Merial offers two powerful and unique medications for equine stomach ulcers — one that heals and one that prevents. Together, they give veterinarians and horse owners the tools to protect horses from stomach ulcers and Equine Gastric Ulcer Syndrome (EGUS), which can affect a wide variety of breeds and ages. In fact, stomach ulcers have been diagnosed in 93% of racehorses, 63% of nonracing competitive horses and 51% of foals. And they can occur in as little as five days.

Merial is dedicated to advancing the partnership between the veterinarian and the horse owner, as well as a healthy bond between horse and owner. GASTROGARD® (omeprazole) and ULCERGARD® (omeprazole) offer two products that provide very different solutions for horse health.

How they’re similar:

- Both are powered by omeprazole as their active ingredient
- Both are FDA-approved — unique among products used for stomach ulcers
- Both can be used while horses continue their regular training regimen
- Both are administered orally
- Both are a cinnamon-flavored paste and are well-accepted by horses
- Both have convenient once-a-day dosing

How they’re different:

<table>
<thead>
<tr>
<th>GastroGard® (omeprazole)</th>
<th>UlcerGard® (omeprazole)</th>
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<tbody>
<tr>
<td><strong>Treat and heal the stomach ulcer (EGUS)</strong></td>
<td><strong>Prevent the stomach ulcer (EGUS)</strong></td>
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<tr>
<td><strong>Focus on clinical signs</strong> for diagnosis, including:</td>
<td><strong>Focus on stress factors</strong> to pre-empt the stomach ulcer:</td>
</tr>
</tbody>
</table>
| - Change in eating and drinking behavior | - Competition
| - Weight loss | - Training
| - Change in attitude (for the worse) | - Travel
| - Recurrent colic | - Limited turnout or grazing
| - Dull hair coat | - Lay-up due to sickness or injury
| - Less-than-optimal performance | - Changes in routine
| **Where it fits:** | **Where it fits:** |
| For use in horses diagnosed with stomach ulcers. | For use in healthy horses. |
| **Regimen:** | **Regimen:** |
| 28-day treatment | As needed for prevention*** |
| **Convenient packaging:** | **Convenient packaging:** |
| One daily dose per syringe for horses weighing up to 1,250 lbs. | Four daily doses per syringe for horses weighing 600 - 1,200 lbs.; administered once daily during stressful period (when horse will be exposed to stress factors listed above) |
| **Prescription only:** | **Non-prescription:** |
| Prescribed by licensed veterinarians. | Sold through licensed veterinarians.****

ULCERGARD® (omeprazole) can be used in horses that weigh at least 600 pounds. The effectiveness of ULCERGARD in the prevention of gastric ulcers in foals and weanlings has not been evaluated. ULCERGARD may be used safely in breeding stallions. Safety in pregnant mares has not been determined.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. GASTROGARD® (omeprazole) is indicated for the treatment and prevention of recurrence of gastric ulcers in horses and foals 4 weeks and older. In efficacy trials, no adverse reactions were observed. Safety in pregnant or lactating mares has not been determined. DO NOT USE IN HORSES INTENDED FOR HUMAN CONSUMPTION. KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.
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.

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

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/kg (4 mg/kg) body weight daily for 28 days and 0.9 mg omeprazole/kg (2 mg/kg) body weight daily for 10 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 canalicular 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 cannulae, 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 89%, 95% and 98% 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/kg 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(∞−∞) vs. AUC(∞−0)). When comparing the individual bioavailability data (AUC(∞−∞) vs. Cmax, and Tmax measurements) across the study days, there was great inter- and intra-subject 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. It is evidenced by the observation that the mean AUC(∞−∞) 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 all breakfast and sweet feed (grain) twice daily. Preclinical status did not affect the rate of drug elimination. The terminal half-life estimates (t1/2) ranged from approximately one-half to eight hours.

Efficacy
Dose Confirmation: GASTROGARD® (omeprazole) Paste, administered to provide omeprazole at 1.8 mg/kg (4 mg/lb) daily for 28 days, effectively healed or reduced the severity of gastric ulcers in 92% of omeprazole-treated horses. In comparison, 32% 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/kg (2 mg/lb) 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/kg (4 mg/lb) 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: antiinfectives, antibiotics, non-steroidal and steroidal anti-inflammatory agents, diuretics, tranquilizers and vaccines.

Diagnostic and Management Considerations:
The following clinical signs may be associated with gastritis ulceration in adult horses: inappetence or decreased appetite, recurrent colic, intermittent loose stool 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/kg 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 tolerability study, adult horses were treated with GASTROGARD Paste at a dosage of 45 mg/kg/day (10x the recommended dose) for 21 days. No treatment-related adverse effects were observed.
• A placebo controlled faecal safety study evaluated the safety of omeprazole at doses of 4, 12 or 20 mg/kg (1X, 3X 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 exagerrated doses of 20 mg/kg (5x the recommended dose). Mean stools 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. Marketed by: Merial Limited, Duluth, GA. 30096-6460

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• Equine Gastric Ulcer Syndrome.
• **ULCERGARD has not been evaluated in foals.
• ***When administered for 8 or 28 days, ULCERGARD is proven to effectively prevent gastric ulcers in horses exposed to stressful conditions.
• ****ULCERGARD is available over the counter for lay use because a diagnosis of gastric ulcer disease is not required in order to prevent the disease.³

⁵GASTROGARD product label.
⁶ULCERGARD product label.
⁹Freedom of information summary for ULCERGARD (NADA 141-227).

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