# Therapeutics for Equine Endocrine Disorders

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**KEYWORDS**

• Equine • Endocrine • PPID • EMS • Diabetes • Therapeutics

**KEY POINTS**

- Endocrine disease is commonly encountered in equine practice.
- Pergolide remains the most popular drug for treating PPID although some alternatives exist if required.
- Equine metabolic syndrome control requires compliance with strict management measures although these may be supplemented by medical therapy in some cases.
- Rarer endocrinopathies such as diabetes mellitus, diabetes insipidus, hyperthyroidism and critical illness-related corticosteroid insufficiency present some therapeutic options but are frequently challenging to manage.

Endocrinopathic causes of laminitis have attracted considerable research interest over the last decade alongside a parallel surge in caseload seen in general equine practice.[1,2] The justification for medical intervention in cases of pituitary pars intermedia dysfunction (PPID) seems to be relatively straightforward, in contrast with the potential danger that equine metabolic syndrome (EMS) cases are medicated as an easier alternative to implementing essential management changes. Such reliance on medical treatment of EMS cases is likely to fail unless administered alongside strict dietary and exercise management.[3] Indeed, dietary management may also play an important role in other rarer endocrine diseases, such as diabetes mellitus (DM) and diabetes insipidus (DI), but such recommendations are beyond the scope of this article.

## PITUITARY PARS INTERMEDIA DYSFUNCTION

PPID is suspected to arise after a loss of dopaminergic neuronal input to the pars intermedia, thus freeing the secretory melanotrope cells from tonic inhibition.[4] This pathophysiology forms the basis for preferential selection of dopaminergic agents in PPID

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cases to moderate excessive pars intermedia secretion.[5,6] There is currently no evidence that medical treatment (**Table 1**) can reduce or reverse the pathologic changes in the affected pars intermedia of PPID cases,[7] although this is a variable but realistic expectation in association with treatment of human prolactinomas with dopamine agonists.[8]

The dopamine agonist pergolide mesylate was first approved for the treatment of Parkinson's disease in humans more than 30 years ago and remains the only equine-licensed drug for the treatment of PPID in horses (Prascend, Boerhinger Ingelheim). The drug acts as a potent agonist of dopamine D2 receptors, but has additional effects on other classes of dopamine receptors as well as adrenergic and 5-hydroxytryptamine receptors. The drug was withdrawn as a human medicine from the United States and Canadian market in 2007 owing to increased risk of cardiac valvulopathy. Similar adverse effects are not recognized in horses, although temporary inappetence is not uncommon after commencement of medication or after dosage increases.[9,10] Pergolide is generally administered at a starting dose of 0.002 mg/kg orally (PO) every 24 hours with clinical and endocrine improvement expected within 1 to 3 months.[9–14] Improvements in signs such as lethargy, hypertrichosis, and polydipsia may be readily noticeable, although it is less easy to judge treatment success based on reduced likelihood of further attacks of laminitis or susceptibility to infections. Hence, there may be value in monitoring endocrine test results, although it should be stated that clinical and endocrine improvements do not always concur. Similarly, in human studies of prolactinomas, there may be poor correlation between clinical signs, prolactin concentrations, and adenoma size after treatment with dopamine agonists.[8] Unpublished data from this author (AE Durham, 2014) monitored endocrine changes between 1 and 2 months after the treatment of 402 PPID cases with 0.002 mg/kg pergolide every 24 hours. This revealed that 30% of cases showed a return of plasma adrenocorticotrophic hormone (ACTH) concentrations to the reference interval. A further 41% of horses showed a greater than 50% decrease in basal ACTH concentrations, but

**Table 1**
**Drug dosages for PPID and EMS in horses**

| | Drug | Dosage | Comments |
|---|---|---|---|
| PPID | Pergolide | 0.002–0.010 mg/kg PO q24h | Begin at lower end of dose range and increase gradually if required. Inappetence not uncommon. |
| | Cyproheptadine | 0.25 mg/kg PO q12–24h | May be used alone or in combination with pergolide. |
| | Bromocryptine | 0.1 mg/kg PO q12h | Alternative dopamine agonist to pergolide. |
| | Trilostane | 0.4–1 mg/kg PO q24h | Only indicated if evidence of hyperadrenocorticism. |
| EMS | Levothyroxine | 0.1 mg/kg PO q24h for 3–6 mon, then taper to 0.05 mg/kg PO q24h for 2 wk, then 0.025 mg/kg PO q24h for 2 wk | Must be used alongside dietary control. |
| | Metformin | 30 mg/kg PO q12h | Ideally, immediately before grazing/feeding |

*Abbreviations*: EMS, equine metabolic syndrome; PO, per os; PPID, pituitary pars intermedia dysfunction.