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Equine Stomach Ulcer Prevalence Remains at 60 Percent ***Nationwide scopings demonstrate all horses at risk***

DULUTH, GA. — March 10, 2010 — For the second year, a nationwide series of more than 160 gastroscopy events showed 60 percent of horses were identified with stomach ulcers.¹

“This is the second year that these scopings were able to show horse owners the type of potentially painful stomach ulcers that their horses have been dealing with,” says April Knudson, DVM, manager, Merial Veterinary Services. “Many times, horses are suffering in silence from stomach ulcers due to their natural tendencies as a prey animal to mask pain. In talking to many of these owners myself, they are frequently surprised to find out their horse had been suffering from stomach ulcers, but the evidence is clear.”

At these events, veterinarians evaluated the horses’ stomachs using gastroscopy, which is the only definitive way to determine if a horse has ulcers, Dr. Knudson says.

Throughout the year, 1,532 horses across the country participated in events. Overall, 922 horses from 37 states had some ulceration as identified by gastroscopy. Horses of varying ages and disciplines were found to have all grades of stomach ulcers, including:¹

- Horses from 2 months to 30 years of age
- 610 horses, or 40 percent, were Grade 0 (healthy, nonulcerated stomach)
- 471 horses, or 31 percent, were Grade 1 (mild ulcers, with small lesions or damaged tissue)
- 319, or 21 percent, were Grade 2 (moderate ulcers with large lesions)
- 132, or 9 percent, were Grade 3 (extensive lesions with deep ulceration and bleeding)
- 86 percent of racing horses had some grade of ulcers (226 total participating)
- 59 percent of eventing horses (113 total participating)
- 59 percent of hunter jumpers (168 total participating)
- 52 percent of barrel racing horses (122 total participating)
- 48 percent of dressage (107 total participating)

(more)

Nationwide Scopings Demonstrate Ulcer Prevalence March 10, 2010

There are many triggers for stomach ulcer development, and stress is an important factor, Dr. Knudson says.

Horses are especially sensitive and may experience stress when exposed to situations you would think of as normal, including competition, training, travel, lay-up due to sickness or injury, shows or events, limited turnout or grazing, or trailering.^{2,3}

Ulcers can develop quickly, too. One study showed that horses can develop stomach ulcers in as little as five days.⁴

“For competitive horse owners, it’s important to think about preventing stomach ulcers, because stomach ulcers can diminish the hard work, training and commitment both horse and rider worked hard to achieve,” Dr. Knudson notes. “Before a complete gastroscopy and treatment regimen is needed, it can pay to help prevent stomach ulcers before they start.”

Before using any products for stomach ulcers, Dr. Knudson recommends only trusting those that are FDA-approved to work safely and effectively.

For those 60 percent of horses diagnosed with ulcers, Dr. Knudson recommends a course of GASTROGARD® (omeprazole) to treat those ulcers. GASTROGARD is the only FDA-approved product to treat and heal stomach ulcers.⁵ However, stomach ulcers can still return even after completion of a successful treatment program, if horses are exposed to stressful situations again.

Preventing stomach ulcers before they start is more cost effective, Dr. Knudson notes. She recommends using ULCERGARD® (omeprazole) during times of stress, which is the only FDA-approved, proven preventive for stomach ulcers.⁶

“Even with top-notch care and regular veterinary visits, many horse owners don’t like to think that stomach ulcers may develop in their horses,” Dr. Knudson says. “But, the results of these scopings confirm what university studies have found previously: horses of all competitive disciplines are at risk for stomach ulcers.”

Merial is a world-leading, innovation-driven animal health company, providing a comprehensive range of products to enhance the health, well-being and performance of a wide range of animals. Merial employs approximately 5,700 people and operates in more than 150 countries worldwide. Its 2009 sales were over \$2.7 billion. Merial is the Animal Health subsidiary of sanofi-aventis. For more information, please see www.merial.com.

IMPORTANT SAFETY INFORMATION:

Caution: Safety of GASTROGARD in pregnant or lactating mares has not been determined.

ULCERGARD can be used in horses that weigh at least 600 pounds. Safety in pregnant mares has not been determined.

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Nationwide Scopings Demonstrate Ulcer Prevalence March 10, 2010

¹Data on file at Merial.

²ULCERGARD product label.

³Murray MJ. Disorders of the stomach. In: Smith BP, ed. *Large Animal Internal Medicine*. St. Louis; CV Mosby, 1990: 710-717.

⁴McClure SR, Carithers DS, Gross SJ, Murray MJ. Gastric ulcer development in horses in a simulated show or training environment. *J Am Vet Med Assoc* 2005;227(5):775-777.

⁵GASTROGARD Oral Paste product label.

⁶Freedom of Information summary for ULCERGARD Oral Paste.

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GastroGard® (omeprazole)

Oral Paste for Horses and Foals

NADA 141-123, Approved by FDA

Caution

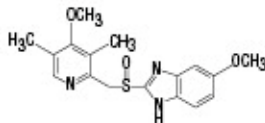
Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description

Chemical name: 5-Methoxy-2-[[[4-methoxy-3,5-dimethyl-2-pyridinyl] methyl]sulthyl]-1H-benzimidazole.

Empirical formula: C₁₉H₁₉N₃O₃S. Molecular weight: 345.42.

Structural formula:



How Supplied

GASTROGARD® (omeprazole) Paste for horses contains 37% w/w omeprazole and is available in an adjustable-dose syringe. Each syringe contains 2.28 g of omeprazole. Syringes are calibrated according to body weight and are available in boxes of 7 units or 72 units.

Storage Conditions

Store at 68°F – 77°F (20-25°C). Excursions between 59°F – 86°F (15-30°C) are permitted.

Indications

For treatment and prevention of recurrence of gastric ulcers in horses and foals 4 weeks of age and older.

Dosage Regimen

For treatment of gastric ulcers, GASTROGARD Paste should be administered orally once-a-day for 4 weeks at the recommended dosage of 1.8 mg omeprazole/lb body weight (4 mg/kg). For the prevention of recurrence of gastric ulcers, continue treatment for at least an additional 4 weeks by administering GASTROGARD Paste at the recommended daily maintenance dose of 0.9 mg/lb (2 mg/kg).

Directions For Use

- GASTROGARD Paste for horses is recommended for use in horses and foals 4 weeks of age and older. The contents of one syringe will dose a 1250 lb (568 kg) horse at the rate of 1.8 mg omeprazole/lb body weight (4 mg/kg). For treatment of gastric ulcers, each weight marking on the syringe plunger will deliver sufficient omeprazole to treat 250 lb (114 kg) body weight. For prevention of recurrence of gastric ulcers, each weight marking will deliver sufficient omeprazole to dose 500 lb (227 kg) body weight.
- To deliver GASTROGARD Paste at the treatment dose rate of 1.8 mg omeprazole/lb body weight (4 mg/kg), set the syringe plunger to the appropriate weight marking according to the horse's weight in pounds.
- To deliver GASTROGARD Paste at the dose rate of 0.9 mg/lb (2 mg/kg) to prevent recurrence of ulcers, set the syringe plunger to the weight marking corresponding to half of the horse's weight in pounds.
- To set the syringe plunger, unlock the knurled ring by rotating it 1/4 turn. Slide the knurled ring along the plunger shaft so that the side nearest the barrel is at the appropriate notch. Rotate the plunger ring 1/4 turn to lock it in place and ensure it is locked. Make sure the horse's mouth contains no feed. Remove the cover from the tip of the syringe, and insert the syringe into the horse's mouth at the interdental space. Depress the plunger until stopped by the knurled ring. The dose should be deposited on the back of the tongue or deep into the cheek pouch. Care should be taken to ensure that the horse consumes the complete dose. Treated animals should be observed briefly after administration to ensure that part of the dose is not lost or rejected. If any of the dose is lost, redosing is recommended.
- If, after dosing, the syringe is not completely empty, it may be reused on following days until emptied. Replace the cap after each use.

Warning

Do not use in horses intended for human consumption. Keep this and all drugs out of the reach of children. In case of ingestion, contact a physician. Physicians may contact a poison control center for advice concerning accidental ingestion.

Adverse Reactions

In efficacy trials, when the drug was administered at 1.8 mg omeprazole/lb (4 mg/kg) body weight daily for 28 days and 0.9 mg omeprazole/lb (2 mg/kg) body weight daily for 30 additional days, no adverse reactions were observed.

Precautions

The safety of GASTROGARD Paste has not been determined in pregnant or lactating mares.

Clinical Pharmacology

Mechanism of Action: Omeprazole is a gastric acid pump inhibitor that regulates the final step in hydrogen ion production and blocks gastric acid secretion regardless of the stimulus. Omeprazole irreversibly binds to the gastric parietal cell's H⁺, K⁺ ATPase enzyme which pumps hydrogen ions into the lumen of the stomach in exchange for potassium ions. Since omeprazole accumulates in the cell canalliculi and is irreversibly bound to the effect site, the plasma concentration at steady state is not directly related to the amount that is bound to the enzyme. The relationship between omeprazole action and plasma concentration is a function of the rate-limiting process of H⁺, K⁺ ATPase activity/turnover. Once all of the enzyme becomes bound, acid secretion resumes only after new H⁺, K⁺ ATPase is synthesized in the parietal cell (i.e., the rate of new enzyme synthesis exceeds the rate of inhibition).

Pharmacodynamics: In a study of pharmacodynamic effects using horses with gastric canulæ, secretion of gastric acid was inhibited in horses given 4 mg omeprazole/kg/day. After the expected maximum suppression of gastric acid secretion was reached (5 days), the actual secretion of gastric acid was reduced by 99%, 95% and 90% at 8, 16, and 24 hours, respectively.

Pharmacokinetics: In a pharmacokinetic study involving thirteen healthy, mixed breed horses (8 female, 5 male) receiving multiple doses of omeprazole paste (1.8 mg/lb once daily for fifteen days) in either a fed or fasted state, there was no evidence of drug accumulation in the plasma when comparing the extent of systemic exposure (AUC_{0-∞}). When comparing the individual bioavailability data (AUC_{0-∞}, C_{max}, and T_{max} measurements) across the study days, there was great inter- and intrasubject variability in the rate and extent of product absorption. Also, the extent of omeprazole absorption in horses was reduced by approximately 67% in the presence of food. This is evidenced by the observation that the mean AUC_{0-∞} values measured during the fifth day of omeprazole therapy when the animals were fasted for 24 hours was approximately three times greater than the AUC estimated after the first and fifteenth doses when the horses were fed hay ad libitum and sweet feed (grain) twice daily. Prandial status did not affect the rate of drug elimination. The terminal half-life estimates (N=38) ranged from approximately one-half to eight hours.

Efficacy

Dose Confirmation: GASTROGARD® (omeprazole) Paste, administered to provide omeprazole at 1.8 mg/lb (4 mg/kg) daily for 28 days, effectively healed or reduced the severity of gastric ulcers in 92% of omeprazole-treated horses. In comparison, 92% of controls exhibited healed or less severe ulcers. Horses enrolled in this study were healthy animals confirmed to have gastric ulcers by gastroscopy. Subsequent daily administration of GASTROGARD Paste to provide omeprazole at 0.9 mg/lb (2 mg/kg) for 30 days prevented recurrence of gastric ulcers in 84% of treated horses, whereas ulcers recurred or became more severe in horses removed from omeprazole treatment.

Clinical Field Trials: GASTROGARD Paste administered at 1.8 mg/lb (4 mg/kg) daily for 28 days healed or reduced the severity of gastric ulcers in 99% of omeprazole treated horses. In comparison, 32.4% of control horses had healed ulcers or ulcers which were reduced in severity. These trials included horses of various breeds and under different management conditions, and included horses in race or show training, pleasure horses, and foals as young as one month. Horses enrolled in the efficacy trials were healthy animals confirmed to have gastric ulcers by gastroscopy. In these field trials, horses readily accepted GASTROGARD Paste. There were no drug related adverse reactions. In the clinical trials, GASTROGARD Paste was used concomitantly with other therapies, which included: anthelmintics, antibiotics, non-steroidal and steroidal anti-inflammatory agents, diuretics, tranquilizers and vaccines.

Diagnostic and Management Considerations: The following clinical signs may be associated with gastric ulceration in adult horses: inappetence or decreased appetite, recurrent colic, intermittent loose stools or chronic diarrhea, poor hair coat, poor body condition, or poor performance. Clinical signs in foals may include: bruxism (grinding of teeth), excessive salivation, colic, cranial abdominal tenderness, anorexia, diarrhea, sternal recumbency or weakness. A more accurate diagnosis of gastric ulceration in horses and foals may be made if ulcers are visualized directly by endoscopic examination of the gastric mucosa. Gastric ulcers may recur in horses if therapy to prevent recurrence is not administered after the initial treatment is completed. Use GASTROGARD Paste at 0.9 mg omeprazole/lb body weight (2 mg/kg) for control of gastric ulcers following treatment. The safety of administration of GASTROGARD Paste for longer than 91 days has not been determined. Maximal acid suppression occurs after three to five days of treatment with omeprazole.

Safety

- GASTROGARD Paste was well tolerated in the following controlled efficacy and safety studies.
- In field trials involving 139 horses, including foals as young as one month of age, no adverse reactions attributable to omeprazole treatment were noted.
- In a placebo controlled adult horse safety study, horses received 20 mg/kg/day omeprazole (5x the recommended dose) for 90 days. No treatment related adverse effects were observed.
- In a placebo controlled tolerance study, adult horses were treated with GASTROGARD Paste at a dosage of 40 mg/kg/day (10x the recommended dose) for 21 days. No treatment related adverse effects were observed.
- A placebo controlled foal safety study evaluated the safety of omeprazole at doses of 4, 12 or 20 mg/kg (1, 3 or 5x) once daily for 91 days. Foals ranged in age from 66 to 110 days at study initiation. Gamma glutamyltransferase (GGT) levels were significantly elevated in horses treated at exaggerated doses of 20 mg/kg (5x the recommended dose). Mean stomach to body weight ratio was higher for foals in the 3x and 5x groups than for controls; however, no abnormalities of the stomach were evident on histological examination.

Reproductive Safety

In a male reproductive safety study, 10 stallions received GASTROGARD Paste at 12 mg/kg/day (3x the recommended dose) for 70 days. No treatment related adverse effects on semen quality or breeding behavior were observed. A safety study in breeding mares has not been conducted.

For More Information

Please call 1-888-637-4251 and please visit our web site at www.gastrogard.com.

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