ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pergoquin 1 mg tablets for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Pergolide 1.0 mg
equivalent to 1.31 mg pergolide mesilate

Excipients:
Iron oxide red (E172) 0.9 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet
Pink round and convex tablet with a cross-shaped break line on one side.

Tablets can be divided into 2 or 4 equal parts.

4. CLINICAL PARTICULARS

4.1 Target species

Horses

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

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 veterinary medicinal product may cause eye irritation, an irritating smell, or headache after dividing the tablets. Avoid contact with the eyes and inhalation when handling the tablets. Minimize exposure risks when dividing tablets, e.g. tablets should not be crushed.
In case of contact with skin, wash exposed skin with water. In the event of eye exposure, flush the affected eye immediately with water and seek medical advice. For nasal irritation, move to fresh air and seek for medical attention if breathing difficulty develops.

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 by wearing gloves when administering the product.

Accidental ingestion, especially by children, may cause adverse reactions. To avoid accidental ingestion, carefully keep the product out of reach and sight of children. Tablet parts should be returned to the open blister space. Blisters should be inserted back into the outer packaging and kept in a safe place. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Do not eat, drink or smoke when using this product. Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Inappetence, transient anorexia and lethargy, mild central nervous system signs (e.g. mild depression and mild ataxia), diarrhoea and colic have been observed in horses in rare cases. Sweating has been reported in very rare cases.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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.

Starting dose
The starting dose is 2 µg pergolide/kg (dose range: 1.7 to 2.5 µg/kg) body weight. Studies from the published literature cite the most common, average dose as 2 µg pergolide/kg with a range from 0.6 to 10 µg pergolide/kg. The starting dose (2 µg pergolide/kg, e.g. one tablet for 500 kg bodyweight) should then be titrated according to the individual response as determined by monitoring (see below).

Starting doses are recommended as follows:

Horse body weight	Number of tablets	Starting dose	Dosage range
200 - 300 kg	½	0.50 mg	1.7 – 2.5 µg/kg
301 – 400 kg	¾	0.75 mg	1.9 - 2.5 µg/kg
401 - 600 kg	1	1.00 mg	1.7 – 2.5 µg/kg
601 - 850 kg	1 ½	1.50 mg	1.8 – 2.5 µg/kg
851 - 1000 kg	2	2.00 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.

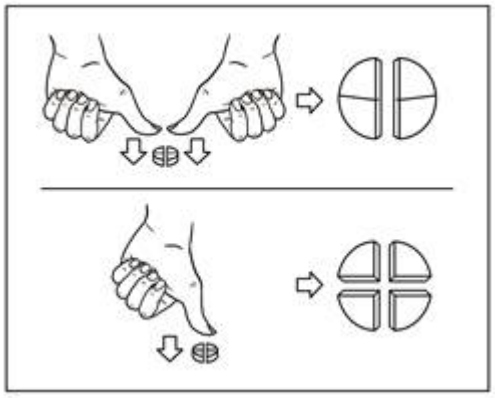
Following initial diagnosis, repeat endocrinologic testing for dose titration and monitoring of treatment at intervals of 4 to 6 weeks until stabilisation or improvement of clinical signs and/or diagnostic testing occurs.

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 0.25 – 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 0.25-0.5 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 0.25-0.5 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.

Tablets can be divided into 2 or 4 equal parts to ensure accurate dosing. Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.



2 equal parts: press down with your thumbs on both sides of the tablet.
4 equal parts: press down with your thumb in the middle of the tablet.

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 (Cmax) 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 (Tmax) 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 (Tmax). 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 (Cmax) following the dose of 4 µg/kg were low and variable with a range from 0.7 to 2.9 ng/ml with a mean of ~ 1.7 ng/ml, and a mean terminal half-life (T ½) of ~ 9 hours. The median time of peak concentration (Tmax) was ~ 0.6 hours and the AUC ~ 4.8 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

Croscarmellose sodium
Iron oxide red (E172)
Lactose monohydrate
Magnesium Stearate
Povidone

6.2 Major incompatibilities

Not applicable

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years
Shelf life of divided tablets after first opening the immediate packaging: 3 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Aluminium-OPA/Aluminium/PVC blisters containing 10 tablets
Cardboard box of 50, 60, 100, 150, 160 or 200 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

Richter Pharma AG
Feldgasse 19
4600 Wels
Austria

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT