

# Esomeprazole in the treatment of equine glandular gastric disease

**Background:** Equine glandular gastric disease is a highly prevalent disease, for which there is no universally effective treatment. Given the widespread use of esomeprazole in the treatment of peptic ulcer disease in humans, its use in horses warrants further investigation.

**Objective:** To assess rates of healing of equine glandular gastric disease using oral esomeprazole.

**Study design:** Retrospective case series.

**Methods:** Medical records and gastroscopy images of horses diagnosed with equine glandular gastric disease and treated with esomeprazole by Avon Ridge Equine Veterinary Services were reviewed.

**Results:** Out of four horses treated with esomeprazole for 28 days, 75% (three) healed and 25% (one) did not improve. Out of three horses treated with esomeprazole for 14 days, 67% (two) healed and 33% (one) did not improve.

**Main limitations:** The study was limited by its retrospective nature and small sample size.

**Conclusions:** Esomeprazole may be a valid first-line treatment option for equine glandular gastric disease.

Larger and more robust studies of esomeprazole are warranted.

<https://doi.org/10.12968/ukve.2021.5.5.216>

**Tania Sundra** BSc(Hons) BVMS MANZCVS (Equine Medicine), Avon Ridge Equine Veterinary Services, Brigadoon, Australia. ORCID ID: <https://orcid.org/0000-0003-0556-4406>. [taniasundra@yahoo.com](mailto:taniasundra@yahoo.com)

**Key words:** equine glandular gastric disease | esomeprazole | gastric ulcer | proton pump inhibitor

Equine glandular gastric disease (EGGD) is a highly prevalent condition in performance horses (Hepburn and Proudman 2014; Sykes et al, 2015a). Studies have detailed the prevalence of EGGD across a variety of equestrian disciplines and horse populations, reporting a prevalence of 47–65% in thoroughbred racehorses (Begg and O’Sullivan 2003; Sykes et al, 2015); 16–35% in endurance horses (Nieto et al, 2004; Tamzali et al, 2011) and 54–57% in leisure horses (Husted et al, 2009; Luthersson et al, 2009; Malmkvist et al, 2012). While acid injury is not thought to initiate EGGD, acid suppression appears to be an important factor in healing these lesions (Sykes et al, 2015a).

Proton pump inhibitors are the mainstay of gastric acid suppression in both human and veterinary medicine. Omeprazole is the only proton pump inhibitor authorised for use in horses and while oral omeprazole results in squamous healing rates of over 70% (Murray et al, 1997; Andrews et al, 1999; Doucet et al, 2003; Lester et al, 2005), it is considered ineffective as monotherapy in the treatment of glandular lesions (Rendle et al, 2018).

A recent consensus paper by Rendle et al (2018) outlined three first-line options for the treatment of glandular disease:

- Oral omeprazole and sucralfate

- Misoprostol
- Long-acting injectable omeprazole.

The highest rates of healing have been reported following the use of long-acting injectable omeprazole (Sykes et al, 2017a; Gough et al, 2019). Reported rates of healing following 4 weeks of oral omeprazole and sucralfate therapy are between 20% and 67.5% and this variation is likely a result of differing definitions of healing between authors (Hepburn and Proudman, 2014; Varley et al, 2019). This combination also presents practical challenges for owners regarding the administration of both medications at different times on an empty stomach. Misoprostol has been reported to result in healing of EGGD in 55–72% cases (Varley et al, 2019; Pickles et al, 2020). However, one study reported that in 42% of cases treated with misoprostol, squamous disease either developed or worsened (Pickles et al, 2020). Furthermore, misoprostol tablets (Cytotec, Pfizer) are increasingly difficult to source and the human health safety concerns must also be considered. Given the lack of robust evidence to support the use of oral omeprazole or misoprostol in the treatment of EGGD, alternative oral preparations should be investigated.

In human medicine newer proton pump inhibitors have been developed, including pantoprazole, rabeprazole and most recently,

esomeprazole (Andersson et al, 2001; Kendall, 2003; Gralnek et al, 2006). Esomeprazole is the S-isomer of omeprazole, which results in more pronounced and consistent acid suppressive effects compared to omeprazole in humans (Lind et al, 2000; Rohss et al, 2001). Evidence to support its use in the treatment of glandular disease is lacking, although esomeprazole has been associated with the healing of both squamous and glandular lesions in 80% of horses that failed to respond to oral omeprazole monotherapy (Rendle, 2017). Given its widespread use in the treatment of peptic ulcer disease in humans (Lenoir et al, 2019; Madi et al, 2019; Thompson, 2019) and the limited efficacy of other oral preparations available for horses, esomeprazole warrants further investigation as an alternative treatment option for EGGD.

The objective of this study was to conduct a retrospective evaluation of EGGD cases treated with esomeprazole. To the author's knowledge, there are no published reports detailing the effectiveness of oral esomeprazole as a first-line treatment option for clinical cases of glandular gastric disease.

## Methods

### Horses

Medical records and gastroscopy images from horses examined between July 2020 and May 2021 by Avon Ridge Equine Veterinary Services were reviewed. Horses diagnosed with EGGD and treated first-line with oral esomeprazole at 4 mg/kg were identified and included in the study.

### Medication

The esomeprazole used was a compounded oral paste containing enteric coated esomeprazole granules (100mg/ml; Bova Aus, Caringbah, New South Wales, Australia).

### Gastroscopy

Following sedation with 0.01mg/kg detomidine hydrochloride (10mg/ml; Dozadine, Virbac Pty Ltd, Sydney, Australia), gastroscopy was performed using a 3.3 m flexible gastroscope (Endo I; Steris, Mentor, Ohio, USA) to visualise the squamous mucosa as well as the glandular mucosa at the level of the margo plicatus and pyloric antrum. The presence of residual fluid in the stomach of all horses obscured the observation of the most ventral portion of the glandular mucosa. Gastroscopy was then repeated within 0–3 days, following the discontinuation of treatment to assess endoscopic response.

### Client Communication

Owners were advised to administer esomeprazole paste in the morning, following an overnight fast and at least 30–60 minutes before feeding. A standard advice sheet was emailed to owners following the gastroscopy procedure to outline management changes including reducing the frequency of exercise to 4 days per week, minimising the number of riders and handlers, and identifying stressors for each individual horse.

Upon follow-up gastroscopy, owners reported that they had complied with medication advice and had made attempts to reduce stressors, but all horses were maintained in their current workload.

## Results

A total of seven horses met the criteria for inclusion, including two Thoroughbreds, one Arabian X, one Welsh Pony, one Riding Pony, one Standardbred and one Warmblood. There were three geldings and four mares, with ages ranging from 8–23 years old. Out of seven horses, four were treated for 28 days and three were treated for 14 days.

Upon follow-up gastroscopy for the four horses treated with esomeprazole for 28 days, glandular lesions were healed in three horses (75%) and one horse (25%) showed no improvement.

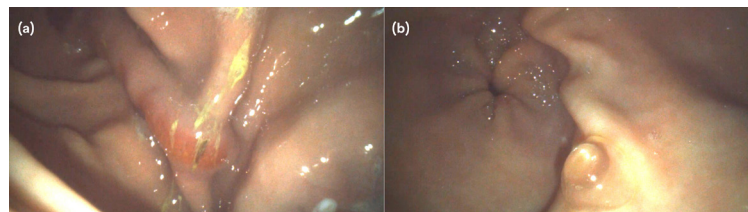


Figure 1. Case 1. 13-year-old Thoroughbred, mare. Before (a) and after (b) treatment with esomeprazole for 28 days.

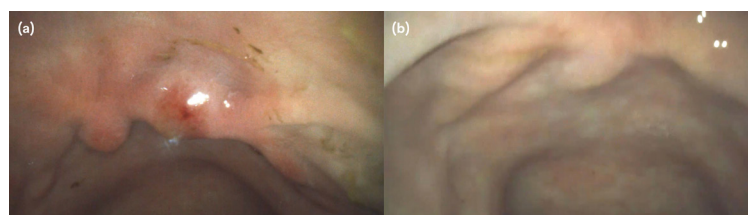


Figure 2. Case 4. 8-year-old Warmblood, gelding. Before (a) and after (b) treatment with esomeprazole for 28 days.

**Table 1. Case details of horses included in the study**

Case	Signalment	Lesion Type	Location	Treatment Duration	Result
1	13-year-old Thoroughbred, mare	Raised, fibrino-suppurative	Pyloric antrum	28 days	Healed (Figure 1)
2	23-year-old Thoroughbred, gelding	Flat, erythematous	Pyloric antrum	28 days	No improvement
3	16-year-old Warmblood X, mare	Flat, erythematous	Pyloric antrum	28 days	Healed
4	8-year-old Warmblood, gelding	Raised, haemorrhagic	Pyloric antrum	28 days	Healed (Figure 2)
5	6-year-old Welsh Pony, mare	Flat, erythematous	Fundus	14 days	Healed (Figure 3)
6	13-year-old Riding Pony, mare	Flat, erythematous	Fundus	14 days	Healed
7	11-year-old Standardbred, gelding	Flat, erythematous	Pyloric Antrum	14 days	No improvement

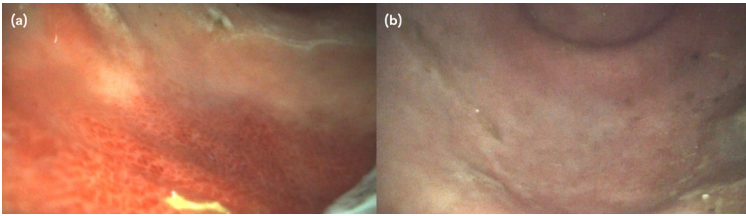


Figure 3. Case 5. 6-year-old, Welsh Pony, mare. Before (a) and after (b) treatment with esomeprazole for 14 days.

On follow-up gastroscopy for the three horses treated with esomeprazole for 14 days, glandular lesions were healed in two horses (67%) and in one horse (33%) there was no improvement.

The owners declined further treatment in cases 2 and 7, both of which showed no improvement following 28 and 14 days of esomeprazole, respectively.

## Discussion

The healing of 75% and 67% of horses with equine glandular gastric disease treated with 28 and 14 days of esomeprazole, respectively, is attributed to the potent acid suppressive effects of esomeprazole. In human medicine, studies have shown that esomeprazole has a more rapid onset of action; is metabolised by the liver much more slowly and results in a three to four times higher area under the curve, compared to omeprazole (Andersson et al, 2001; Kendall, 2003). A higher plasma concentration allows more drug to enter the parietal cell to inhibit hydrochloric acid production. In horses, esomeprazole has also been demonstrated to be superior to omeprazole in its ability to increase gastric pH (Pereira et al, 2009; Videla et al, 2011; Sykes et al, 2017b).

The rate of healing following 28 days of treatment with esomeprazole is similar to rates reported using long-acting injectable omeprazole (Sykes et al, 2017a; Rendle et al, 2018), albeit in a much smaller number of horses. While there exists a growing body of evidence to suggest that long-acting injectable omeprazole is the most effective treatment option for EGGD (Sykes et al, 2017a; Gough et al, 2019, 2020), esomeprazole may provide a valid alternative for horses which are refractory to intramuscular injection or racehorses that cannot be treated with long-acting injectable omeprazole because of withdrawal times and rules of racing. The rates of healing observed in this study also compare very favourably with rates of healing for oral omeprazole and sucralfate (Hepburn and Proudman, 2014; Varley et al, 2019; Kranenburg et al, 2020). Treatment with esomeprazole is only required once daily, as opposed to three treatments required with an omeprazole and sucralfate combination. Therefore, esomeprazole is much easier for owners and handlers to administer regular and its use would likely be associated with higher levels of compliance.

Glandular gastric disease in horses shares similarities to peptic ulcer disease in humans (Sykes et al, 2015b) in that rates of healing are thought to be directly proportional to the length of time within a 24-hour period that the intra-gastric pH remains above level 4 (Lind et al, 2000). Duration of intra-day acid suppression is one of the factors which may account for the poor response of EGGD to oral omeprazole (Sykes et al, 2015c). In human studies, the percentage of a 24-hour period for which intragastric pH remained

above level 4 was significantly higher for esomeprazole compared to omeprazole. A similar effect was also demonstrated in horses by Sykes et al (2017b) with enteric coated esomeprazole at 2 mg/kg maintaining pH>4 at the mucosal surface for 80% of a 24-hour period, compared to only 40% for oral omeprazole (Sykes et al, 2017). The increased efficacy is likely because of esomeprazole's lower first-pass hepatic metabolism, increased area under the curve and slower plasma clearance compared to omeprazole (Andersson et al, 2001). More robust clinical trials are required, but the data from this study suggests that esomeprazole as a monotherapy may be a viable treatment option for EGGD and combination with sucralfate, to further increase rates of healing, is a logical option which should be explored further.

The esomeprazole paste used in this study was formulated as an enteric coated preparation which may have favoured rates of healing despite any potential compliance issues. Studies have demonstrated superior bioavailability of enteric coated products compared to buffered or plain omeprazole (Birkmann et al, 2014; Sykes et al, 2016) and the absorption of coated preparations also appears to be less affected by feeding (Sykes et al, 2015c).

A minimum treatment duration of 28 days is recommended for the treatment of glandular disease (Sykes et al, 2015b; Rendle et al, 2018). However, owing to financial constraints, it was not possible to treat all horses for 28 days. Those cases which did heal after 14 days of treatment, had atypical lesions located in the fundus which may have affected the treatment outcomes. Anecdotally, these lesions appear to be more responsive to acid suppression and easier to treat compared to those located at the pyloric antrum.

The main limitation of this study was the small sample size and its retrospective nature. A second limitation of this study was that all horses were maintained at their full working regime, as exercise has been shown to be a risk factor (Sykes et al, 2019) for the development of glandular lesions and this may have negatively impacted treatment outcomes. However, it could be argued that this represents a more realistic scenario and good rates of healing were still achieved in this study, despite no reduction in exercise.

## Conclusions

This study suggests that esomeprazole could be considered as a valid first-line treatment option for glandular gastric disease in horses. However, case numbers were low and the study was subject to a number of limitations. Larger, blinded, randomised clinical trials of esomeprazole are warranted. **EQ**

## Conflicts of interest

The author has previously received payment for consultancy services provided to Virbac Australia, who produce oral omeprazole.

## References

- Andersson T, Rohss K, Bredberg E, Hassan-Alin M. Pharmacokinetics and pharmacodynamics of esomeprazole, the S-isomer of omeprazole. *Alimentary Pharmacol Ther.* 2001;15(10):1563–1569. <https://doi.org/10.1046/j.1365-2036.2001.01087.x>
- Andrews FM, Sifferman RL, Bernard W et al. Efficacy of omeprazole paste in the treatment and prevention of gastric ulcers in horses. *Equine Vet J Suppl.* 1999;(29):81–86.
- Begg LM, O'Sullivan CB. The prevalence and distribution of gastric ulceration in 345 racehorses. *Aust Vet J.* 2003;81(4):199–201. <https://doi.org/10.1111/j.1751-0813.2003.tb11469.x>
- Birkmann K, Junge HK, Maischberger E, Eser MW, Schwarzwald CC. Efficacy of omeprazole powder paste or enteric-coated formulation in healing of gastric

- ulcers in horses. *J Vet Intern Med.* 2014;28(3):925–933. <https://doi.org/10.1111/jvim.12341>
- Doucet MY, Veins AA, Dionne R, Alva R, Ericsson G. Efficacy of a paste formulation of omeprazole for the treatment of naturally occurring gastric ulcers in training standardbred racehorses in Canada. *Can Vet J.* 2003;44(7):581–585.
- Gough S, Hallowell G, Rendle D. Treatment of equine glandular gastric disease with long acting injectable and oral omeprazole. In Press. 2019.
- Gough S, Hallowell G, Rendle D. A study investigating the treatment of equine squamous gastric disease with long-acting injectable or oral omeprazole. *Vet Medicine Sci.* 2020;6(2):235–241. <https://doi.org/10.1002/vms3.220>
- Gralnek IM, Dulai GS, Fennerty MB, Spiegel BMR. Esomeprazole Versus Other Proton Pump Inhibitors in Erosive Esophagitis: A Meta-Analysis of Randomized Clinical Trials. *Clin Gastroenterol H.* 2006;4(12):1452–1458. <https://doi.org/10.1016/j.cgh.2006.09.013>
- Hepburn RJ, Proudman CJ. 2014. Treatment of ulceration of the gastric glandular mucosa: Retrospective evaluation of omeprazole and sucralfate combination therapy in 204 sport and leisure horses (Abstract). Presented at proceedings of the International Colic Symposium, Dublin, Ireland, July 8–10th 2014
- Husted L, Sanchez LC, Baptiste KE, Olsen SN. Effect of a feed/fast protocol on pH in the proximal equine stomach. *Equine Vet J.* 2009;41(7):658–662. <https://doi.org/10.2746/042516409x416431>
- Kendall MJ. Esomeprazole – the first proton pump inhibitor to be developed as an isomer. *Aliment Pharmacol Ther.* 2003;17:1–4. <https://doi.org/10.1046/j.1365-2036.17.s1.1.x>
- Kranenburg LC, Scheepbouwer JHT, van den Boom R. Retrospective study of combined sucralfate and omeprazole therapy compared with omeprazole monotherapy for equine glandular disease. Presented at proceedings of the 13th Annual European College of Equine Internal Medicine Congress, Online, 2020. <https://doi.org/10.1111/jvim.16066>
- Lenoir C, Biali ME, Luthy C, Grosgrin O, Desmeules JA, Rollason V. Snapshot of proton pump inhibitors prescriptions in a tertiary care hospital in Switzerland: less is more? *Int J Clin Pharm.* 2019;41(6):1634–1641. <https://doi.org/10.1007/s11096-019-00929-w>
- Lester GD, Smith RL, Robertson ID. Effects of treatment with omeprazole or ranitidine on gastric squamous ulceration in racing Thoroughbreds. *J Am Vet Med Assoc.* 2005;227(10):1636–1639. <https://doi.org/10.2460/javma.2005.227.1636>
- Lind T, Kyleback A, Rydberg L et al. Esomeprazole provides improved acid control vs omeprazole in patients with symptoms of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther.* 2000;118(4):A18. [https://doi.org/10.1016/s0016-5085\(00\)82139-3](https://doi.org/10.1016/s0016-5085(00)82139-3)
- Luthersson N, Nielsen KH, Harris P, Parkin TDH. Risk factors associated with equine gastric ulceration syndrome in 201 horses in Denmark. *Equine Vet J.* 2009;41(7):625–630. <https://doi.org/10.2746/042516409x441929>
- Madi L, Elhada AA, Alrawashdeh H, Ahmed A. Prescribing pattern of proton pump inhibitors in Qatar rehabilitation institute: A retrospective study. *J Res Pharm Pract.* 2019;8(2):101. [https://doi.org/10.4103/jrpp.jrpp\\_18\\_79](https://doi.org/10.4103/jrpp.jrpp_18_79)
- Malmkvist J, Poulsen JM, Luthersson N, Palme R, Christensen JW, Søndergaard E. Behaviour and stress responses in horses with gastric ulceration. *Appl Anim Behav Sci.* 2012;142(3–4):160–167. <https://doi.org/10.1016/j.applanim.2012.10.002>
- Murray MJ, Haven ML, Eichorn ES, Zhang D, Eagleson J, Hickey GJ. Effects of omeprazole on healing of naturally-occurring gastric ulcers in Thoroughbred racehorses. *Equine Vet J.* 1997;29(6):425–429. <https://doi.org/10.1111/j.2042-3306.1997.tb03153.x>
- Nieto JE, Snyder JR, Beldomenico P, Aleman M, Kerr JW, Spier SJ. Prevalence of gastric ulcers in endurance horses—a preliminary report. *Vet J.* 2004;167(1):33–37. <https://doi.org/10.1016/j.tvjl.2003.09.005>
- Pereira MC, Levy FL, Valadão CAA, Ferraz GC, Queiroz-Neto A. Preliminary Study of the Gastric Acidity in Thoroughbred Horses at Rest after Enteral Administration of Esomeprazole Magnesium (Nexium). *J Equine Vet Sci.* 2009;29(11):791–794. <https://doi.org/10.1016/j.jevs.2009.10.006>
- Pickles KJ, Black K, Brunt O, Crane M. Retrospective study of misoprostol treatment of equine glandular gastric disease. Presented at proceedings of the 13th Annual European College of Equine Internal Medicine Congress, Online, 2020. <https://doi.org/10.1111/jvim.16066>
- Rendle D, Bowen M, Brazil T et al. Recommendations for the management of equine glandular gastric disease. *UKVE.* 2018;2(Sup1):2–11. <https://doi.org/10.12968/ukve.2018.2.s1.3>
- Rendle DI. Oral Esomeprazole as a treatment for equine gastric ulcer syndrome refractory to oral omeprazole. *Equine Vet J.* 2017;49(S51):25–26. [https://doi.org/10.1111/evj.47\\_12732](https://doi.org/10.1111/evj.47_12732)
- Rendle DI, Gosling L, Platt A, Duff A. Efficacy of long-acting injectable omeprazole (LAIOME) in the management of equine glandular gastric disease (EGGD)

## KEY POINTS

- Equine glandular gastric disease is a highly prevalent condition for which there is no universally effective treatment.
- In this study, 75% (3/4) and 67% (2/3) of horses with equine glandular gastric disease healed following treatment with oral esomeprazole for 28 and 14 days, respectively.
- The study was limited by its small sample size and retrospective nature.
- Esomeprazole may be a valid first-line treatment option for equine glandular gastric disease and warrants further consideration.

- and equine squamous gastric disease. *Equine Vet J.* 2018;50:14–14. [https://doi.org/10.1111/evj.20\\_13008](https://doi.org/10.1111/evj.20_13008)
- Röhss K, Wilder-smith C, Claarnilsson C, Lundin C, Hasselgren G. Esomeprazole 40mg provides more effective acid control than standard doses of all other proton pump inhibitors. *Gastroenterology.* 2001;120(5):A419–A419. <https://doi.org/10.1007/s00228-004-0804-6>
- Sykes BW, Hewetson M, Hepburn RJ, Luthersson N, Tamzali Y. European College of Equine Internal Medicine Consensus Statement—Equine Gastric Ulcer Syndrome in Adult Horses. *J Vet Intern Med.* 2015a;29(5):1288–1299. <https://doi.org/10.1111/jvim.13578>
- Sykes BW, Sykes KM, Hallowell GD. 2015. A comparison of three doses of omeprazole in the treatment of equine gastric ulcer syndrome: A blinded, randomised, dose-response clinical trial. *Equine Vet J.* 2015b;47(3):285–290. <https://doi.org/10.1111/evj.12287>
- Sykes BW, Underwood C, McGowan CM, Mills PC. Pharmacokinetics of intravenous, plain oral and enteric-coated oral omeprazole in the horse. *J Vet Pharmacol Ther.* 2015c;38(2):130–136. <https://doi.org/10.1111/jvp.12169>
- Sykes BW, Underwood C, Greer R, McGowan CM, Mills PC. Pharmacokinetics and bioequivalence testing of five commercial formulations of omeprazole in the horse. *J Vet Pharmacol Ther.* 2016;39(1):78–83. <https://doi.org/10.1111/jvp.12240>
- Sykes BW, Kathawala K, Song Y, Garg S, Page SW, Underwood C, Mills PC. Preliminary investigations into a novel, long-acting, injectable, intramuscular formulation of omeprazole in the horse. *Equine Vet J.* 2017a;49(6):795–801. <https://doi.org/10.1111/evj.12688>
- Sykes BW, Underwood C, Mills PC. The effects of dose and diet on the pharmacodynamics of esomeprazole in the horse. *Equine Vet J.* 2017b;49(5):637–642. <https://doi.org/10.1111/evj.12670>
- Sykes BW, Bowen M, Habershon-Butcher JL, Green M, Hallowell GD. Management factors and clinical implications of glandular and squamous gastric disease in horses. *J Vet Intern Med.* 2019;33(1):233–240. <https://doi.org/10.1111/jvim.15350>
- Tamzali Y, Marguet C, Priymenko N, Lyazrhi F. Prevalence of gastric ulcer syndrome in high-level endurance horses. *Equine Vet J.* 2011;43(2):141–144. <https://doi.org/10.1111/j.2042-3306.2010.00129.x>
- Thompson A. Monitoring the growing use of esomeprazole. *Prescriber.* 2019;30(4):37–39. <https://doi.org/10.1002/psb.1757>
- Varley G, Bowen IM, Habershon-Butcher JL, Nicholls V, Hallowell GD. Misoprostol is superior to combined omeprazole-sucralfate for the treatment of equine gastric glandular disease. *Equine Vet J.* 2019;51(5):575–580. <https://doi.org/10.1111/evj.13087>
- Videla R, Sommardahl CS, Elliott SB, Vasili A, Andrews FM. Effects of Intravenously Administered Esomeprazole Sodium on Gastric Juice pH in Adult Female Horses. *J Vet Intern Med.* 2011;25(3):558–562. <https://doi.org/10.1111/j.1939-1676.2011.0716.x>

# Call for case reports

[www.ukvet.co.uk](http://www.ukvet.co.uk)

Equine wants YOUR case reports, please contact [ella.mackenzie@markallengroup.com](mailto:ella.mackenzie@markallengroup.com)