

[Version 9,10/2022]

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Trilotab 120 mg chewable tablets for dogs (NL/AT/BE/CZ/DE/ES/FR/HU/IE/IT/PL/PT/SK/UKNI)
Trilotab vet 120 mg chewable tablets for dogs (FI/ SE/ DK)
Trilotab vet chewable (EE/ LT/ LV)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Trilostane 120 mg

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate
Starch, pregelatinised
Hydroxypropylcellulose
Silica, colloidal hydrated
Sodium starch glycolate (Type A)
Magnesium stearate
Chicken flavour

Off-white to light brown with brown spots, round and convex tablet with a cross-shaped break line on one side. Tablets can be divided into 2 or 4 equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For the treatment of pituitary-dependent and adrenal-dependent hyperadrenocorticism (Cushing's disease and syndrome).

3.3 Contraindications

Do not use in animals suffering from primary hepatic disease and/or renal insufficiency.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

An accurate diagnosis of hyperadrenocorticism is essential.
Where there is no apparent response to treatment, the diagnosis should be re-evaluated. Dose increases may be necessary.
Veterinarians should be aware that dogs with hyperadrenocorticism are at increased risk of pancreatitis. This risk may not diminish following treatment with trilostane.

3.5 Special precautions for use

Special precautions for safe use in the target species:

As the majority of cases of hyperadrenocorticism are diagnosed in dogs between the ages of 10-15 years, other pathological processes are frequently present. It is particularly important to screen cases for primary hepatic disease and renal insufficiency as the product is contraindicated in these cases. Subsequent close monitoring during treatment should be carried out. Particular attention should be paid to liver enzymes, electrolytes, urea and creatinine.

The presence of diabetes mellitus and hyperadrenocorticism together requires specific monitoring. If a dog has previously been treated with mitotane, its adrenal function will have been reduced. Experience in the field suggests that an interval of at least a month should elapse between cessation of mitotane and the introduction of trilostane. Close monitoring of adrenal function is advised, as dogs may be more susceptible to the effects of trilostane.

The product should be used with extreme caution in dogs with pre-existing anaemia as further reductions in packed-cell volume and haemoglobin may occur. Regular monitoring should be undertaken.

The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Accidental ingestion of the product can cause gastrointestinal effects, such as nausea and vomiting. Avoid hand to mouth contact. To avoid accidental ingestion, especially by a child, unused tablet parts should be placed back into the blister and carton and carefully kept away from children. Part used tablets should be used at the time of the next dose.

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

Wash hands with soap and water after use.

Trilostane may decrease testosterone synthesis and has anti-progesterone properties.

Women who are pregnant or are intending to become pregnant should avoid handling the product.

The product may cause skin and eye irritation. After contact of the product with eyes or skin, wash with plenty of water. If irritation persists, seek medical advice.

This veterinary medicinal product may cause hypersensitivity reactions. People with known hypersensitivity to trilostane should avoid contact with the product. If you develop allergic symptoms such as a skin rash, swelling of the face, lips or eyes following exposure to the product, seek medical advice and show the package leaflet or label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Ataxia, Muscle tremor Hypersalivation, Bloating Generalised skin reaction
Undetermined frequency (cannot be estimated from the available data)	Adrenal gland disorders, Hypoadrenocorticism ^{1,2} and Addison disease ³ Sudden death Lethargy ⁴ , Anorexia ⁴

¹: Signs associated with iatrogenic hypoadrenocorticism, including weakness, lethargy, anorexia, vomiting and diarrhoea (particularly if monitoring is not adequate, see section 3.9 'Administration routes and dosage'. Signs are generally reversible within a variable period following withdrawal of treatment.).

²: possible result from adrenal necrosis

³: Acute Addisonian crisis (collapse) (see section 3.10 'Symptoms of overdose (and where applicable, emergency procedures and antidotes)').

⁴: in the absence of evidence of hypoadrenocorticism.

Corticosteroid withdrawal syndrome or hypocortisolaemia should be distinguished from hypoadrenocorticism by evaluation of serum electrolytes.

Subclinical renal dysfunction may be unmasked by treatment with the product.

Treatment may unmask arthritis due to a reduction in endogenous corticosteroid levels.

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 the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

Do not use during pregnancy and lactation.

Fertility:

Do not use in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

The possibility of interactions with other medicinal products has not been specifically studied. Given that hyperadrenocorticism tends to occur in older dogs, many will be receiving concurrent medication. In clinical studies, no interactions were observed.

The risk of hyperkalaemia developing should be considered if trilostane is used in conjunction with potassium-sparing diuretics or ACE inhibitors. The concurrent use of such drugs should be subject to a risk-benefit analysis by the veterinary surgeon, as there have been a few reports of deaths (including sudden death) in dogs when treated concurrently with trilostane and an ACE inhibitor.

3.9 Administration routes and dosage

Oral use.

Administer once daily with a meal.

The starting dose for treatment is approximately 2 mg trilostane /kg bodyweight, based on available combinations of (divided) tablet sizes. This tablet strength is therefore not appropriate for dogs weighing less than 15 kg.

Titrate the dose according to individual response, as determined by monitoring (see below). If a dose increase is required, use combinations of (divided) tablet sizes to slowly increase the once daily dose. A wide range of divisible tablet sizes enables optimum dosing for the individual dog. Administer the lowest dose necessary to control the clinical signs.

Ultimately, if symptoms are not adequately controlled for an entire 24 hour inter-dose period, consider increasing the total daily dose by up to 50% and dividing it equally between morning and evening doses.

A small number of animals may require doses significantly in excess of 10 mg per kg body weight per day. In these situations appropriate additional monitoring should be implemented.

Monitoring:

Samples should be taken for biochemistry (including electrolytes) and an ACTH stimulation test pre-treatment and then at 10 days, 4 weeks, 12 weeks, and thereafter every 3 months, following initial diagnosis and after each dose adjustment. It is imperative that ACTH stimulation tests are performed 4 – 6 hours post-dosing to enable accurate interpretation of results. Dosing in the morning is preferable as this will allow your veterinary surgeon to perform monitoring tests 4-6 hours following administration of the dose. Regular assessment of the clinical progress of the disease should also be made at each of the above time points.

In the event of a non-stimulatory ACTH stimulation test during monitoring, treatment should be stopped for 7 days and then re-started at a lower dose. Repeat the ACTH stimulation test after a further 14 days. If the result is still non-stimulatory, stop treatment until clinical signs of hyperadrenocorticism recur. Repeat the ACTH stimulation test one month after re-starting treatment.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Overdose may lead to signs of hypoadrenocorticism (lethargy, anorexia, vomiting, diarrhoea, cardiovascular signs, collapse). There were no mortalities following chronic administration at 36 mg of trilostane /kg to healthy dogs, however mortalities may be expected if higher doses are administered to dogs with hyperadrenocorticism.

There is no specific antidote for trilostane. Treatment should be withdrawn and supportive therapy, including corticosteroids, correction of electrolyte imbalances and fluid therapy may be indicated depending on the clinical signs.

In cases of acute overdose, induction of emesis followed by administration of activated charcoal may be beneficial.

Any iatrogenic adrenocortical insufficiency is usually quickly reversed following cessation of treatment. However in a small percentage of dogs, effects may be prolonged. Following a one week withdrawal of trilostane treatment, treatment should be reinstated at a reduced dose rate.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION**4.1 ATCvet code: QH02CA01****4.2 Pharmacodynamics**

Trilostane selectively and reversibly inhibits the enzyme system 3 beta hydroxysteroid isomerase, thus blocking the production of cortisol, corticosterone and aldosterone.

It reduces the production of glucocorticoid and mineralocorticoid steroids in the adrenal cortex.

Circulating concentrations of these steroids are thus reduced.

Trilostane also antagonises the activity of exogenous adrenocorticotrophic hormone (ACTH). It has no direct effect on either the central nervous or cardiovascular systems.

4.3 Pharmacokinetics

Pharmacokinetic data in dogs have demonstrated large inter-individual variability.

Following a single oral dose at 6.7 mg/kg bw in fed laboratory beagles, AUC is about 5400 ng.h/mL.

Generally, trilostane is rapidly removed from the plasma with concentrations in the plasma reaching a

maximum at 45 min with a Cmax about 5100 ng/mL and are below 20 ng/mL (the limit of quantification) by 6 to 12 hours after administration.

An oral bioavailability study in dogs demonstrated that trilostane was absorbed more extensively when administered with food.

The primary active metabolite of trilostane, ketotrilostane follows a similar pattern. Furthermore, there was no evidence that trilostane or its metabolites accumulated with time.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 34 months

5.3 Special precautions for storage

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

Any remaining portions of divided tablets should be returned to the opened blister and given at the next administration.

5.4 Nature and composition of immediate packaging

Aluminium-PVC/Aluminium/oPA blisters, containing 10 tablets.

Cardboard box of 30 or 100 tablets

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

CP-Pharma Handelsgesellschaft mbH

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (<https://medicines.health.europa.eu/veterinary>).