SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pergocoat 2 mg film-coated tablets for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Pergolide	2.0 mg
equivalent to 2.62 mg pergolide mesilate	

Excipients:

Core:	
Iron oxide yellow (E172)	0.24 mg
Coating:	
Iron oxide yellow (E172)	0.66 mg
Titanium dioxide (E171)	5.06 mg
Ferrosofferic oxide	0.28 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet
Green sphere shaped, film-coated tablet

4. CLINICAL PARTICULARS

4.1 Target species

Horses (non food-producing).

4.2 Indications for use, specifying the target species

Symptomatic treatment of clinical signs associated with Pituitary Pars Intermedia Dysfunction (PPID) (Equine Cushing's Disease).

4.3 Contraindications

Do not use in horses with known hypersensitivity to pergolide mesilate or other ergot derivatives or to any of the excipients.
Do not use in horses less than 2 years of age.

4.4 Special warnings for each target species

Appropriate endocrinologic laboratory tests should be conducted as well as evaluation of clinical signs in order to establish a diagnosis of PPID.

4.5 Special precautions for use

Special precautions for use in animals
As the majority of cases of PPID are diagnosed in aged horses, other pathological processes are frequently present. For monitoring and frequency of testing, see section 4.9.

Special precautions to be taken by the person administering the medicinal product to animals
This product may cause hypersensitivity (allergy) reactions. People with known hypersensitivity to pergolide or other ergot derivatives should avoid contact with the veterinary medicinal product.

This product may cause adverse effects due to decreased prolactin levels, which poses a particular risk to pregnant and lactating women. Pregnant or lactating women should avoid dermal contact or hand-to-mouth contact and wear gloves when administering the product.

Accidental ingestion, especially by children, may cause adverse reactions such as emesis, dizziness, lethargy or low blood pressure. To avoid accidental ingestion, the blister should be replaced into the carton and carefully kept away from children. Avoid hand-to-mouth contact. Do not eat, drink or smoke when using this product. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

This product may cause eye irritation. Avoid contact with the eyes including hand-to-eye contact when handling the tablets. Minimize exposure risks when dissolving the tablets, e.g. tablets should not be crushed. In case of contact of the dissolved product with skin, wash exposed skin with water. In the event of eye exposure, flush the affected eye immediately with water and seek medical advice.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Horses:

Rare (1 to 10 animals / 10,000 animals treated):	Inappetence, anorexia[1], lethargy[1]. Central nervous system signs[2] (e.g. depression[2], ataxia[2]). Diarrhoea, colic.
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Sweating.

[1] transient
[2] mild

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See also section 'contact details' of the package leaflet for respective contact details.

4.7 Use during pregnancy or lactation

Pregnancy:
Use only according to the benefit/ risk assessment by the responsible veterinarian. The safety of this veterinary medicinal product has not been demonstrated in pregnant mares. Laboratory studies in mice and rabbits have not produced any evidence of teratogenic effects. Reduced fertility was seen in mice at a dose of 5.6 mg/kg body weight per day.

Lactation:
The use is not recommended in lactating horses, in which the safety of this veterinary medicinal product has not been demonstrated. In mice, reduced body weights and survival rates in the progeny were attributed to the pharmacological inhibition of prolactin secretion resulting in lactation failure.

4.8 Interaction with other medicinal products and other forms of interaction

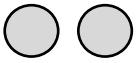
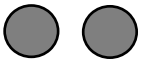
Use with caution in case the veterinary medicinal product is co-administered with other drugs known to affect protein binding.
Do not administer concurrently with dopamine antagonists, such as neuroleptics (phenothiazines - e.g. acepromazine), domperidone, or metoclopramide, as these agents may reduce the effectiveness of pergolide.

4.9 Amounts to be administered and administration route

Oral use, once daily.
To facilitate administration, the required daily dose should be placed in a small amount of water and/or mixed with molasses or other sweetener and agitated until dissolved. In this case, the dissolved tablets should be administered with a syringe. The whole amount should be administered immediately. Tablets should not be crushed, see section 4.5.

Starting dose
The starting dose is about 2 µg pergolide/kg (dose range: 1.3 to 2.5 µg/kg; see table below). The maintenance dose should then be titrated according to the individual response as determined by monitoring (see below), resulting in an average maintenance dose of 2 µg pergolide/kg bodyweight with a dose range of 0.6 to 10 µg pergolide/kg bodyweight.

Starting doses are recommended as follows:

Horse body weight	0.5 mg tablet		1 mg tablet	2 mg tablet	Starting dose	Dosage range
200 - 400 kg					0.5 mg	1.3 – 2.5 µg/kg
401 - 600 kg					1.0 mg	1.7 – 2.5 µg/kg
or						
401 - 600 kg					1.0 mg	1.7 – 2.5 µg/kg
601 - 850 kg		+			1.5 mg	1.8 – 2.5 µg/kg
or						
601 - 850 kg					1.5 mg	1.8 – 2.5 µg/kg
851 - 1000 kg					2.0 mg	2.0 – 2.4 µg/kg
or						
851 - 1000 kg					2.0 mg	2.0 – 2.4 µg/kg

Maintenance dose
Lifelong treatment is anticipated for this disease.
Most horses respond to therapy and are stabilised at an average dose of 2 µg pergolide/kg body weight. Clinical improvement with pergolide is expected within 6 to 12 weeks. Horses may respond clinically at lower or varying doses; it is therefore recommended to titrate to the lowest effective dose per individual based on response to therapy, whether it is effectiveness or signs of intolerance. Some horses may require doses as high as 10 µg pergolide/kg body weight per day. In these rare situations, appropriate additional monitoring is advised.

Following initial diagnosis, repeat endocrinologic testing for dose titration and monitoring of treatment at intervals of 4 to 6 weeks until stabilisation or improvement of clinical signs and/or diagnostic testing occurs.

If clinical signs or diagnostic testing have not yet improved at the first 4 to 6 week interval, the total daily dose may be increased by 0.50 mg. In case clinical signs have improved but are not yet normalised, the veterinarian may decide to titrate or not to titrate the dose, considering the individual’s response/tolerance to the dose.

In case clinical signs are not adequately controlled (clinical evaluation and/or diagnostic testing) it is recommended to increase the total daily dose by 0.5 mg increments (if the drug is tolerated at that dose) every 4 to 6 weeks until stabilisation occurs. If signs of dose intolerance develop, treatment should be stopped for 2 to 3 days and reinstated at one-half of the previous dose. The total daily dose may then be titrated back up to the desired clinical effect by 0.5 mg increments every 2 to 4 weeks. If a dose is missed, the next scheduled dose should be administered as prescribed.

Following stabilisation, regular clinical assessment and diagnostic testing should be performed every 6 months to monitor treatment and dose. Where there is no apparent response to treatment, the diagnosis should be re-evaluated.

4.10 Overdose (symptoms, emergency procedures, antidotes)

No information available.

4.11 Withdrawal period(s).

Not authorised for use in horses intended for human consumption.
Treated horses may never be slaughtered for human consumption.
The horse must have been declared as not intended for human consumption under national horse passport legislation.
Not authorised for use in mares producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Nervous system, dopamine agonist
ATCvet code: QN04BC02

5.1 Pharmacodynamic properties

Pergolide is a synthetic ergot derivative and is a potent, long-acting dopamine receptor agonist. Both *in vitro* and *in vivo* pharmacological studies have demonstrated the activity of pergolide as a selective dopamine agonist with little or no effect on norepinephrine, epinephrine or serotonin pathways at therapeutic doses. As with other dopamine agonists, pergolide inhibits the release of prolactin. In horses with Pituitary Pars Intermedia Dysfunction (PPID) pergolide exerts its therapeutic effect by stimulating dopamine receptors. Further, in horses with PPID, pergolide has been shown to decrease the plasma levels of ACTH, MSH and other pro-opiomelanocortin peptides.

5.2 Pharmacokinetic particulars

Pharmacokinetic information in the horse is available for oral doses of 2, 4 and 10 µg pergolide/kg body weight. It has been demonstrated that pergolide is rapidly absorbed with a short time to peak concentration.

Peak concentrations (C_{max}) following the dose of 10 µg/kg were low and variable with a mean of ~ 4 ng/ml and a mean terminal half-life (T ½) of ~ 6 hours. The median

time of peak concentration (T_{max}) was ~ 0.4 hours and the area under the curve (AUC) was ~ 14 ng x hours/ml.

In a more sensitive analytical assay, plasma concentrations following the dose of 2 µg pergolide/kg were very low and variable with peak concentrations ranging from 0.138 to 0.551 ng/ml. The peak concentrations occurred at 1.25 +/- 0.5 hours (T_{max}). Plasma concentrations in most horses were quantifiable for only 6 hours post dose. However, one horse had quantifiable concentrations for 24 hours. Terminal half-lives were not calculated as there was incomplete elucidation of the plasma concentration-time curve for most horses.

Peak concentrations (C_{max}) following the dose of 4 µg/kg were low and variable with a range from 0.4 – 4.2 ng/mL with a mean of 1.8 ng/mL, and a mean terminal half-life (T ½) of ~ 6 hours. The median time of peak concentration (T_{max}) was ~ 0.6 hours and the AUC_t ~ 3.4 ng x h/ml.

Pergolide mesilate is approximately 90% associated with plasma proteins in humans and laboratory animals. The route of elimination is via the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Lactose monohydrate
Croscarmellose sodium
Povidone
Magnesium stearate
Iron oxide yellow (E172)

Coat:
Polyvinylalcohol
Talc
Titanium dioxide (E171)
Glycerol monocaprylocaprate
Sodium laurilsulfate
Iron oxide yellow (E172)
Ferrosofferic oxide

6.2 Major incompatibilities

Not applicable

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months

6.4 Special precautions for storage

Store in the original package, in order to protect from light.

6.5 Nature and composition of immediate packaging

PVC/PE/PVDC-aluminium blisters, containing 10 tablets each.
OPA/aluminium/PVC-aluminium blisters, containing 10 tablets each.
Carton box of 10, 30, 60, 90, 100, 120, 160 or 240 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 36408/5024

9. DATE OF FIRST AUTHORISATION

08 October 2021

10. DATE OF REVISION OF THE TEXT

August 2023

Approved 07 August 2023