Recommendations for the Diagnosis and Management of Pituitary Pars Intermedia Dysfunction (PPID)

EQUINE ENDOCRINOLOGY GROUP

2025

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Revised October 2025

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The Equine Endocrinology Group (EEG) is composed of experts in the field of equine endocrinology who provide advice in the form of written guidelines to help veterinary practitioners diagnose and manage equine endocrine disorders. Guidelines are updated every two years and can be found on the EEG website: https://equineendocrinologygroup.org/

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Summary

- Pituitary pars intermedia dysfunction (PPID) is a slowly progressive, age-related degenerative disease of dopaminergic neurons in the hypothalamus.
- This hypothalamic degeneration results in hyperplasia and adenoma formation of the pars intermedia of the pituitary gland, which then releases increased amounts of ACTH (adrenocorticotropic hormone) and other related peptides, such as CLIP (corticotropin-like intermediate peptide), alpha-MSH (alpha-melanocyte-stimulating hormone), and beta-endorphin **(Figure 2)**.
- PPID prevalence increases with age, reaching 20% in equids >15 years of age and 30% in equids >30 years of age.
- Hypertrichosis, a long hair coat that fails to shed, is a classic clinical sign of PPID, but many other clinical signs are also described **(Figures 1 & 3; Table 1)**.
- Documentation of increased plasma ACTH concentrations at rest and/or after TRH stimulation testing is currently the most practical diagnostic test for PPID. However, season and breed impact ACTH concentrations, and there is some overlap in concentrations between healthy and PPID populations.
- Consideration of the clinical context of the patient (including signalment, severity of clinical signs, comorbidities, and intended purpose) and the season in which testing is taking place are crucial for accurate interpretation of ACTH results to decide whether to treat, monitor, or re-test **(Figures 4 & 5, Tables 2 & 3)**.
- PPID is often accompanied by insulin dysregulation, so assessing insulin dynamics in concert with PPID testing is also very important (see the EEG Recommendations for Diagnosis and Management of Equine Metabolic Syndrome).
- The mainstay of treatment for PPID is daily oral administration of the dopaminergic agonist pergolide mesylate, combined with appropriate dietary management and general wellness care.

Figure 1 – Hypertrichosis, altered shedding patterns, and muscle loss are classic clinical signs of PPID

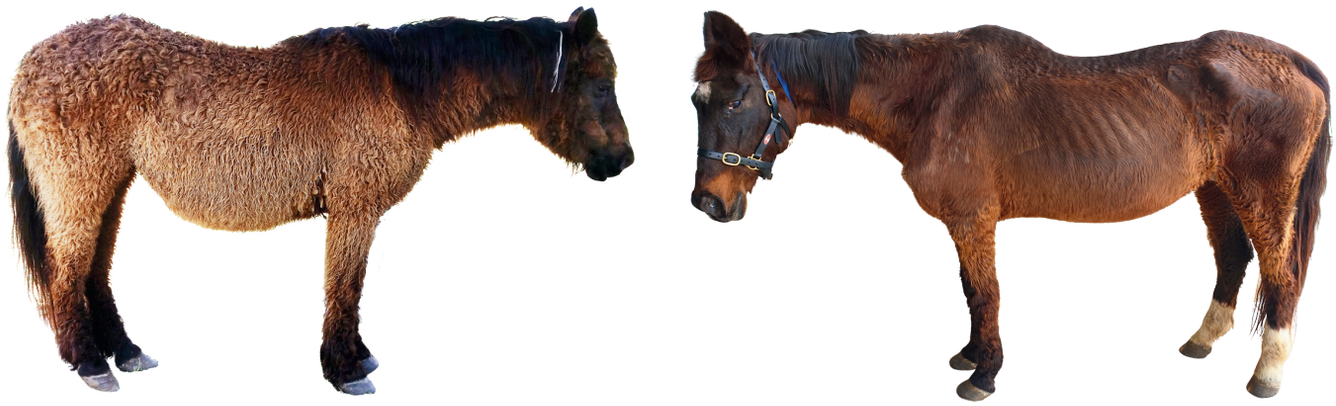

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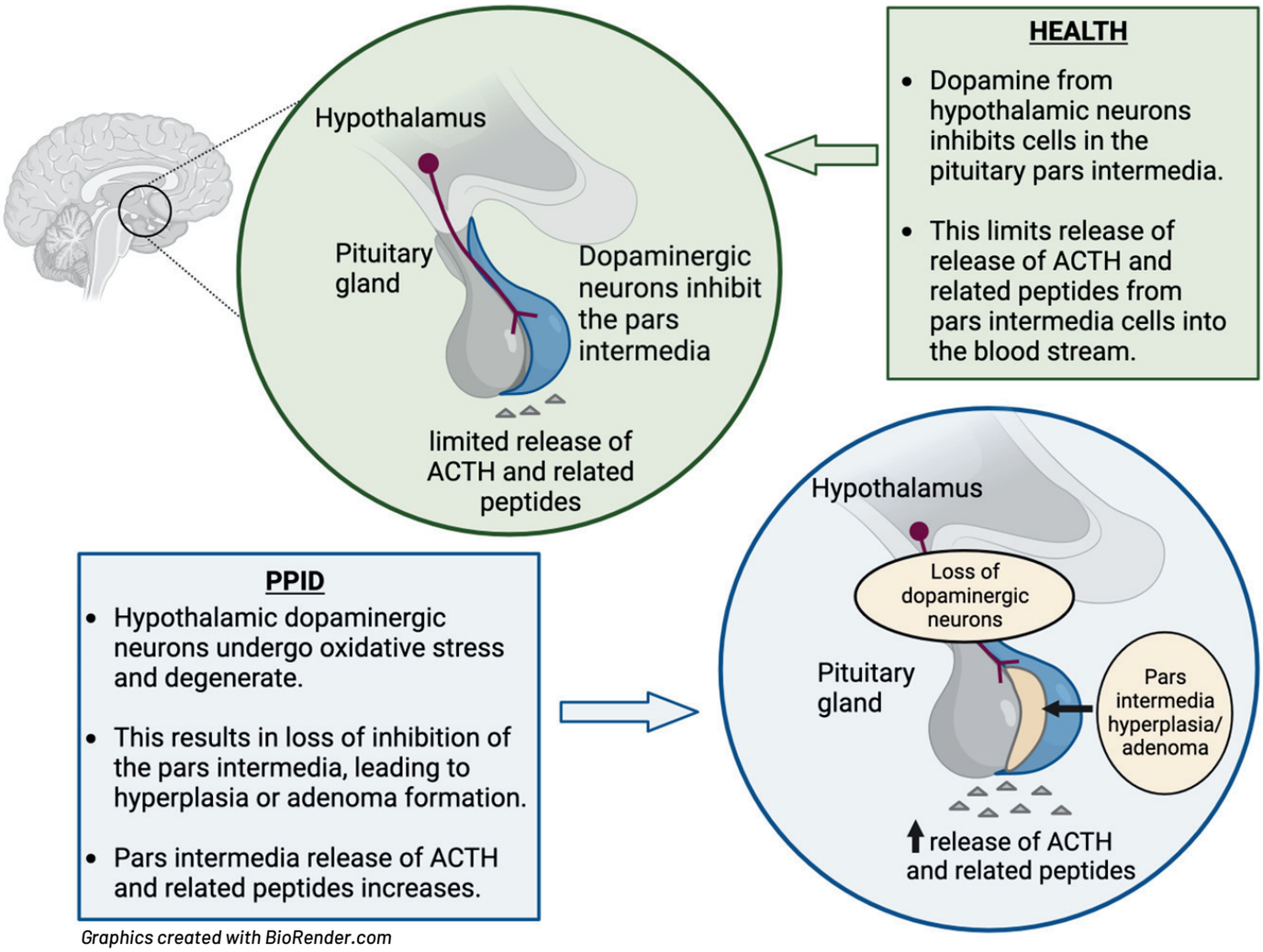
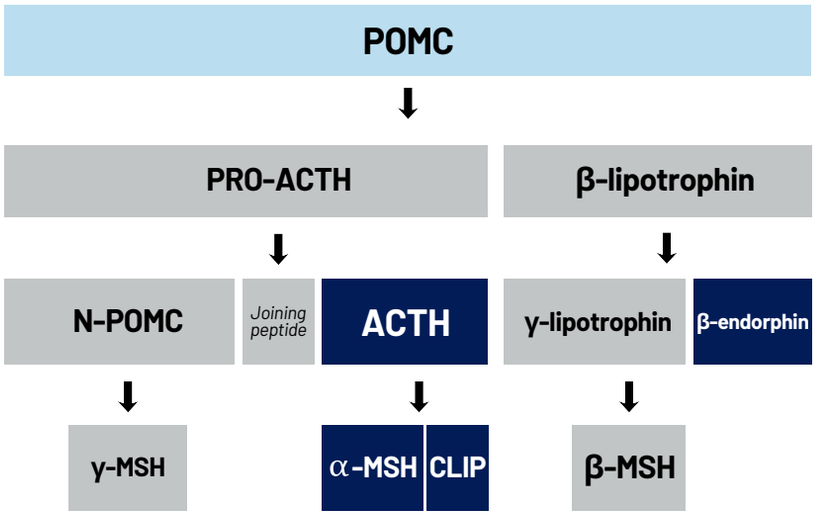
Figure 2 – Overview of PPID Pathogenesis



Graphics created with BioRender.com



Overview of Pituitary Hormone Production

- ACTH is produced by cleavage of the precursor protein POMC (pro-opiomelanocortin).
- The related peptide hormones α-MSH, CLIP, and β-endorphin, along with other peptides, are also produced in this process.
- **In PPID, ACTH and/or these related peptides increase.**
- The specific role that each of these play in PPID pathogenesis is not yet fully defined.
- ACTH and CLIP can be measured with currently available diagnostic tests.

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Figure 3 – Clinical signs and syndromes with PPID vary in affected equids

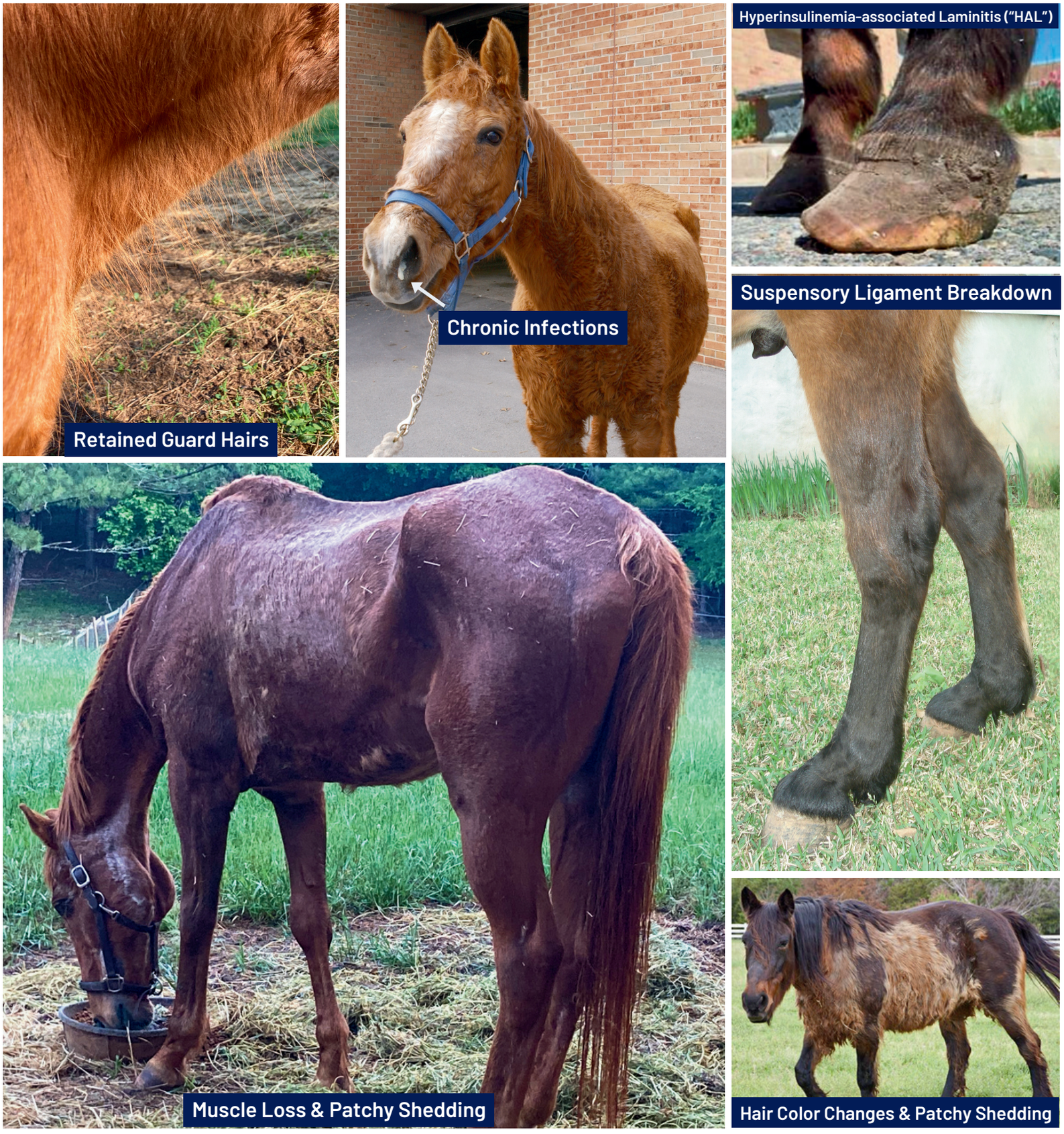

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Table 1 – Clinical spectrum of PPID

	EARLY/SUBTLE CLINICAL FINDINGS	ADVANCED CLINICAL FINDINGS
Strongly Suggestive	Regional hypertrichosis/ delayed shedding	Generalized hypertrichosis
Suggestive	Some loss of topline muscle Change in attitude/lethargy Decreased performance Abnormal sweating (increased or decreased)	Topline muscle atrophy Altered mentation Exercise intolerance Abnormal sweating (increased or decreased) Rounded abdomen Polyuria/polydipsia Recurrent infections
Possible Comorbidities	Infertility Desmitis/tendonitis/laxity Regional adiposity High fecal egg count Hyperglycemia Hypertriglyceridemia Hyperinsulinemia-associated laminitis Insulin dysregulation	Infertility Desmitis/tendonitis/laxity Regional adiposity High fecal egg count Hyperglycemia Hypertriglyceridemia Hyperinsulinemia-associated laminitis Insulin dysregulation Recurrent corneal ulcers Recurrent infections Parasitism Poor wound healing Increased mammary gland secretions

Practice Tip:

Increasing animal age and number and advancement of clinical signs increase the likelihood that these clinical signs are truly associated with PPID.

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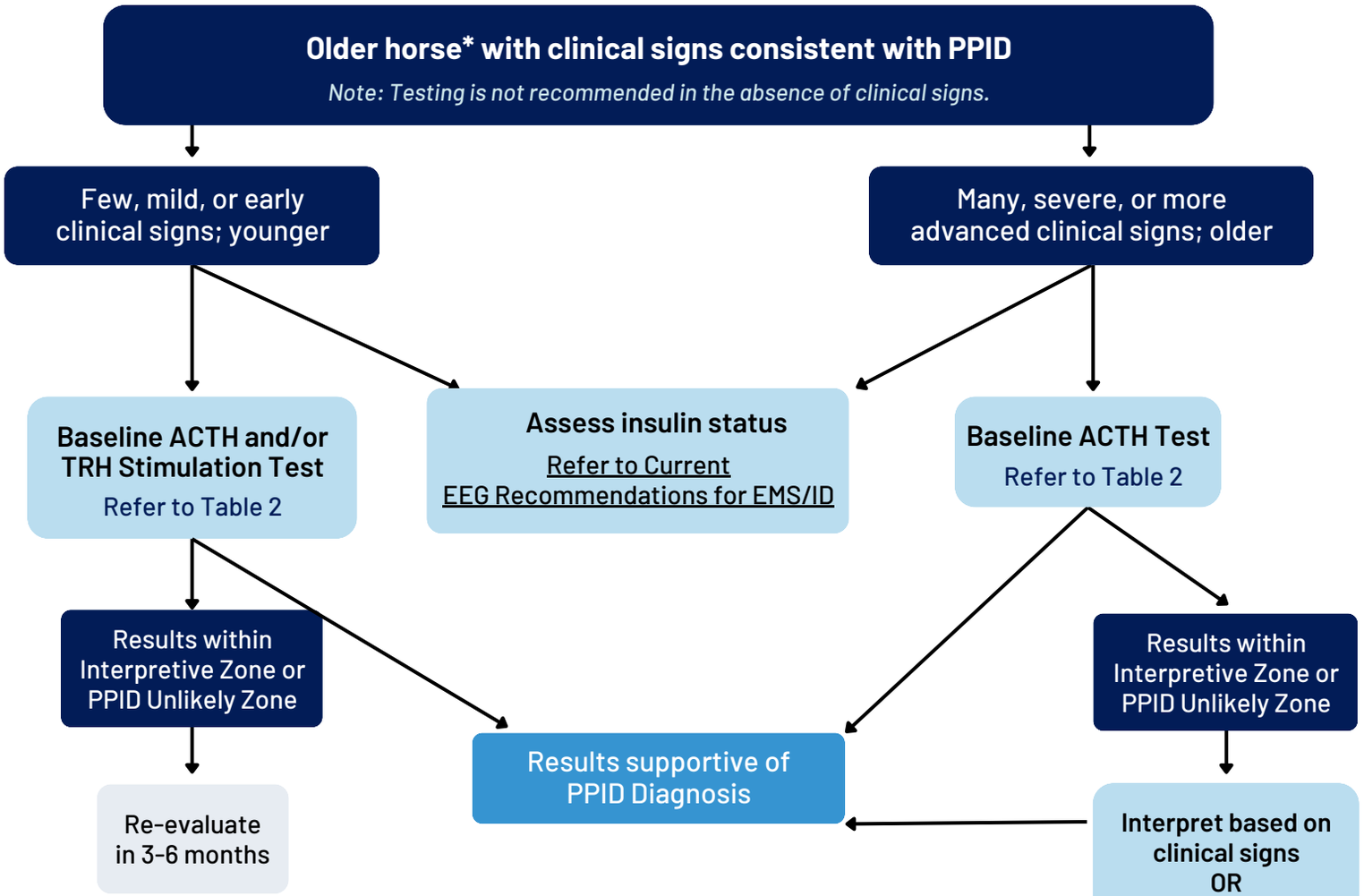
Figure 4 – Algorithm for the diagnosis of PPID



Practice Tips:

- ***This algorithm can also be applied to other equids (ponies, donkeys, and mules).***
- In aged horses with advanced clinical signs, a clinical diagnosis without testing may also be made.
- Baseline ACTH alone may be less supportive of diagnosis in the earlier stages of the disease than TRH stimulation testing.
- False positive and false negative results are possible. Treatment trial, or monitoring and repeat testing, are both acceptable approaches if the clinical picture and test results seem incompatible.

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Table 2 – Baseline ACTH and TRH stimulation test protocols

BASELINE ACTH

- Ensure that the animal is as unstressed as possible, since ACTH may transiently increase with stress or excitement
- Collect into EDTA-containing tube (purple top) at any time of day
- Keep samples cool (ice packs or refrigerator) at all times
- Centrifuge and separate EDTA plasma prior to shipping and within 24 hours of collection. Gravity separation of chilled plasma within 4 hours of collection is also acceptable if centrifugation is not available, but ensure the non-centrifuged sample does not freeze to avoid spuriously high ACTH levels.
- Ship via overnight mail with ice packs
- EDTA plasma can be frozen (centrifuged samples only), but avoid freeze-thaw cycles

TRH STIMULATION TEST

- Administer 0.5 mg (equids <250 kg) or 1.0 mg (equids >250 kg) of TRH intravenously. Side effects after administration are transient and include coughing, flehmen response, and yawning.
- Collect blood into EDTA-containing tubes (purple top) at 0 and exactly 10 minutes after TRH administration. A second sample may also be collected 30 minutes after TRH administration if desired, and may more consistently identify positive cases than the 10 minute sample.
- Horses can be tested after hay is fed, but not within 4 hours after a grain meal. Testing can be performed immediately before an oral sugar test ("OST"), but do not perform within 12 hours after an OST.

Table 3 – Seasonal interpretation of baseline ACTH* concentrations (also refer to Figure 5)

	TIME OF YEAR	PPID UNLIKELY	INTERPRETIVE ZONE: *Consider clinical signs and signalment*	PPID LIKELY
Baseline ACTH or TRH time 0 (pg/mL)	**Dec. - Jun.**	**< 15**	15 - 40	**> 40**
	July & November	**< 15**	15 - 50	**> 50**
	August	**< 20**	20 - 75	**> 75**
	Sept. - Oct.	**< 30**	30 - 90	**> 90**
ACTH 10 min. after TRH (pg/mL)	**Jan. - June**	**< 100**	**100 - 200**	**> 200**
	July - Dec.	**< 100**	TRH stimulation testing is most useful to identify negative cases in these months. **See below for more information.	
ACTH 30 min. after TRH (pg/mL)	**Jan. - June**	**< 40**	**40 - 90**	**> 90**
	July - Dec.	**< 40**	TRH stimulation testing is most useful to identify negative cases in these months. **See below for more information.	

** ACTH concentrations provided here are based on values determined by the Immulite 2000xpi analyzer. Additional information on interpreting test results from other equine ACTH analyzers is provided in Table 5 - Frequently Asked Questions.*

Specific months provided here are accurate for the northern hemisphere, but require seasonal correction for southern hemisphere interpretation. An alternate version of this table with ACTH concentrations reported in SI units (pmol/L) is included at the end of document (see Figure 7 and Table 6).

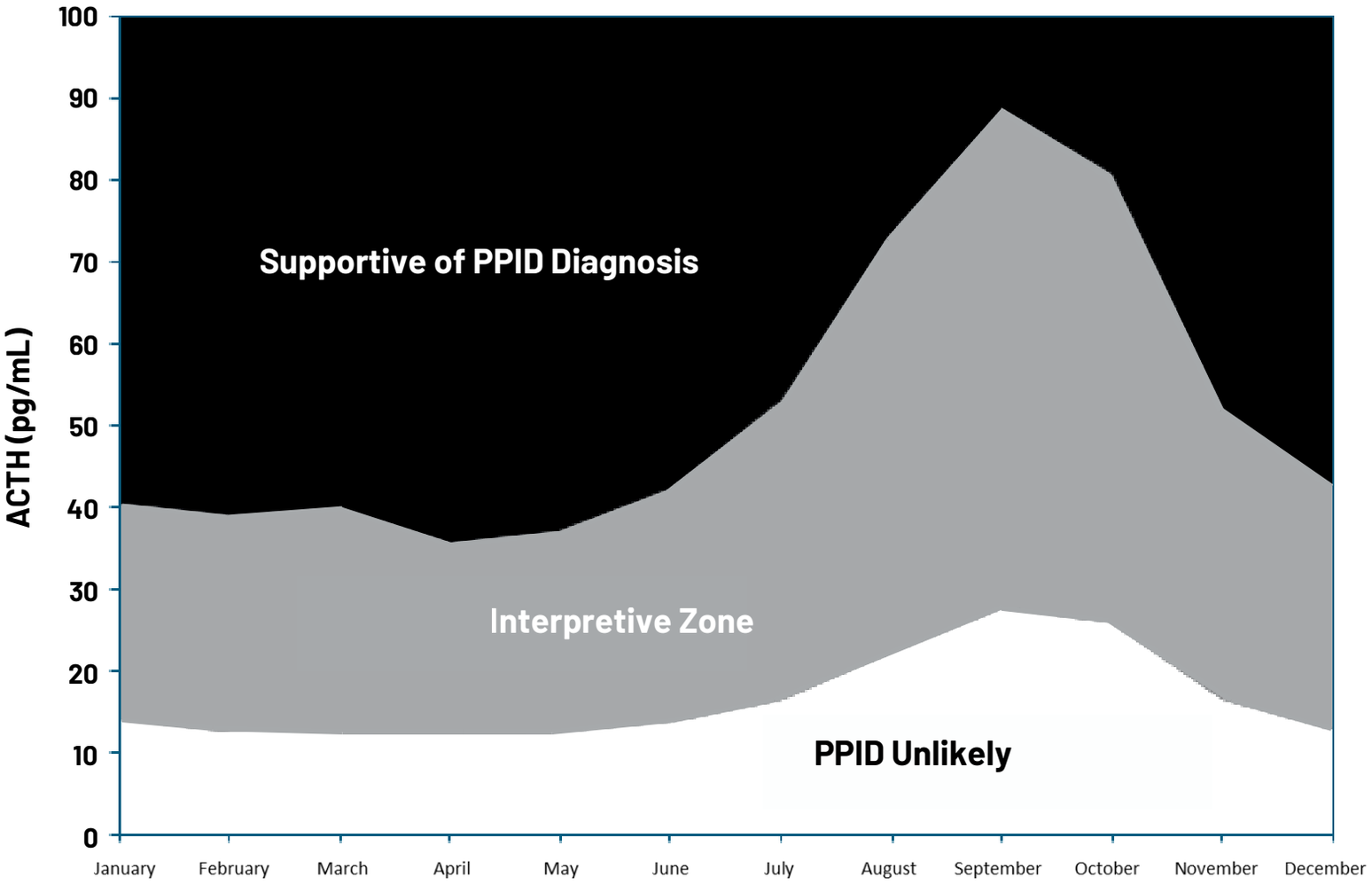
*** Many healthy animals have variably exaggerated ACTH responses to TRH in the autumn. 10-minute ACTH concentrations >500 pg/mL in the autumn may be consistent with PPID, but much variability within and among horses is described. Thus, interpretation of TRH stimulation test results in the autumn can be a challenge, and repeat testing at a later date should be considered if clinical signs and test results are inconsistent.*

Practice Tip: Healthy animals of certain breeds may have results that fall within the interpretive zone, or even the PPID likely range. Specifically, Arabian horses and donkeys may have higher ACTH concentrations in any season. Welsh and Shetland ponies often have higher ACTH concentrations only in the autumn months. Thus, PPID diagnosis should be made with caution in these breeds unless clinical signs are also present.

Figure 5 – Seasonal interpretation of baseline ACTH concentrations

Note: ACTH values presented here were determined using the Immulite 2000xpi analyzer. ACTH concentrations falling in the black shaded area are supportive of PPID diagnosis, and those falling in the white shaded area suggest a PPID diagnosis is unlikely at that time. ACTH concentrations falling in the grey area require further interpretation based on the clinical picture of the animal. The upper and lower limits of the interpretive zone were defined as thresholds that were shown to respectively maximize diagnostic specificity and sensitivity in a study using a large laboratory database of equine plasma ACTH concentrations (Durham et al, Equine Vet J, 2020).

An alternate version of this figure with ACTH concentrations reported in SI units is available at the end of the document (see Figure 7).



Practice Tips:

- For <u>older horses with many and/or advanced clinical signs, the lower threshold</u> of the interpretative zone may be used to support a PPID diagnosis.
- For <u>younger horses with few and/or early clinical signs, the upper threshold</u> of the interpretative zone may be used to support a PPID diagnosis.

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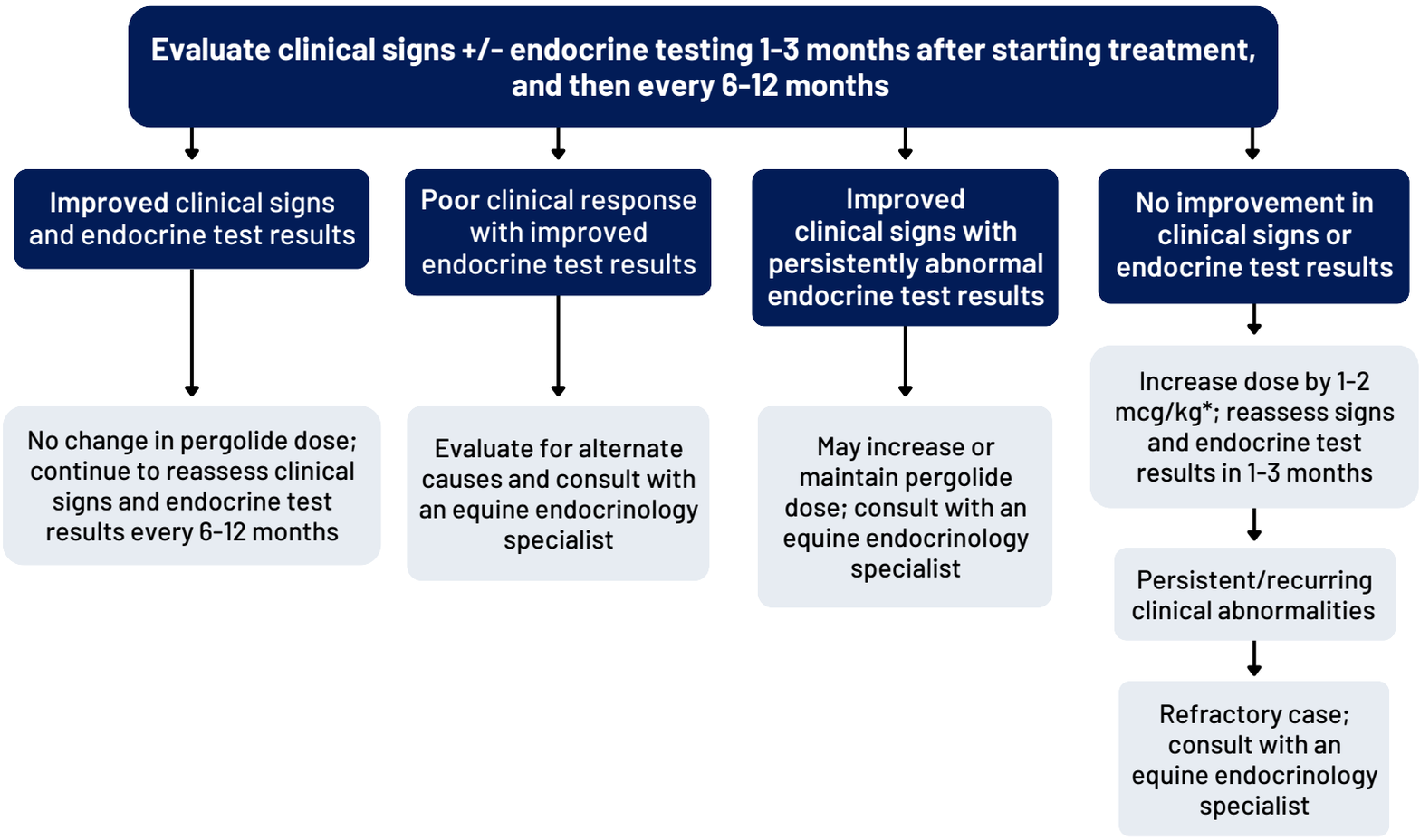
Figure 6 – Treatment and monitoring of PPID

Initial Treatment Plan	PRASCEND® (pergolide tablets); Boehringer Ingelheim Animal Health USA Inc. is approved for treatment of PPID in horses and is recommended at an initial dose of 2 mcg/kg once daily (0.5 mg for a 250 kg pony and 1.0 mg for a 500 kg horse).



**Note, pergolide doses above 4 mcg/kg per day are considered extra-label use in the United States and Canada, as the manufacturer's recommendations are not to exceed 4 mcg/kg daily.*

Practice Tips:

- Improvement in clinical signs is the most important indicator of response to treatment.
- Given the impact of season on ACTH, monitoring in the same season from year to year is important.
- ACTH concentrations may not return to the "PPID unlikely" range despite clinical improvement, and do not always warrant a dose increase. Some horses with PPID show good long-term control of their signs and never require a dose increase.

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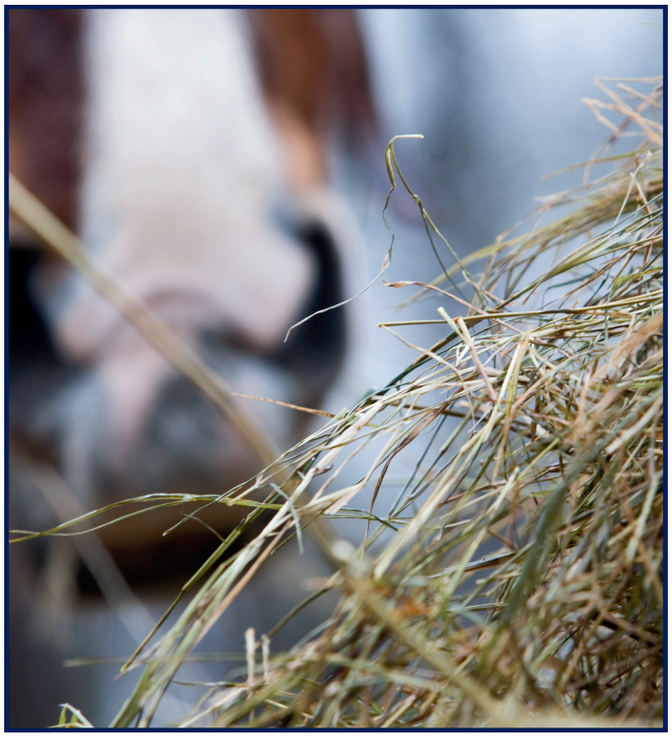
Table 4 – Other considerations for managing horses with PPID

DIET RECOMMENDATIONS

- Feed selection in horses with PPID should be based on body condition and the presence or absence of concurrent insulin dysregulation.
- Horses with PPID and concurrent insulin dysregulation require lower non-structural carbohydrate feeds and limited pasture access, but it is important to note that horses with PPID that have normal insulin regulation as confirmed with dynamic testing (e.g. OST) do not need a carbohydrate-restricted diet.
- Many horses with PPID are lean and/or have muscle wasting and benefit from an increase in dietary fat, protein, and caloric intake via good quality senior feeds, pasture grazing, fat supplements, and/or alfalfa-based feeds.
- Since feed requirements of aged horses--especially those with PPID--may change over time, frequent monitoring of body condition by owners is recommended.



QUALITY OF LIFE AND GENERAL WELLNESS CARE

- The vast majority of owners of PPID-positive horses report their horses have a good quality of life, and PPID does not necessarily result in a decreased life span.
- However, the majority of horses with PPID are aged and will continue to be susceptible to age-related non-PPID conditions.
- Special attention should be paid to body condition, hoof care, dentistry, and parasite control.
- Inadequately-controlled PPID horses are also at risk for bacterial infections.
- An equine quality of life assessment tool for equids with PPID has recently been validated and incorporates assessment of demeanor, attitude, and appetite, among other health factors (Bouquet et al., Equine Vet J, 2025).
- Careful monitoring of these parameters, in addition to complete assessment of overall health as detailed above, can guide decision-making in PPID cases.

MANAGEMENT OF GLUCOSE, INSULIN, AND LIPID DISORDERS

- Assessment for insulin dysregulation should also be pursued in all patients with PPID (see Equine Endocrine Group Recommendations for Diagnosis and Management of Equine Metabolic Syndrome).
- In horses with PPID and concurrent insulin dysregulation, pergolide treatment reduces post-prandial hyperinsulinemia. However, it is important to note that this effect is not observed in horses with insulin dysregulation that do not have PPID.

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Table 5 – Frequently Asked Questions

How is testing for PPID impacted by stress, sedation, pain, and diet?

- Stress, excitement, and trailering can result in a transient increase in ACTH concentrations.
- Samples for PPID diagnosis using baseline ACTH should not be collected within 30 minutes of trailering or in an animal that is visually excited.
- Sedation may impact endocrine responses. If baseline ACTH testing is pursued after sedation with xylazine or detomidine, with or without butorphanol, samples should be collected within 5 minutes after sedation to limit changes that could impact test interpretation.
- TRH stimulation testing and assessment of insulin status are impacted by sedation for several hours; thus, it is ideal to avoid diagnostic testing for PPID and insulin status until at least 24 hours after sedation.
- Mild or moderate pain of at least 24 hours duration does not appear to impact diagnostic testing. Testing may be performed in laminitic horses, but it is ideal to postpone testing until severe pain is controlled.

What are some strategies for dealing with horses that become inappetant with pergolide treatment?

- Some horses show a transient reduction in appetite with initial pergolide therapy or with dosage increases. This is often self-limiting.
- Some strategies used by the EEG for addressing persistent inappetence with pergolide treatment include:
  - Pausing administration for 3-7 days, then restarting administration at a lower dose and gradually increasing to the desired dose over 1-2 weeks
  - Dividing the total daily dose into twice daily administration *(Note, this is considered extra-label use as the manufacturer's recommendations are for once daily administration.).*
  - Administering the medication once daily at a different time than the horse's normal mealtimes
- Consult with an equine internal medicine specialist for specific recommendations if inappetence is persistent in horses receiving pergolide.

A number of analyzers and assays for equine ACTH are now available. How do they compare to traditional reference laboratory testing?

- The diagnostic criteria provided in these recommendations are based on the Immulite 2000xpi analyzer. This assay is used globally for equine ACTH measurement, and is known to have some degree of cross-reactivity with the related pituitary peptide CLIP, which is also variably increased in PPID.
- The TOSOH AIA-900 analyzer has been validated and is now used by some laboratories for analysis of equine ACTH. This assay does not have any cross-reactivity with CLIP, and cutoffs will be lower than those used for the Immulite 2000XPi. An advantage of the TOSOH AIA-900 is that measured ACTH appears less susceptible to degradation during shipping to the laboratory, although chilling is still recommended.
- The TRUFORMA equine ACTH assay is a point-of-care assay available in North America and Europe that concurrently measures ACTH and CLIP in a single sample and provides a composite "eACTH" value. This assay appears to perform reliably with good agreement with the Immulite 2000xpi.

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Table 5 – Frequently Asked Questions (cont.)

What are some approaches for managing refractory cases of PPID? Are there other treatment options for PPID?

- Ensure pergolide tablets are being handled and stored appropriately in provided packaging until administration.
- Strategies* used by the EEG for managing refractory cases of PPID include:
  - Gradually increasing pergolide to 4-6 mcg/kg/day and adding cyproheptadine (0.25 mg/kg PO BID or 0.5 mg/kg PO SID)
  - **OR** gradually increasing pergolide to 10 mcg/kg
  - **These dosages are considered extra-label in the U.S., where the manufacturer's recommendations are not to exceed 4 mcg/kg daily.*
- Cabergoline is another dopamine agonist that has been compounded for administration via once-weekly injection to horses with PPID. This is sometimes suggested for refractory PPID cases or in horses in which daily oral medication administration is not possible, but convincing safety and efficacy data is not yet available. Inappetence was also reported in 30-60% of horses receiving cabergoline in one study.
- Dietary supplements have also been suggested for the management of PPID, but scientific evidence for their efficacy is lacking.

Can pergolide be used in breeding animals?

- The safety and efficacy of pergolide in breeding, pregnant, and lactating animals has not been assessed.
- Group members are aware of pergolide use in a small number of breeding stallions and broodmares, but effects on fertility, lactation, and fetal development are not known.
- In pregnant mares, withdrawal of pergolide treatment 30-60 days prior to expected parturition may theoretically limit drug suppression of lactation or potential impacts on fetal adrenal axis development, but scientific evidence for this approach is lacking.

What happens when horses are removed from pergolide treatment?

- In the event a horse on pergolide treatment misses a dose, ACTH concentrations may begin to increase within 48 hours.
- Drug clearance varies substantially among individual horses and can result in detectable drug levels much longer than 48 hours in some animals.
- If horses are unable to receive pergolide for some period for medical reasons (e.g. colic), a brief pause in treatment is usually well tolerated. There is also data to support sublingual drug absorption in equids. Thus, administration via dissolving the tablet in a small amount of water into the sublingual space may also be attempted in horses who cannot receive oral medications.

Disclosures

Andy Durham is affiliated with the Liphook Equine Hospital and this institution offers endocrine testing.

Boehringer Ingelheim facilitates the development of EEG guidelines by supporting travel expenses for participants but does not influence the recommendations made by the group.

Acknowledgements

The authors thank Rachel Lemcke of Amwell Data Services LLC for helping design this document.

Figure 7 – Seasonal interpretation of baseline ACTH concentrations in SI units

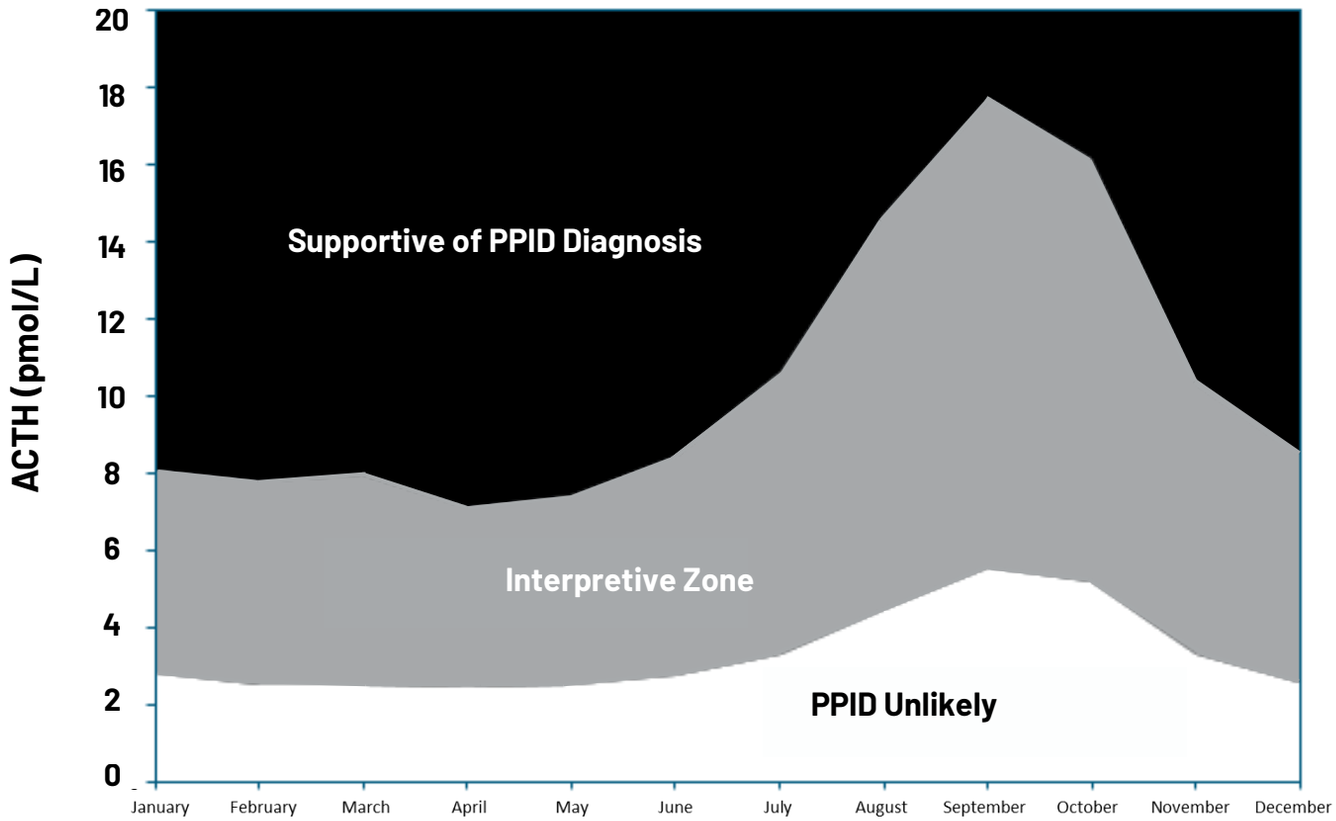


Table 6 – Seasonal interpretation of baseline ACTH* concentrations in SI units (also refer to Figure 7 above)

	TIME OF YEAR	PPID UNLIKELY	INTERPRETIVE ZONE: Consider clinical signs and signalment	PPID LIKELY
Baseline ACTH or TRH time 0 (pmol/L)	Dec. - Jun.	< 3.3	3.3 - 8.8	> 8.8
	July & November	< 3.3	3.3 - 11	> 11
	August	< 4.4	4.4 - 16.5	> 16.5
	Sept. - Oct.	< 6.6	6.6 - 19.8	> 19.8
ACTH 10 min. after TRH (pmol/L)	Jan. - June	< 22	22 - 44	> 44
	July - Dec.	< 22	TRH stimulation testing is most useful to identify negative cases in these months. **See below for more information.	
ACTH 30 min. after TRH (pmol/L)	Jan. - June	< 8.8	8.8 - 19.8	> 19.8
	July - Dec.	< 8.8	TRH stimulation testing is most useful to identify negative cases in these months. **See below for more information.	

** ACTH concentrations provided here are based on values determined by the Immulite 2000xpi analyzer. Additional information on interpreting test results from other equine ACTH analyzers is provided in Table 5 - Frequently Asked Questions.*

Specific months provided here are accurate for the northern hemisphere, but require seasonal correction for southern hemisphere interpretation. An alternate version of this table with ACTH concentrations reported in metric units (pg/mL) is included earlier in the document (see Figure 5 and Table 3).

*** Many healthy animals have variably exaggerated ACTH responses to TRH in the autumn. 10-minute ACTH concentrations >110 pmol/L in the autumn may be consistent with PPID, but much variability within and among horses is described. Thus, interpretation of TRH stimulation test results in the autumn can be a challenge, and repeat testing at a later date should be considered if clinical signs and test results are inconsistent.*

Table 7 – Suggested further reading

1. Adams AA, Siard-Altman MH, Reedy SE, Barker D, Elzinga S, Sanz MG, Urschel K, Ireland JL. Evaluation of seasonal influences on adrenocorticotropic hormone response to the thyrotropin-releasing hormone stimulation test and its accuracy for diagnosis of pituitary pars intermedia dysfunction. Vet J. 2023 Oct 5;300-302:106035. doi: 10.1016/j.tvjl.2023.106035.

2. Bamford NJ, Stewart AJ, El-Hage CM, Bertin FR, Bailey SR. Investigation of breed differences in plasma adrenocorticotropic hormone concentrations among healthy horses and ponies. Vet J. 2023 Jun-Jul;296-297:105995. doi: 10.1016/j.tvjl.2023.105995.

3. Bouquet A, Nicol C, Knowles EJ, Schofield I, Menzies-Gow NJ. Development of a health-related quality-of-life assessment tool for equines with pituitary pars intermedia dysfunction. Equine Vet J. 2025 May 2. doi: 10.1111/evj.14513. Epub ahead of print. PMID: 40314080.

4. Durham AE, Potier JF, Huber L. The effect of month and breed on plasma adrenocorticotropic hormone concentrations in equids. Vet J. 2022 Aug;286:105857. doi: 10.1016/j.tvjl.2022.105857.

5. Durham AE, Clarke BR, Potier JFN, Hammarstrand R, Malone GL. Clinically and temporally specific diagnostic thresholds for plasma ACTH in the horse. Equine Vet J. 53(2): 250-260. 2021. DOI: 10.1111/evj.13292

6. Galinelli NC, Bamford NJ, Erdody ML, Mackenzie SA, Warnken T, Harris PA, Sillence MN, Bailey SR. Effect of pergolide treatment on insulin dysregulation in horses and ponies with pituitary pars intermedia dysfunction. Equine Vet J. 2025 Nov;57(6):1612-1622. doi: 10.1111/evj.14468. Epub 2025 Feb 18. PMID: 39967360; PMCID: PMC12508286.

7. Hodge E, Kowalski A, Torcivia C, Lindborg S, Stefanovski D, Hart K, Frank N, van Eps A. Effect of thyrotropin-releasing hormone stimulation testing on the oral sugar test in horses when performed as a combined protocol. J Vet Intern Med. 2019 Sep;33(5):2272- 2279. DOI: 10.1111/jvim.15601.

8. Horn R, Stewart AJ, Jackson KV, Dryburgh EL, Medina-Torres CE, Bertin FR. Clinical implications of using adrenocorticotropic hormone diagnostic cutoffs or reference intervals to diagnose pituitary pars intermedia dysfunction in mature horses. J Vet Intern Med. 2021 Jan;35(1):560-570. DOI: 10.1111/jvim.16017

9. Horner A, Bamford NJ, Stear MJ, Piedrafita D, Jabbar A, Hughes KJ, El-Hage CM, Preston S. Strongyle egg shedding and egg reappearance periods in horses with pituitary pars intermedia dysfunction. Vet Parasitol. 2024 Jun;328:110176. doi: 10.1016/j.vetpar.2024.110176. Epub 2024 Mar 28. PMID: 38603926.

10. Ireland JL, Lester A, Banse HE. Factors affecting measurement of basal adrenocorticotropic hormone in adult domestic equids: A scoping review. Vet J. 2024 Apr;304:106071. doi: 10.1016/j.tvjl.2024.106071. Epub 2024 Feb 8. PMID: 38341024.926

11. Kam YN, McKenzie K, Coyle M, Bertin FR. Repeatability of a thyrotropin-releasing hormone stimulation test for diagnosis of pituitary pars intermedia dysfunction in mature horses. J Vet Intern Med. 2021 Nov;35(6):2885-2890. doi: 10.1111/jvim.16281.

12. Menzies-Gow NJ, Banse HE, Duff A, Hart N, Ireland JL, Knowles EJ, McFarlane D, Rendle D. BEVA primary care clinical guidelines: Diagnosis and management of equine pituitary pars intermedia dysfunction. Equine Vet J. 2023 Oct 5. doi: 10.1111/evj.14009.

Table 7 – Suggested further reading (cont.)

13. Pinn-Woodcock TL, Llanos-Soto SG, Ivanek R, Goodrich E, Frye E, Wells A, Mullen K, Arbittier E, Hughes L, Berryhill E, Brosnahan P, Buslinger L, Schnabel L, DeNotta S, Mallicote M, Peek S, Place NJ. Seasonal elevation in equine adrenocorticotropic hormone occurs throughout the contiguous United States and is influenced by latitude and age. J Am Vet Med Assoc. 2025 Aug 1:1-10. doi: 10.2460/javma.25.04.0223. Epub ahead of print. PMID: 40749730.int.

14. Schott HC 2nd, Strachota JR, Marteniuk JV, Refsal KR. Long-term response of equids with pituitary pars intermedia dysfunction to treatment with pergolide. J Vet Intern Med. 2025 May-Jun;39(3):e70109. doi: 10.1111/jvim.70109. PMID: 40317948; PMCID: PMC12046498.: 40314080

15. Stewart AJ, Ireland JL, Durham AE, McGowan CM. Diagnosis of equine pituitary pars intermedia dysfunction. Vet J. 2023 Oct 5:106036. doi: 10.1016/j.tvjl.2023.106036.

16. Tadros EM, Fowlie JG, Refsal KR, Marteniuk J, Schott HC. Association between hyperinsulinemia and laminitis severity at the time of pituitary pars intermedia dysfunction diagnosis. Equine Vet J. 51: 52-56. 2019. DOI: 10.1111/evj.12963

17. Tatum RC, McGowan CM, Ireland JL. Efficacy of pergolide for the management of equine pituitary pars intermedia dysfunction: A systematic review. Vet J. 2020 Dec:266:105562. DOI: 10.1016/j.tvjl.2020.105562

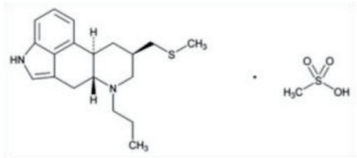
18. Vaughn SA, Lemons MB, Hart KA. The effect of season and breed on hypothalamic-pituitary-adrenal axis hormones, metabolic hormones, and oxidative markers in ponies and horses. J Vet Intern Med. 2025 Mar-Apr;39(2):e70047. doi: 10.1111/jvim.70047. PMID: 40048369; PMCID: PMC11884412.: 40314080

19. Vorster DM, Wang W, Kemp KL, Bamford NJ, Bertin FR. Clinical implications of imprecise sampling time for 10- and 30-min thyrotropin-releasing hormone stimulation tests in horses. Equine Vet J. 2023 Aug 30. doi: 10.1111/evj.13991.

Dopamine receptor agonist for oral use in horses only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: PRASCEND Tablets are rectangular light red colored, half-scored tablets containing 1 mg pergolide, as pergolide mesylate. Pergolide mesylate is a synthetic ergot derivative and is a potent dopamine receptor agonist. The chemical name of pergolide mesylate is 8β-[(Methylthio) methyl]-6-propylergoline monomethanesulfonate. The chemical structure is:



Indication: For the control of clinical signs associated with Pituitary Pars Intermedia Dysfunction (Equine Cushing's Disease) in horses.

Dosage and Administration: Administer orally at a starting dose of 2 mcg/kg once daily. Dosage may be adjusted to effect, not to exceed 4 mcg/kg daily.

It has been reported that pergolide tablets may cause eye irritation, an irritating smell, or headache when PRASCEND Tablets are split or crushed. PRASCEND Tablets should not be crushed due to the potential for increased human exposure and care should be taken to minimize exposure when splitting tablets.

The tablets are scored and the calculated dosage should be provided to the nearest one-half tablet increment (see Table 1).

Table 1 Dosing Table

Body weight	Dosage	
	2 mcg/kg	4 mcg/kg
136 - 340 kg (300 - 749 lb)	0.5 tablet	1 tablet
341 - 567 kg (750 - 1,249 lb)	1 tablet	2 tablets
568 - 795 kg (1,250 - 1,749 lb)	1.5 tablets	3 tablets
796 - 1,022 kg (1,750 - 2,249 lb)	2 tablets	4 tablets

Dosing should be titrated according to individual response to therapy to achieve the lowest effective dose. Dose titration is based on improvement in clinical signs associated with Pituitary Pars Intermedia Dysfunction (PPID) and/or improvement or normalization of endocrine tests (for example, dexamethasone suppression test or endogenous ACTH test).

In some cases, adverse events were reported after a dose increase (see **Post-Approval Experience**).

If signs of dose intolerance develop, the dose should be decreased by half for 3 to 5 days and then titrated back up in 2 mcg/kg increments every 2 weeks until the desired effect is achieved.

Contraindications: PRASCEND is contraindicated in horses with hypersensitivity to pergolide mesylate or other ergot derivatives.

Warnings: Do not use in horses intended for human consumption.

Keep PRASCEND in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Dogs have eaten PRASCEND tablets that were placed in food intended for horses or dropped during administration of the tablets to the horses. Adverse reactions may occur if animals other than horses ingest PRASCEND tablets (see **Post-Approval Experience**).

Human Warnings: Not for use in humans. Do not ingest the product. Keep this and all medications out of the reach of children. PRASCEND should not be administered by persons who have had adverse reactions to ergotamine or other ergot derivatives.

Pergolide, like other ergot derivatives, may cause emesis, dizziness, lethargy or low blood pressure.

Pregnant or lactating women should wear gloves when administering this product. It has been reported that pergolide tablets may cause eye irritation, an irritating smell, or headache when PRASCEND Tablets are split or crushed. PRASCEND Tablets should not be crushed due to the potential for increased human exposure and care should be taken to minimize exposure when splitting tablets. Store this product separately away from human medicinal products and handle this product with care to avoid accidental ingestion.

In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

Precautions: Treatment with PRASCEND may cause inappetence.

The use of PRASCEND in breeding, pregnant, or lactating horses has not been evaluated. The effects of pergolide mesylate on breeding, pregnant, or lactating horses are not known; however, the pharmacologic action of pergolide mesylate suggests that it may interfere with reproductive functions such as lactation.

PRASCEND is approximately 90% associated with plasma proteins. Use caution if administering PRASCEND with other drugs that affect protein binding. Dopamine antagonists, such as neuroleptics (phenothiazines, domperidone) or metoclopramide, ordinarily should not be administered concurrently with PRASCEND (a dopamine agonist) since these agents may diminish the effectiveness of Prascend.

Adverse Reactions:
Pre-Approval Experience: A total of 122 horses treated with PRASCEND Tablets for six months were included in a field study safety analysis.

Table 2 Summary of the most common adverse reactions (N=122)

Clinical sign	# Cases	Cases (%)
Decreased appetite	40	32.8
Lameness	22	18.0
Diarrhea/Loose stool	12	9.8
Colic	12	9.8
Lethargy	12	9.8
Abnormal Weight Loss	11	9.0
Laminitis*	10	8.2
Heart murmur	10	8.2
Death	8	6.6
Tooth disorder	8	6.6
Skin abscess	7	5.7
Musculoskeletal pain	6	4.9
Behavior change	6	4.9

*Three new cases and 7 pre-existing, recurring cases

Inappetence or decreased appetite occurred at one or more meals in 40 of 122 horses treated with Prascend. At the baseline evaluation 1.6% of owners reported a history of inappetence or decreased appetite as compared to the 32.8% of horses that experienced inappetence or decreased appetite during the study. Most cases of inappetence were transient and occurred during the first month of treatment; however, some horses experienced sporadic inappetence throughout the study. Two horses required a temporary reduction in dose due to inappetence during the first month of the study. Both horses returned to their original dose within 30 days.

Weight loss occurred in more than half of the horses in this study; however, weight loss that was considered abnormal was only reported in 11 horses.

Lethargy was reported in 9.8% of horses during the study, and was not reported in any horses at the baseline evaluation.

Behavioral changes were noted in 6 horses including aggression, kicking, agitation, nervous behavior and increased activity. One horse required a temporary reduction in dose due to energetic behavior during the first month of the study.

Eight horses died or were euthanized during the study due to worsening of pre-existing conditions (laminitis, dental disease, septic tenosynovitis) or colic (strangulating lipomas, large colon volvulus).

One mare was inadvertently enrolled in the study while pregnant and experienced dystocia resulting in the death of the foal.

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Post-Approval Experience (2019):

The following adverse events are based on post approval adverse drug experience reporting for PRASCEND. Not all adverse events are reported. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events in horses are categorized in order of decreasing reporting frequency by body system and in decreasing order of reporting frequency within each body system:

General: anorexia, lethargy, weight loss
Gastrointestinal: diarrhea, abdominal pain/colic
Dermatological: alopecia, hyperhidrosis, dermatitis
Musculoskeletal: laminitis, muscle stiffness/soreness
Neurological: ataxia, seizure, muscle tremors
Behavioral: aggression (to other horses and humans), hyperactivity (anxiety, agitation), other behavioral changes (stud-like behavior, spooky, unpredictable, confused)
Clinical pathology: anemia, elevated liver enzymes, thrombocytopenia

The above adverse events were reported in some horses at starting dose levels, while in the others following a dose increase.

Death (including euthanasia) has been reported.

Adverse events have been reported in dogs following ingestion of tablets prepared for administration to horses.

To report suspected adverse reactions, to obtain a Safety Data Sheet (SDS), or for technical assistance, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact the FDA at 1-888-FDA-VETS or online at http://www.fda.gov/reportanimalae.

Clinical Pharmacology: Pergolide mesylate is a synthetic ergot derivative and is a potent dopamine receptor agonist. As with other dopamine agonists, pergolide inhibits the release of prolactin which suggests that it may interfere with lactation. In horses with PPID, pergolide is believed to exert its therapeutic effect by stimulating dopamine receptors, and has been shown to decrease the plasma levels of adrenocorticotropic hormone (ACTH), melanocyte stimulating hormone (MSH), and other pro-opiomelanocortin peptides.[1]

Pharmacokinetic information in the horse is based on a study using single oral doses of 10 mcg/kg in six healthy mares between 3 and 17 years of age.[2] Pergolide was rapidly absorbed; the mean maximum concentration (Cmax) was 4.05±2.02 ng/mL with the median time to maximum concentration (Tmax) being 0.415 hours.

The area under the curve (AUC) was 14.08±7.46 hr·ng/mL. The mean half life (T1/2) was 5.86±3.42 hours; the mean apparent oral clearance (CL/F) was 1204 mL/kg/hr; and the mean apparent volume of distribution (V/F) was 3082±1354 mL/kg.

Effectiveness: An open-label, historical control, field study evaluated the effectiveness of PRASCEND for the control of clinical signs of PPID. A total of 122 horses with PPID were enrolled in the study, 113 of which were included in effectiveness evaluations. The success of each horse was based on results of endocrinology testing (dexamethasone suppression test or endogenous ACTH test) and/or improvement in clinical signs related to PPID (hirsutism, hyperhidrosis, polyuria/polydypsia, abnormal fat distribution, and/or muscle-wasting) on the Day 180 evaluation. Based on endocrine testing and investigators' clinical assessment scores, 86 (76.1%) of the 113 evaluable cases were treatment successes.

Table 3 Proportion of Treatment Successes on Day 180

Percent success	Lower bound: one-sided 95% confidence interval
76.1% (86/113)	68.6%

Enrolled horses were diagnosed with PPID based on the presence of hirsutism and an abnormal pre-study endocrine test result. All horses were treated with 2 mcg/kg PRASCEND (to the nearest one-half tablet) orally once daily for the first three months. If the endocrine test result on Day 90 was normal or adequately improved, the horse continued on the same dose through Day 180. If the endocrine test result on Day 90 was abnormal, the dose increased to 4 mcg/kg given once daily through Day 180.
Forty-seven (41.6%) of the 113 horses included in the effectiveness database required a dose increase at Day 90.

Improvement was noted in scores for all clinical sign categories and in mean results for endocrine tests.

Table 4 Percent of Animals with Improvement in Clinical Signs Relative to Baseline Scores

Clinical sign	Day 90±7 (%)	Day 180±7 (%)
Hirsutism	32.7%	89.2%
Hyperhidrosis	27.4%	42.3%
Polyuria / polydypsia	31.0%	34.2%
Abnormal fat distribution	21.2%	33.3%
Muscle wasting	36.3%	46.0%

Table 5 Endocrine test results (mean values)

Test	# Animals	Baseline	Day 90	Day 180
ACTH (pg/mL)	20	73.53	51.12	45.08
DST** (mcg/dL)	93	3.12	1.39	1.47

** Dexamethasone suppression test: Post dexamethasone cortisol concentration

Animal Safety: In a six month target animal safety study healthy adult horses received PRASCEND administered orally, once daily, at doses of either 0 mcg/kg, 4 mcg/kg, 6 mcg/kg, or 8 mcg/kg (0X, 1X, 1.5X, or 2X the maximum recommended dose). There were eight healthy horses (four males and four females) in each treatment group. Doses were prepared by dissolving tablets in approximately 10 mL of a 50% sugar water solution.

PRASCEND treated groups had lower mean heart rates and higher mean temperatures than the control group. Horses in all treatment groups had minimum heart rates within the normal range and maximum temperatures below 101.5°F. One 1.5X horse experienced a mild episode of spasmodic colic on Day 3 that resolved after treatment with flunixin meglumine.

Mean red blood cell counts and hemoglobin values were lower in PRASCEND treated groups as compared to the control group. Other hematology parameters including hematocrit, white blood cells, absolute neutrophils, and absolute lymphocytes exhibited mild, transient decreases as compared to the control group. The hematology parameters generally decreased over the first 30 to 60 days after treatment initiation and then returned to values similar to pre-treatment levels. No treatment related alterations were identified on histopathology evaluation of bone marrow.

Storage: Store at or below 25°C (77°F).

How Supplied: PRASCEND Tablets are available in 1 mg strength - packaged 10 tablets per blister and 60 or 160 tablets per carton.
NDC 0010-4489-01 - 60 tablets
NDC 0010-4489-02 - 160 tablets

Approved by FDA under NADA # 141-331

References:
[1] Orth, D.N., Holscher, M.A., Wilson, M.G., et al. (1982) Equine Cushing's Disease: Plasma Immunoreactive Proopiolipomelanocortin Peptide and Cortisol Levels Basally and in Response to Diagnostic Tests. Endocrinology. 110(4):1430-41
[2] Wright A, Gehring R, Coetzee H (2008.) Pharmacokinetics of pergolide in normal mares. American College of Veterinary Internal Medicine Forum, Abstract #36, San Antonio, TX.

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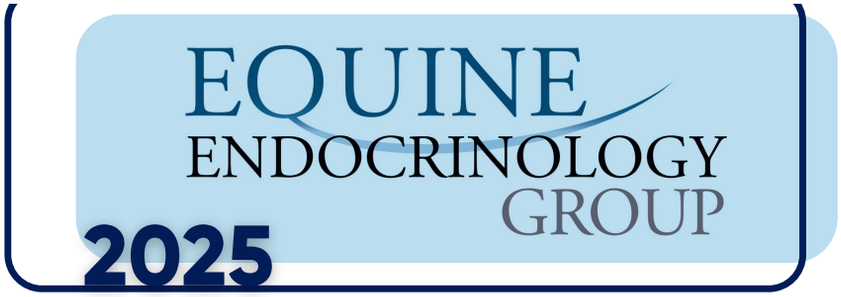
Notes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