

## **Efficacy of Equidone® for Treatment of Equine Fescue Toxicosis**

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Equidone® (domperidone) is an experimental drug currently undergoing testing for approval as a new animal drug by the FDA for fescue toxicosis in pregnant mares (Equi-Tox, Incorporated, 112 Central Road, Central, South Carolina – 864-646-6443).

### **DOPAMINE RECEPTOR INVOLVEMENT IN FESCUE TOXICOSIS**

The consistent observation of decreased serum prolactin levels in animals receiving diets of endophyte infected (E+) tall fescue (Porter et al., 1985; Monroe et al., 1988; Redmond et al., 1991a; Redmond et al., 1991b) indicates the involvement of dopamine receptors in tall fescue toxicosis. This conclusion, based on reduced serum prolactin levels, is derived from dopamine's involvement in the control of prolactin secretion *in vivo*. Also, several recent studies provide further evidence of dopamine receptor involvement in tall fescue toxicosis. Strickland et al. (1992) used isolated pituitary cell preparations and provided evidence that the alkaloids of tall fescue serve as dopamine agonists to effect a reduction in prolactin production from the lactotroph cells.

### **USE OF DOMPERIDONE**

Redmond et al. (1992) demonstrated that a selective D2 dopamine receptor antagonist, domperidone, was capable of eliminating fescue toxicosis in pregnant mares.

Strickland et al. (1994) studied the effects of ergot and loline alkaloids of E+ fescue on prolactin release by isolated and perfused rat pituitary cells. The ergot alkaloids had prolactin lowering effects. The use of a D2 dopamine receptor antagonist (domperidone) blocked the effect of the ergot alkaloids and prevented their prolactin lowering effect. Domperidone is a D2 dopamine receptor blocker that does not cross the blood brain barrier and elicit neuroleptic side effects.

### **STUDIES WITH HORSES**

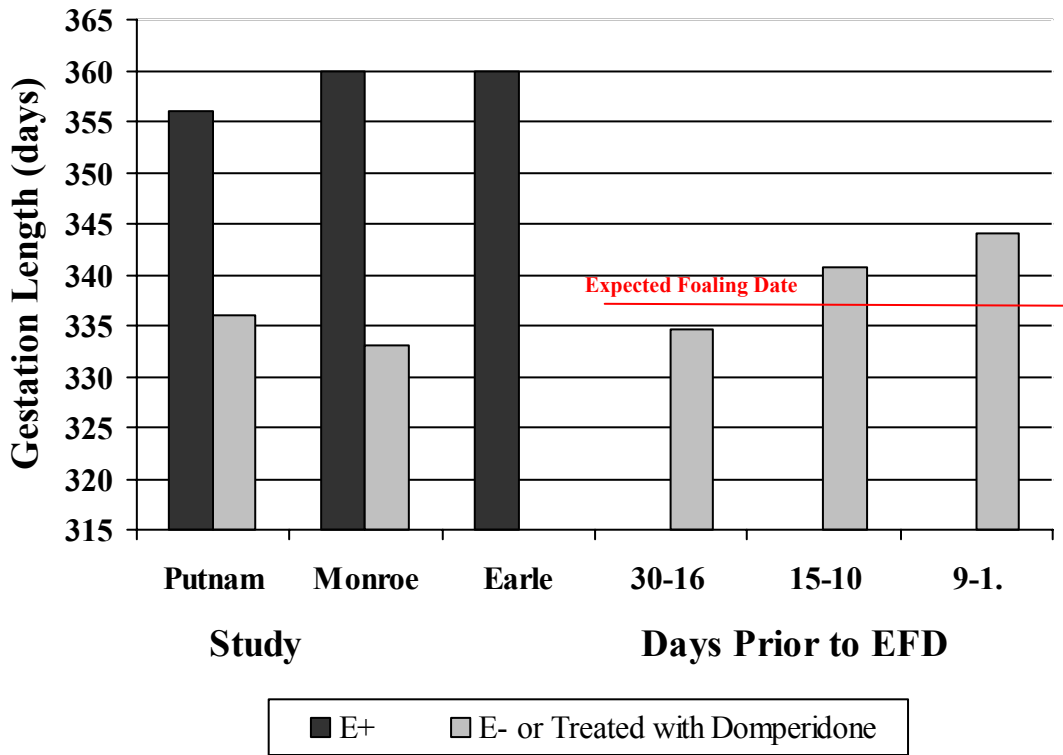
Domperidone was administered orally (1.1 mg/kg body weight) to gravid mares grazing E+ tall fescue. The first *in vivo* study using domperidone was conducted by Redmond et al., 1992. Domperidone increased serum prolactin and progesterone and provided what seemed to be nearly complete recovery of gravid mares from tall fescue toxicosis without side effects of the drug. Treated mares had near normal endocrine levels, milk, live, healthy foals, and gestation length similar to the calculated gestation length. Subsequently, a dose titration study was conducted to determine the minimum effective dose of domperidone for treating tall fescue toxicosis (Redmond et al., 1993). Again, domperidone provided recovery from tall fescue toxicosis in gravid mares and the minimum effective oral dose was 1.1 mg/kg body weight when administered daily starting

30 days before foaling. An additional dose/titration study was conducted to verify the minimum effective dose (Campbell et al., 1996). Subsequently, a short duration dosing study was conducted to evaluate the effectiveness of dosing for either 10 to 15 days prior to expected foaling date (Dooley, 1998).

**CLINICAL TESTING**

The efficacy and safety of domperidone was evaluated under clinical conditions utilizing pregnant mares in various regions of the United States. The study involved the treatment of 1423 mares under local veterinary supervision.

In a controlled study by Monroe et al. (1988), mares grazing (E+) tall fescue had gestation lengths averaging 27 days longer than mares grazing endophyte-free (E-) fescue. Similar results were observed by Putnam et al., (1991) and Earle et al. (1990). Under clinical conditions, mares treated with Equidone® (domperidone) for 10 to 15 days prior to expected foaling, foaled near their expected foaling date (Figure 1). Approximately 80% of mares had normally or rapidly developing udders after the initiation of domperidone therapy, with an additional 13% having a “good” udder at foaling (93% total). More than 98% of mares treated with domperidone had live foal births.



**Figure 4.** Gestation lengths for mares consuming endophyte-infected tall fescue (E+) and mares consuming endophyte-free tall fescue (E-) in three separate control studies; and mares consuming endophyte-infected tall fescue in a clinical study (1423 mares), receiving domperidone at different days prior to the expected foaling date (EFD). (Expected foaling date for this study is based on a 337.5 day gestation length.)

In the study by Earle et al. (1990), 86% of foals delivered on E+ fescue pasture died. In the study by Monroe et al. (1988), 50% of mares on E+ fescue pastures had stillborn foals. In this study, 1.9% of mares did not have live foals.

When asked whether the treatment was effective for treatment/prevention of fescue toxicosis, 94.5% of veterinarians and/or mare owners felt domperidone therapy was effective.

## References

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