Pharmacokinetic and Bioequivalence of Ulcershield®, a Novel Omeprazole Product

Sharanne L. Raidal1, Frank M. Andrews2, Gareth D. Trope1
1School of Animal and Veterinary Sciences, Veterinary Clinical Centre, Charles Sturt University, Agriculture Avenue, Locked Bag 588, Wagga Wagga NSW, Australia; 2Equine Health Studies Program Dept of Veterinary Clinical Sciences, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA., USA.

Introduction
Equine Gastric Ulcer Syndrome (EGUS) is common and prevalence ranges from 60 to 90%. Ulcers occur in the nonglandular (squamous) and glandular stomach due to its lack of resistance due to the erosive effects of gastric acids (hydrochloric, volatile fatty and bile acids). Horses with this condition perform poorly which makes it a significant economical problem within the horse industry. Omeprazole, a potent antiulcer medication, is highly effective in treating and preventing stomach ulcers by increasing stomach pH setting up a permissive environment for healing. Ulcershield®, a novel formulation of omeprazole paste, is a potent antiulcer medication and promotes healing of stomach ulcers in horses. The purpose of this study was to compare the pharmacokinetics (PK) Ulcershield® (Randlab Pty Ltd, Chipping Norton, NSW, Australia) to an existing registered omeprazole product (Ceva Omoguard Paste).

Materials and Methods
Twelve healthy Thoroughbred and Standardbred horses (7 geldings and 5 females), aged 3 to 8 years (5.25 ± 2.00 years, mean ±SD), weighing 365-548 kg (461.9 ± 53.9 kg) with no abnormalities on physical examination, haematology or serum biochemistry were included in the study. Horses were acclimatised to box stalls (Day -7) for at least 1 week before treatment, and were fed pelleted feed (1 kg, twice daily; Coprice, Leeton NSW) and oaten hay (1.5 - 2% bwt) divided twice daily. Horses were turned out into a dirt yard for a least 1 hour daily. Water was supplied ad lib, and horses were monitored daily for clinical signs or adverse events. The study was performed as a masked, randomized, 2-period, 2-treatment crossover design so that all horses received the two formulations of omeprazole (4.0 mg/kg, orally, q24h) from Days 0 to 5, 6 daily doses. Jugular catheters were placed aseptically at 8am on Days 0 and 6. Approximately 10mL of venous blood was collected from the catheters and placed into blood tubes containing lithium heparin prior to treatment (t=0h), and following treatment at 15 min, 30 min, 45 min, 60 min, 75 min, 90 min, 105 min, 120 min, 135 min, 150 min, 165 min, 180 min, 3.5h, 4h, 4.5h, 5h, 6h, 7h, 8h, 12h, 24h. Blood samples were stored on ice until centrifugation within four hours of collection. Plasma was collected and stored -20°C until shipment. Omeprazole concentrations in plasma were determined in duplicate using a validated analytical method based on instrumental determination using Ultra High Performance Liquid Chromatography tandem mass spectrometry (PIA PHARMA PTY LTD, Gladesville, NSW). The omeprazole time/concentration results were plotted and the area under the curve (AUC) and maximal plasma concentration (Cmax) were calculated for each horse. The AUC and Cmax data were converted to natural log and analysed by analysis of variance.

Results
Pharmacokinetic data is listed in Table 1. Analysis of lnAUC, indicated there was no statistically significant difference in between products (Figure 1). There was significant difference between individual animals. There was no statistically significant difference in log-transformed maximal plasma concentrations attributed to animals, sequences, periods or treatments. Ulcershield® showed a shorter time to maximum concentration (Tmax) and a higher maximum concentration (Cmax) than Omoguard®, but these values were not significantly different.

Conclusion
• Ulcershield® was safe and no adverse responses were seen in the treated horses.
• Ulcershield® and Omoguard® treatments resulted in statistically equivalent plasma concentrations.
• Ulcershield® and Omoguard® mean residency time and half-lives confirmed similarity of the two products.
• Ulcershield® demonstrated statistical similarity to the reference product and non-inferiority (related to pH studies) of the test product relative to Omoguard®.
• Ulcershield® would perform in a similar manner to the reference product when used according to label directions.
• Ulcershield® is pharmacodynamically bioequivalent to Omoguard® and shows beneficial effects on the treatment of gastric ulcers in horses.

References

Ulcershield® is a registered trademark of Randlab Pty LTD. Ulcershield® APVMA #81799/104073. Omoguard® is a registered trademark of Ceva Animal Health.