A recent study found that nutritional management can impact both a horse's gastrointestinal health and caretaker costs

ANNE M. EBERHARDT

Individual Commitment

TAILORING **FEED PROGRAM** TO EACH HORSE CAN **PAY DIVIDENDS**

By **AMANDA DUCKWORTH**

A HORSE'S DIETARY needs vary depending on the lifestyle it leads. However, well-intentioned nutrition plans sometimes are based on traditional practices that might or might not be right for the animal in question. Working with someone who best understands a specific horse's requirements is the first step in developing a feeding plan, but it's also important to focus on continual education regarding equine nutrition.

Worldwide research is being done that examines common management practices, with an eye toward how they might or might not impact overall health as well as ways to improve them.

One such recent study, "A Survey of Pennsylvania Horse Management: Part One—Nutrition," was published in December 2022 by the *Journal of Equine Veterinary Science*.

"Various aspects of nutritional management can impact both a horse's gastrointestinal health and caretaker costs," researchers explained. "The objective of this study was to characterize the feeding management and GI issues of horses in Pennsylvania."

Researchers devised an online survey and used Kruskal-Wallis and Mann-Whitney tests to analyze the data resulting from the 470 collected responses. The majority of horses in the survey were Quarter Horses and Thoroughbreds.

"Of the 345 horses who received premixed feed, 81% were fed on a volume basis," researchers noted. "Most horses (95%) received hay on a volume basis, and 57% of horses were fed hay on the ground rather than in a feeder. No difference was detected in the number of scoops of premixed feed or the flakes of hay per day between horses in different exercise categories. The frequency of reported GI issues was 10%.

"No statistical difference was detected in the number of scoops of premixed feed fed per day between horses with or without GI issues. Horses were provided the same amount of premixed feed and forage regardless of reported exercise category. Most equine caretakers fed concentrates on volume rather than weight, a common practice despite most feeding requirements being based on feed weights."

In January 2023 *Animals (Basel)* published "Validating a Thoroughbred Racehorse Welfare Index through Horse Behavior and Trainers' Reports of Welfare Issues in Their Horses." This wide-ranging study covered a number of categories, including nutrition.

"The racing industry is continually challenged to improve Thoroughbred racehorse conditions both in training and race procedures, particularly those identified as welfare issues," explained researchers. "The training of (Thoroughbred racehorses) is often based on management and husbandry methods that have been determined over many

A Novel Approach to Gastric Ulcer Management

The presence and severity of equine gastric ulcer syndrome (EGUS) depends largely on a horse's breed, use, and disposition. While gastric ulcers can affect all classes of horses, they are especially widespread among performance horses. In some high-performance disciplines, such as racing, gastric ulcers are commonplace. When severe enough, gastric ulcers can completely sideline a horse, making prevention or resolution of them paramount.

ReSolvin EQ™ is a research-proven supplement that reduces the severity of ulceration and prevents new ulcers from developing in the squamous portion of the stomach. In a study performed by Kentucky Equine Research, severe squamous gastric ulcers completely resolved in 80% of horses in the study (Thoroughbreds) after 90 days of supplementation with ReSolvin EQ.

Developed by: Kentucky Equine Research®

In summary, targeted supplementation with ReSolvin EQ, a blend of the long-chain polyunsaturated fatty acids GLA (gamma-linolenic acid), EPA (eicosapentaenoic acid), and DHA (docosahexaenoic acid), provides potent anti-inflammatory protection for horses predisposed to gastric ulcers.

KERx is a division of KER Targeted Nutrition featuring products developed by Kentucky Equine Research and recommended by veterinarians to support specific nutrition-related challenges.

Learn more at ker.com/resolvin.

years to be convenient to humans but not necessarily scientifically evaluated."

Researchers in Australia developed a welfare index through expert opinion on horse behavior recorded in a range of training stables, then surveyed trainers to investigate the environment and management systems for Thoroughbred racehorses. While different areas were examined in the study, and some fared better than others, the majority of trainers handled nutrition as a prioritized, individualized matter.

"Regarding nutrition, most trainers (78%) said that they paid attention to the requirements of individual horses, as determined by age and training, balancing fiber/grain intake, and providing access to additional green forage," researchers found. "Some (17%) paid attention to individual horses' needs but only provided infrequent access to green forage. Just 2% of trainers did not supply any green forage and did not pay attention to individual horses' requirements.

"The time budget of the Thoroughbred racehorse is influenced by the management system, but they often only spend 10%-40% of the day consuming their ration of concentrates and hay, in contrast to free-ranging or feral horses, who typically spend 70% of the day foraging."

ANNE M. EBERHARDT

At the track, horses spend 10%-40% of the day consuming their ration of concentrates and hay, in contrast to free-ranging or feral horses, who typically spend 70% of the day foraging, according to a study

Hay is a vital part of a horse's nutritional program. As the American Association of Equine Practitioners explains in its overview "Hay Quality and Horse Nutrition: Evaluating Your Horse's Nutritional Needs," horses are foragers by nature.

"Horses are most content when they can nibble almost constantly," explains the AAEP. "As an added benefit, horses that are allowed to graze continuously will typically have less dental problems. Although it's not always possible to let our domesticated friends graze to their hearts' content, one way to satisfy their urge to chew and provide essential nutrients is to feed high-quality hay.

"Hay generally falls into one of two categories—grasses or legumes. Horse hay is often a mixture of the two. What

Doc's Products OCD Pellets

OCD Pellets (Optimal Cartilage Development) are proven to increase comfort associated with daily activities to help maintain a mobile, sound, pain-free horse.

Building healthy bone requires the proper activity of bone-building nutrients, hormones, and cells. OCD Pellets, a 2-in-1 supplement, support the bone and joint health of horses in all stages of life. The dual-action of OCD Pellets supplies the building blocks necessary for the formation and maintenance of healthy cartilage and bone. Since inflammation interferes with bone remodeling and accelerates bone loss, OCD Pellets rely on Corta-Flx, a clinically proven formula, as a source of nutrients that addresses inflammation of the joint.

Studies demonstrate chondroitin, glucosamine, and hyaluronic acid are large molecules that are difficult to absorb. OCD Pellets do not rely on these large molecules for absorption. Our formula is micro-sized isolates of the active ingredients of chondroitin and glucosamine, resulting in higher levels of assimilation and absorption. No other products with glucosamine and chondroitin—regardless of milligram strength—can match the effectiveness of the OCD Pellets.

Effective in the treatment of OCDs, epiphysitis, DJD, bucked shins, sesamoiditis, bone cysts, bone bruising, navicular syndrome, and more, OCD Pellets provide the nutritional requirements for the development, maintenance, and repair of bones and joints, keeping your horse sound and pain free at all stages of life.

Visit OCDPellets.com to order and receive four pounds of OCD Pellets free with your first order.

The most common nutritional risk factors for equines are related to a decrease in forage intake

is readily available and most cost-effective generally depends on the part of the country in which you live."

A number of factors can influence price points and what hay varieties are available at any given time, which can lead to potential switches in a horse's diet. In June 2022, the *Journal of Equine Veterinary Science* published "When Changing the Hay Makes a Difference: A Series of Case Reports."

"Dry hay (composed of grass, legumes, or a mixture of the two) provides the primary source of alimentary fiber in stabled horses with limited access to fresh pasture," explains the case study. "However, hay can also give rise to health problems in the horse, depending on the quality and quantity of its components. Pathologies might be rooted in biological problems, such as inadequate digestion disturbances, or reflect mechanical difficulties, for example, due to the presence of sharp plant parts that irritate the oral mucosa or due to physical intake problems that inhibit consumption."

Case 1 dealt with unwanted plants in the hay, which caused stomatitis. Case 2 examined the results of horse dysphagia, which is defined as a difficulty in ingesting feed through the mouth and esophagus. Case 3 pertained to free fecal water syndrome (FFWS) and whether or not hay quality plays a key role.

"The most common nutritional risk factors for equines are related to a decrease in forage intake, an altered nutritional value of the forage, or its poor hygienic quality," said researchers. "In particular, the poor nutritional and hygienic quality of hay has been shown to be responsible for a number of health disorders, including gastric ulcers, colic, diarrhea, and recurrent airway obstruction.

"This case series highlights the importance of hay quality and of providing an appropriate and adequate fiber intake. Moreover, good hay management becomes crucial when horses are affected by contextual pathologies, such as stomatitis, dysphagia, or FFWS."

Horses are sensitive to the dust often found in hay and bedding. With racehorses, this is doubly problematic, as being able to breathe easily is obviously important while competing at high speeds.

"Effects of low-dust forages on dust exposure, airway cytology, and plasma omega-3 concentrations in Thoroughbred racehorses: A randomized clinical trial," was published by the *Journal of Veterinary Internal Medicine* in January 2023.

"Racehorses commonly develop evidence of mild asthma in response to dust exposure," explained researchers. "Diets deficient in omega-3 polyunsaturated fatty acids (Ω-3) might exacerbate this response."

For the study, researchers compared dust exposure, bronchoalveolar lavage fluid cytology, and plasma Ω-3 and specialized pro-resolving mediators (SPM) concentrations amongst 43 Thoroughbred racehorses fed dry hay, steamed hay, and haylage. The horses involved were randomly assigned to be fed one of the three hay varieties for six weeks, and measures of exposure to dust in the breathing zone were obtained twice.

"Respirable dust was significantly higher for horses fed hay when compared with steamed hay or haylage," researchers concluded. "At week six, bronchoalveolar lavage fluid neutrophil proportions in horses eating haylage were significantly lower compared with baseline and horses eating hay. Plasma eicosapentaenoic acid to arachidonic acid ratios were higher in horses eating haylage for six weeks when compared with baseline and horses eating steamed or dry hay.

"Steamed hay and haylage reduce dust exposure compared with dry hay, but only haylage increased the ratio of anti-inflammatory to pro-inflammatory lipids while reducing BAL neutrophil proportions within six weeks."

Thoroughbreds often receive supplements to their standard diet, which is something that also needs to be properly managed. In September 2022, *Animals (Basel)* published "Dietary Iron Unlikely to Cause Insulin Resistance in Horses."

"Racehorses are often supplemented extra iron with the expectation that the iron will improve overall performance and health," explained researchers.

RICK SAMUELS

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, which limits amino acid in horses. All feeds are formulated and fortified through 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.

Recent studies suggest benefits in creating feed plans suited for each individual horse

For the study, researchers surveyed 120 U.S. Thoroughbred trainers from a variety of regions. A total of 1,978 Thoroughbreds were represented in the survey, which was conducted to determine the average amount of dietary iron fed to Thoroughbred racehorses per day.

"Survey results indicated racehorses were fed an average of 3,900 mg of iron per day from hay and grain alone," researchers found. "This exceeds the 0.8 mg/kg BW or 400 mg for a 500 kg working horse that the NRC 2007 recommends per day. Supplements increased the daily average intake of iron by an additional 500 mg Fe. Some equine nutritionists propose that excess dietary iron (might) be a causative factor in insulin resistance.

"However, the occurrence of insulin resistance in Thoroughbred racehorses is very rare. This study did not find one confirmed veterinary diagnosis of insulin resistance in any of the surveyed trainers' Thoroughbred horses, whether racing, on a layoff, or retired. Given the iron content in these diets easily exceeds the NRC minimum daily requirements, it seems unlikely that dietary iron is an independent causative factor in insulin resistance."

Hydration is another important part of proper nutrition. As the old saying goes "you can lead a horse to water, but you can't make it drink." A recent study suggests that the horse might be too hungry to drink. In January 2021, the *Equine Veterinary Journal* published "Effect of feed deprivation on daily water consumption in healthy horses."

"Measurements of water consumed by fed, healthy horses might not apply to horses that are unwilling or unable to drink or are not fed for any reason," explained researchers.

In a randomized crossover designed study, eight healthy Thoroughbred geldings were used. Researchers measured water intake, bodyweight, physical findings, and vital signs during four days of being fed properly as well as during four days of feed deprivation.

"Daily measurements during the trial periods were PCV, TPP, electrolytes,

osmolality, and triglycerides," explained researchers. "Plasma and extracellular fluid volumes were measured in the last eight hours of the trial periods. Data were analyzed with a two-way analysis of variance with repeated measures, and statistical significance was $P \leq .05$. Feed deprivation immediately and persistently reduced water consumption to ~16% of fed values, with laboratory evidence of mild dehydration on day four.

"Changes in total body water and in water and electrolyte excretion or conservation through feces and urine were not measured. Feed consumption has a marked effect on water

TOP: SKIP DICKSTEIN; BOTTOM: ANNE M. EBERHARDT

requirements in healthy horses. Because current guidelines for water needs were obtained in the fed state, they might not apply to horses that are denied feed for any reason or have reduced feed intake. This study provides new information on water consumption in horses that should apply to this essential nutrient in health and disease."

Access and being comfortable in their surroundings also have an impact on the willingness of horses to drink. In November 2022, the *Journal of Equine Veterinary Science* published "The Behavior of Horses Stabled in a Large Group at Essential Resources (Watering Point and Lying Halls)."

For the study, researchers observed the behavior of 51 horses that were kept in one group. Drinking events, interactions between horses, and time spent at the accessible water were analyzed for 18 days.

"The time period had significant effects on drinking events with visible interactions," researchers explained. "The highest least square means and standard errors of drinking events with and without visible interaction were observed between noon-2 p.m., which was also the time period of main occupancy of the watering point. About 57% of drinking events were classed as with visible interaction, of which more than 90% were mild (i.e. laying back of ears, tightening of face)."

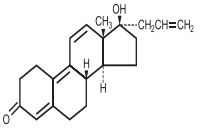
Keeping a horse at peak fitness is a multi-faceted endeavor. There is no magic feeding plan that is appropriate for all horses, but working with professionals and staying up to date on the latest research are key steps in understanding how to best meet an individual horse's needs. BH

> **"HORSES ARE MOST CONTENT WHEN THEY CAN NIBBLE ALMOST CONSTANTLY. AS AN ADDED BENEFIT, HORSES THAT ARE ALLOWED TO GRAZE CONTINUOUSLY WILL TYPICALLY HAVE LESS DENTAL PROBLEMS."**
>
> —AAEP

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

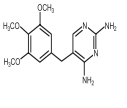


Figure 2. Structure of trimethoprim

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.auroraphar maceutical.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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