

## FACT SHEET

# Pituitary Pars Intermedia Dysfunction

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Early diagnosis and appropriate management, including pergolide, can help improve PPID horses' quality of life

As many as one-quarter of all horses 15 years of age or older are affected by pituitary pars intermedia dysfunction (PPID), formerly known as equine Cushing's disease.<sup>1,2</sup> This condition results in the overproduction of stress hormones, which can have many negative effects on a horse's body.

### Brain Wiring Gone Wrong

The pars intermedia is a region of the pituitary gland located in the base of the brain. During times of stress, the hypothalamic-pituitary-adrenal axis activates, resulting in the release of ACTH (adrenocorticotropic hormone). ACTH then circulates through the bloodstream and stimulates the adrenal glands near the kidneys to secrete cortisol and other glucocorticoid hormones.<sup>1</sup>

The pars intermedia is innervated by dopaminergic neurons that release dopamine, which stimulates D2 receptors on cells called melanotropes in the pars intermedia. Upon stimulation, melanotropes inhibit ACTH production. This is important because PPID is caused by the loss of dopaminergic inhibition, which results in the pars intermedia releasing high levels of ACTH. The loss of dopaminergic inhibition also results in hyperplasia (excessive growth) and micro- and macroadenoma (noncancerous mass) formation.<sup>1,3</sup>

The hypothalamic-pituitary-adrenal axis is closely linked with the hypothalamic-pituitary-thyroid axis. In healthy horses, glucocorticoids such as cortisol inhibit the hypothalamic-pituitary-thyroid axis by minimizing thyrotropin-releasing hormone (TRH) secretion from the hypothalamus. When administered to horses, TRH binds to and stimulates melanocytes in the pars intermedia, resulting in increased ACTH production.

### Clinical Signs of PPID

A pot-bellied, sway-backed, hairy horse suffering from chronic laminitis is the poster child for

severe PPID. Up to 69.9% of horses with PPID show signs of hypertrichosis—excessive hair growth and abnormal shedding.<sup>1</sup> Other signs of PPID include:

- Epaxial muscle wasting, other muscle mass loss, and general weight loss.
- Hyperhidrosis (excessive sweating) and anhidrosis (inability to sweat).
- Excessive drinking and urination.
- Lethargy and exercise intolerance.
- Abnormal fat depositions.
- Infertility.
- Suspensory ligament breakdown.
- Behavior changes.
- Recurrent skin infections and other signs of immune dysfunction.

Despite these seemingly obvious signs, early PPID can be easily missed, meaning many affected horses go untreated.

### A Diagnostic Challenge

The goal with PPID is to diagnose affected horses prior to severe or end-stage disease. Early diagnosis allows veterinarians and owners to institute appropriate therapies to improve an affected horse's quality of life. Any older horse showing the clinical signs described should be tested for PPID.<sup>4</sup>

The first-line test for suspected PPID is simple: Measure resting ACTH levels.<sup>1,5</sup> To do this, a veterinarian draws a single blood sample at any time of the day and sends it to a commercial laboratory. ACTH levels will be low (PPID is unlikely) or high (PPID is likely), based on established cutoff values, or in the equivocal range. Veterinarians usually recommend a TRH stimulation test if levels are equivocal. To perform this test, the veterinarian collects a blood sample immediately before administering TRH intravenously. Exactly 10 minutes after that injection, he or she collects a second blood sample and sends both to the laboratory

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Veterinarians run ACTH level and TRH stimulation tests on horses' blood samples to diagnose PPID.

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to measure ACTH levels. If the ACTH levels remain low, PPID is unlikely. But if ACTH levels are higher than normal reference range, PPID is considered likely.

Veterinarians also recommend performing the TRH stimulation test in horses exhibiting only a few clinical signs of PPID, including hypertrichosis.

If TRH test results are equivocal, owners can retest in three to six months while monitoring clinical signs (in otherwise healthy horses) or initiate treatment, monitor signs, and conduct follow-up testing in three to six months. Either choice is also reasonable in cases with equivocal ACTH values that did not have TRH testing performed.

Most important is being consistent with the test and laboratory used, especially when monitoring horses over time or in response to treatment.

### Treating PPID

Pergolide mesylate is the treatment of choice and only approved drug for PPID. It binds to the D2 receptors on melanocytes to inhibit ACTH production, essentially replacing the role of the dopaminergic neurons in the pars intermedia.

Pergolide is registered "for the control of clinical signs associated with pituitary pars intermedia dysfunction in horses."<sup>6</sup> It will not cure hypothalamic adenoma (an abnormal growth in the gland), but it can help slow the progression of disease.

Kirkwood et al. (2022) relayed data from multiple systematic reviews and reported improved short-term survival, reduced clinical signs in 40-100% of treated horses, and decreased rate of laminitis in 32-75% of treated horses. Muscle wasting, lethargy/poor performance, and hyperhidrosis also improved. According to data collected during the FDA approval process, horses showed marked improvements in hirsutism (abnormal shedding/hair coats), hyperhidrosis, excessive drinking and

# EVERY DAY COUNTS.



**CONTINUED TREATMENT IS CRUCIAL TO MAINTAINING A HEALTHY HORSE AND CONTROLLING THE SIGNS OF PPID.**



**CONTROLLED SIGNS:**

Clinical signs improved within 3 months and continued through 6 months.<sup>1</sup>



**PROVEN SUCCESS:**

3 out of 4 horses evaluated were considered treatment successes.<sup>1</sup>



**CLEAR IMPROVEMENT:**

Hypertrichosis (delayed shedding) improved in 89% of treated horses within 6 months.<sup>1</sup>

**IMPORTANT SAFETY INFORMATION:** PRASCEND has not been evaluated in breeding, pregnant, or lactating horses. Treatment with PRASCEND may cause loss of appetite. Most cases are mild. PRASCEND tablets should not be crushed due to the potential for increased human exposure. Keep PRASCEND in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose. Adverse reactions may occur if animals other than horses ingest PRASCEND tablets. Not for human use. Do not ingest the product. Refer to the package insert for complete product information.

<sup>1</sup>Prascend® (pergolide tablets) [Freedom of Information Summary]. St. Joseph, MO; Boehringer Ingelheim Inc.; 2011.

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urination, abnormal fat deposition, and muscle wasting after 90 and 100 days of treatment.<sup>1,6</sup>

Currently, the starting dose of pergolide is 2 µg/kg, which is equivalent to 0.5 milligrams for a pony and 1 milligram for an average 1,100-pound horse.<sup>1,5,6</sup> The maximum dose is 4 µg/kg once daily.

One of the most common side effects associated with pergolide is transient hyporexia (decreased appetite). If this occurs, veterinarians recommend lowering the pergolide dose, then increasing it to the recommended dose slowly over a longer period.<sup>1</sup>

It is also important to manage affected horses on appropriate diets, clip their coats in warm months, ensure they have access to plenty of water and shade, and keep them up to date on vaccinations and deworming.

**Monitoring, Compliance Key to Success**

Starting pergolide is not the end of management. Veterinarians should monitor horses closely with follow-up testing (ACTH or TRH stimulation) one month after starting therapy.<sup>1,5</sup> They should then follow horses' treatment progress regularly and titrate the pergolide dose until clinical signs resolve and ACTH concentrations fall within normal ranges. Once a horse stabilizes, practitioners typically recheck horses one to two times per year in case dose adjustments might be necessary due to disease progression.

Not all horses, however, receive appropriate follow-up. Steel et al. (2022) reported only 77 (48.1%) of 160 PPID horses had follow-up basal ACTH testing within the first one to three months of diagnosis.<sup>2</sup> Owner compliance is also critical to managing these horses successfully. Hague et al. (2021) found only 52% of the 110 horses in their study had compliant owners who gave ≥ 90% of the veterinary-recommended dose of pergolide.<sup>7</sup>

**Summary**

Pituitary pars intermedia dysfunction often occurs in older horses. Hypertrichosis is the most common and easily recognizable clinical sign, and laminitis can be one of the most important sequelae. The goal is to diagnose PPID cases early and initiate treatment with pergolide when indicated. Owner compliance and follow-up monitoring play key roles in optimal management and maintaining a PPID horse's quality of life.

**References**

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