally made, top-quality, fresh feed. Our start was from the vision of Thoroughbred racehorse owners wanting a locally milled fresh feed.

OBS feeds feature quality protein sources and added lysine, the first limiting amino acid for horses. All feeds are formulated and fortified with a partnership with Kentucky Equine Research (KER) to support the specific needs of equine athletes, with proven results year after year. Feeding racehorses was their foundation, and today many breeds rely on OBFS for fresh, top-quality feed.

The two retail stores carry a full line of animal health supplies and supplements, bedding, feeders, waterers, hay, and tack. In addition to the OBS brand horse feeds, Purina and Manna Pro feeds are stocked along with a large variety of pet, aviary, poultry, and livestock feeds.

The staff is knowledgeable and friendly and strives to know each customer's name and needs. A steadfast commitment to customer service and a product line that meets the needs of our clientele makes OBFS your one-stop shop for your farm and pet needs.