The American Association of Equine Practitioners has published updated guidelines on parasite control

Staying a Step Ahead

PROTOCOLS TO **CONTROL PARASITES** CONTINUE TO EVOLVE

By **AMANDA DUCKWORTH**

WHILE HORSE FARMS understand parasite control should be included in any horse health plan, comprehending the best approach to properly manage these unwanted guests is evolving. Some approaches that worked in the past are no longer effective, and research shows the need to continue to improve awareness of this evolving reality across the globe and across breeds.

Parasites are extremely common in horse herds. That fact, in and of itself, is not problematic. Owners, however, do need to work with veterinarians to properly manage a parasite burden before it has negative effects on the equine hosts.

The American Association of Equine Practitioners has published updated guidelines for dealing with parasites. It outlines multiple approaches, and many of the guidelines should be viewed as suggestions because no "one size fits all" program exists. Knowing that, it is important to work with trusted veterinarians and keep up to date on the latest research.

"Commonly used strategies for parasite control in adult horses are based largely on knowledge and concepts that are more than 50 years old," the AAEP explains in its internal parasite control guidelines. "However, much has changed in this time, necessitating a reexamination of recommendations for parasite control."

That paper notes that cyathostomins (small strongyles) are viewed differently today than in past decades.

"It is noteworthy that cyathostomins were not considered important pathogens at that time, as their pathogenic potential was overshadowed by Strongylus vulgaris. However, that situation has changed, and currently, cyathostomins are recognized as a primary equine parasite pathogen."

Drug resistance to traditional deworming methods has increasingly become a problem because of blanket rotational treatments for entire herds. Veterinarians have urged adopting the fecal-egg-count method to treat horses based on need, as opposed to administering blindly. Numerous research efforts spanning multiple aspects of this parasite reality highlight the necessity to be aware of problems related to drug-resistant parasites.

In December 2022 the *International Journal for Parasitology: Drugs and Drug Resistance* published "Anthelmintic resistance in equine nematodes: Current status and emerging trends" as a review of the current state of play when it comes to drug resistance.

"Anthelmintic resistance is reported in equine nematodes with increasing frequency in recent years, and no new anthelmintic classes have been introduced during the past 40 years," explained Dr. Martin Nielsen, who published the review. "This manuscript reviews published literature describing anthelmintic resistance in cyathostomins, Parascaris spp., and Oxyuris equi with special emphasis on larvicidal efficacy against encysted cyathostomin larvae and strongylid egg reappearance periods (ERP).

"Multi-drug resistance is becoming

ANNE M. EBERHARDT

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the norm in managed cyathostomin populations around the world, and a similar pattern may be emerging in Parascaris spp. More work is required to understand the mechanisms behind the shortened ERPs, and researchers and veterinarians around the world are encouraged to routinely monitor anthelmintic efficacy against equine nematodes."

In January 2023 *Veterinary Parasitology* published "Molecular diagnostics for gastrointestinal helminths in equids: Past, present and future," as researchers turned an eye toward methods of diagnosing when parasites have gone from present to problematic.

"This review is aimed to appraise the literature on the use of molecular techniques for the detection, quantification, and differentiation of gastrointestinal helminths (GIH) of equids; identify the knowledge gaps; and, discuss diagnostic prospects in equine parasitology," explained researchers.

Drug resistance to traditional deworming methods is a concern

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For the study, researchers evaluated 54 previously conducted studies, and of those, 50 were done using horses and four involved donkeys and zebras. They found Polymerase chain reaction (PCR) was employed in all of the studies whereas PCR amplicons were sequenced in only 18 of them.

"Overall, to date, the majority of

The American Association of Equine Practitioners notes that when it comes to controlling parasites there is no "one size fits all" program

molecular studies have focused on the diagnosis and identification of GIHs of equids (i.e., species of Anoplocephala, Craterostomum, cyathostomins, Oesophagodontus, Parascaris, Strongylus, Strongyloides, and Triodontophorus), with a recent shift toward investigations on anthelmintic resistance and the use of high-throughput nemabiome metabarcoding.

"With the increasing reports of anthelmintic resistance in equid GIHs, it is crucial to develop and apply techniques such as advanced metabarcoding for surveillance of parasite populations in order to gain detailed insights into their diversity and sustainable control. To the best of our knowledge, this is the first systematic review that evaluates molecular investigations published on the diagnosis and quantification of equid GIHs and provides useful insights into important knowledge gaps and future research directions in equid molecular parasitology."

Understanding the current parasitic threats to horses and how best to deal with them remains an area of high concern. The *International Journal for Parasitology* published "Shortened egg reappearance periods of equine cyathostomins following ivermectin or moxidectin treatment: morphological and molecular investigation of efficacy and species composition" in November 2022.

"Equine cyathostomins are truly ubiquitous in grazing horses around the world," explained researchers. "With 14 genera and 40 species reported to infect horses, this subfamily is particularly complex and diverse with 15–25 species often coinfecting an individual host.

"The cyathostomins include a remarkably large number of species co-infecting the horse, but knowledge about the role of individual species is strikingly limited. A recent meta-analysis described global prevalence and relative abundance of cyathostomin species, and determined that just three species, Cylicocyclus (Cyc.) nassatus, Cylicostephanus (Cys.) longibursatus, and Cyathostomum (Cya.) catinatum, comprise approximately 55% of recovered specimens, while an additional five species contribute 21% of most populations."

In treating cyathostomin, researchers note, many have relied on moxidectin, which unlike ivermectin, has exhibited efficacy against encysted cyathostomin larvae and is reported to have persistent efficacy through substantially longer egg reappearance periods.

"However, shortened egg reappearance periods have been reported recently for both macrocyclic lactones, and these findings have raised several questions," explained researchers. "One, are egg reappearance period patterns different after ivermectin or moxidectin treatment? Two, are shortened egg reappearance periods associated with certain cyathostomin species or stages? Three, how does moxidectin's larvicidal efficacy affect egg reappearance period?"

The study used 36 horses that lived in Lexington and ranged from 2-5 years old. The study spanned three months in 2019. The horses were randomly assigned to one of three treatment groups: moxidectin, ivermectin, and the untreated control. FEC were done weekly, and researchers found that the egg reappearance period was five weeks for both compounds.

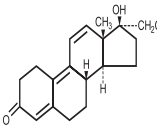
"Moxidectin and ivermectin were 99.9% and 99.7% efficacious against adults at two weeks post treatment, whereas the respective efficacies against luminal L4s were 84.3% and 69.7%," concluded researchers. "At five weeks PT, adulticidal efficacy was 88.3% and 57.6% for moxidectin and ivermectin, respectively, while the efficacy against luminal L4s was 0% for both drugs. Moxidectin reduced early L3 counts by 18.1% and 8.0% at two or five weeks, while the efficacies against late L3s and mucosal L4s were 60.4% and 21.2% at the same intervals, respectively. The luminal L4s surviving ivermectin treatment were predominantly Cylicocyclus (Cyc.) insigne.

"The ITS-2 rDNA metabarcoding was in good agreement with morphologic species estimates but suggested differential activity between moxidectin and

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

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

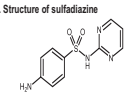
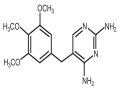


Figure 2. Structure of trimethoprim



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.auroraharmaceutical.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.

01/2021

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.

Draw-off Cap

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Please read and follow all label directions
09/2022 ad000176

ivermectin for several species, most notably Cyc. insigne and Cylicocyclus nassatus. This study was a comprehensive investigation of current macrocyclic lactone efficacy patterns and provided important insight into potential mechanisms behind shortened egg reappearance periods."

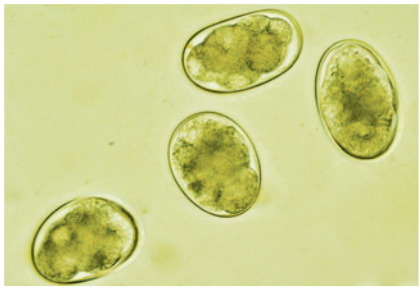
The problems with parasite resistance are by no means restricted to the United States or to Thoroughbreds, and studies are being done around the globe and on multiple breeds. One recent example is "Anthelmintic efficacy in strongyles of horses in Northern Minas Gerais, Brazil," which was published in November 2022 by *Veterinary Parasitology: Regional Studies and Reports.*

"The intensive use of anthelmintics has resulted in resistant parasite populations in horses," explained researchers. "The objective of this trial was to evaluate the anthelmintic efficacies of the anthelmintics fenbendazole, ivermectin, and abamectin in 24 horse farms in Northern Minas Gerais."

For the study, egg counts per gram of feces (EPG) were performed on 619 individual horses, and of those 436 were found to have EPG higher than 150. As a result, they were used in the tests aimed at fecal egg count reduction (FECR).

"These animals received the anthelmintics, fenbendazole, ivermectin, and abamectin," said researchers. "Feces was collected 14 days after the administration of anthelmintics to perform the EPG. Pre- and post-treatment EPG counts were used to calculate the FECR for each anthelmintic group, and fecal culture was used to identify the strongyles.

"The resistance status was evaluated based on the FECR and LCL95%. Fenbendazole was effective in 11 (45.8%) of the horse farms. Ivermectin was effective in 17 (77.3%) and abamectin in 17 (74%) of the farms; side-resistance was detected in three (12.5%) of the farms. Intestinal strongyle resistance to anthelmintics was observed in 14 (58.3%) of the farms. Cyathostomin larvae were found in 100% of the farms, Strongylus vulgaris in 13 (54.2%), and S. equinus in three (12.5%). Only cyathostomins larvae were detected post-treatment with ivermectin and abamectin."



A microscopic look at cyathostomins (small strongyles), which are viewed differently today by veterinarians than in past decades

Because parasites impact all types of horses, the continual research being done on the topic has far-reaching implications. For example, in May 2022, *Schweizer Archiv für Tierheilkunde* published "Helminths and their management in Swiss Army horses: differences between riding horses and pack horses evidence the need of improvement." The study highlighted how differences in planning do make an impact.

"Intestinal helminth management in horses has both clinical and epidemiologic relevance, in additional association with anthelmintic resistance," explained researchers.

For the study, researchers compared husbandry conditions and intestinal helminth management used by the Swiss Army. Within that group, 53 military-owned horses are used as riding horses and 130 are privately owned equines used as pack horses. The two groups are brought together for service periods of up to 12 weeks.

Researchers studied the difference between the two, using both a questionnaire and analyzing fecal samples. They found that the riding horses only had cyathostomin infections while the pack horses had cyathostomins as well as Parascaris sp. and Strongylus vulgaris.

"Pasture management, hygiene, and deworming practices were highly variable for pack horses, while for riding horses there was an overall concept," said researchers. "This included a selective deworming strategy with fecal egg counts (FECs) of strongyles prior to deworming, applying a threshold of 200 eggs per gram of feces (epg). Anthelmintic treatments based on FECs, weekly faeces removal on pastures, the use of macrocyclic lactones and deworming horses regularly were identified as protective factors regarding the 200 epg threshold for strongyle eggs. Accordingly, the mean epg for strongyle eggs between the groups (111 and 539 in riding and pack horses, respectively) was significantly different.

Understanding the current parasitic threats to horses and how best to deal with them remains an area of high concern

TOP: GETTY IMAGES/TODOREAN GABRIEL; BOTTOM: ANNE M. EBERHARDT

"Overall, intestinal helminth management in pack horses showed room for improvement regarding pasture hygiene, the used anthelmintics, and the frequency of deworming, from which all Swiss Army horses would benefit, as they share pastures during their service, therefore entailing the risk of parasite transmission."

Parasites are not going anywhere, and using technology to understand their relationship with their host continues to be important, especially in breeding stock. In July 2022, *Animal Biotechnology* published the study "Genome-wide association study in Thoroughbred horses naturally infected with cyathostomins."

"Cyathostomins are considered one of the most important parasites of horses," researchers said. "A group of horses within a herd can be responsible for eliminating the majority of parasite eggs. This phenotype might be explained by genetic factors. This study aimed to identify genomic regions associated with fecal egg count (FEC) and hematological parameters by performing a genomic-wide association study (GWAS) in Thoroughbred horses naturally infected with cyathostomins."

In total, 90 horses were used for the study, and researchers determined their packed cell volume (PCV), differential leukocyte, and FEC. Genomic (co)variance and SNP effects were estimated by a single step methodology.

"The five genomic windows that have explained the highest percentage of the additive genetic variance of a specific trait (top five) were further explored to identify candidate genes," explained researchers. "A total of 33, 21, 30, 21, and 19 genes were identified for FEC, PCV, eosinophils, neutrophils, and lymphocyte count, respectively. The top five marker regions explained 2.86%, 2.56%, 2.73%, 2.33%, and 2.37% of the additive genetic variation of FEC, PCV, eosinophils, neutrophils, and lymphocytes count, respectively.

"This is the first study correlating phenotypic horse health traits to GWAS analysis, which may be used for animal breeding activities, reducing losses due to parasite infections."

Through continual research, horse owners and veterinarians can work to balance the reality of parasites with ways to manage them effectively. BH