

# Advanced Equine Reproduction Course

By

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**What is Domperidone? What is it used for in the broodmare? and Why?  
Where can it be obtained?  
(or... why are we administering an antiemetic to a species that doesn't vomit?!?)**

Developed in the early 1980's by Janssen Pharmaceutica of Belgium, domperidone is a dopaminergic antagonist which has been marketed for several years, in Europe and Canada, as a human antiemetic. Domperidone was primarily designed to block the chemoreceptor trigger zone (CTZ) in patients who were suffering from nausea and vomiting associated with cytotoxic chemotherapeutic regimens. Unlike metoclopramide, which exhibits similar pharmacologic activity at dopamine receptors, domperidone blocks activity selectively at peripheral D<sub>2</sub> sites without crossing the blood brain barrier. This attribute reduces CNS toxicity, which can be associated with metoclopramide therapy. In humans, peak plasma levels are reached in 30 minutes or less after oral or intramuscular administration. Metabolism occurs via hepatic conjugation and subsequent renal elimination with less than 1% of the drug excreted unchanged in the urine. The clearance of secondary metabolites is complete in approximately 96 hours.<sup>1</sup>

Of course, the equine veterinary profession is not interested in the antiemetic properties of domperidone. Dopamine antagonism has been determined as a viable means of treating the symptoms of tall fescue toxicosis, a syndrome of agalactia and reproductive dysfunction in the mare. Tall fescue (*Festuca arundinaceae*), a highly adaptable, perennial grass estimated to cover 35 million acres in the U.S., is probably the most prevalent source of equine forage in the Southeastern and Pacific Northwest regions. Fescue grass is

frequently symbiotized by the fungal endophyte *Acremonium coenophilum*, which produces ergot alkaloids. These alkaloids, when consumed by gravid broodmares, have been linked to multiple reproductive anomalies, including agalactia, increased placental thickness, abortion, and neonatal weakness. The gestation length of broodmares grazing infected pastures may be extended by as much as 10%.<sup>2</sup>

The mechanism described for fescue agalactia involves dopamine receptor agonism by the endophyte ergot alkaloids at the lactotrophic cells of the anterior pituitary that are normally responsible for prolactin synthesis. Prolactin is a peptide hormone responsible for the initiation of lactogenesis in mammals. Autogenous control of prolactin secretion has been linked to tonic inhibition by dopamine normally produced in the hypothalamus and posterior pituitary. In addition, serum progesterone, which is associated with mammary ductal and secretory structure development in response to prolactin priming is reduced in late term mares consuming contaminated fescue sources. These reduced levels of progesterone may result in the prolongation of pregnancy mentioned above. The mechanism for dopamine agonism has been successfully simulated by the administration of bromocriptine to gravid mares, producing similar clinical signs to those seen with fescue toxicosis.<sup>3</sup>

Studies have shown that by removing the mares from contaminated pastures 60-90 days prior to foaling, symptoms of fescue toxicosis can be minimized. If exposure cannot be avoided, recent research indicates that domperidone, when administered at a dose of 1.1 mg/kg PO QD for 10 days (minimum of 5 days) prior to parturition, alleviates the majority of clinical signs associated with ergot alkaloid toxicosis. If treatment is initiated after parturition, the course may need to be extended over a longer period. Sulpiride, another dopamine antagonist,

created an increase in prolactin as well, but took significantly longer to produce results. <sup>4,5</sup>

Domperidone research is continuing. The drug is currently classified as experimental by the FDA and is available from:

[EQUI-TOX, INC.](#)  
CENTER FOR APPLIED TECHNOLOGY-MBX2  
511 WESTINGHOUSE ROAD  
PENDLETON, SC 29670  
(864) 646-6443

The current form for distribution is 5mls of a molasses based paste containing 550mg domperidone prepackaged in a syringe. This corresponds to 1.1mg/kg for a 500 kg horse once daily, starting 10 days prior to expected foaling and continuing up until parturition. If premature colostral leakage is evident, the dose may be split in half and administered twice daily. If administered post-foaling, give the same dose for a minimum of 5 days. The cost per 5ml syringe is \$5.00. A "Clinical Observations" form must be submitted to Dr. D.L Cross at the Animal, Dairy, and Veterinary Services Dept. of Clemson University, in order to document clinical results for NADA clearance. This technology is protected by U.S. Patent No. 5,372,818. <sup>6</sup>

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<sup>1</sup>Olin, R. B., et al, eds. Drug Facts and Comparisons. St. Louis. JB Lippencott Co. 1996. p.771.

<sup>2</sup>Putnam, M.R., T.R. Boosinger, and J.T. Vaughan. Effects of the fungal endophyte *Acermonium coenophialum* in fescue on pregnant mares and foal viability. Am. Journ. of Vet. Res. Vol 52, No.12, December 1991, pp. 2071-2074.

<sup>3</sup>Cross, D.L., L.M. Redmond, and J. R. Strickland. Equine Fescue Toxicosis: Signs and Solutions. Journ. Anim. Sci. 1995. 73:899-908.

<sup>4</sup>Redmond, L.M., D.L. Cross, J.R. Strickland, and S.W. Kennedy. Efficacy of domperidone and sulipride as treatments for fescue toxicosis in horses. Amer. Journ. Vet. Res. Vol. 55, No. 5, May 1994, pp. 722-729.

<sup>5</sup>Brendemuehl, J.P. Reproductive Aspects of Fescue Toxicosis. Current Therapy in Equine Medicine 4. N.E. Robinson, ed., W.B. Saunders Co. 1997. pp. 571-573.

<sup>6</sup>Cross, D.L. Updated Instructions to Veterinarians: Domperidone for Treatment of Equine Fescue Toxicosis and Agalactia. EQUI-TOX, INC. 1997.