1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetoryl 120 mg chewable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:
Trilostane 120 mg

Excipients:

Qualitative composition of excipients and other constituents
Maize starch
Lactose, monohydrate
Cellulose, microcrystalline
Sodium starch glycolate (type A)
Silica, colloidal hydrated
Magnesium stearate
Yeast (dried)
Chicken flavour

Light brown with brown spots, round and convex flavoured 15 mm chewable 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

Dog.

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.
Do not use in dogs weighing less than 5 kg.

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 veterinary medicinal 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 veterinary medicinal product should be used with extreme caution in dogs with pre-existing anaemia as further reductions in packed-cell volume and haemoglobin may occur. Dogs should be monitored at regular intervals for primary hepatic disease, renal disease, and for diabetes mellitus.
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:
Trilostane may decrease testosterone synthesis and has anti-progesterone properties. Women who are pregnant or are intending to become pregnant should avoid handling the veterinary medicinal product. Wash hands after use. People with known hypersensitivity to trilostane or any of the excipients should avoid contact with the veterinary medicinal product.
To prevent children from having access to the tablets, used blister packs should be stored in the original carton out of sight and reach of children.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or label to the physician. Accidental ingestion may cause adverse effects including vomiting and diarrhoea.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dog:

Uncommon (1 to 10 animals / 1,000 animals treated):	Lethargy[a,b], Anorexia[a,b], Vomiting[a,b], Diarrhoea[a,b]
Rare (1 to 10 animals / 10,000 animals treated):	Hypoadrenocorticism[c], Hypersalivation[d], Bloated[d], Ataxia[d], Muscle tremor[d], Skin disorders[d], Renal insufficiency[e], Arthritis[e], Weakness[a,b]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Adrenal necrosis[f], Sudden death

[a] associated with iatrogenic hypoadrenocorticism, particularly if monitoring is not adequate (see section 3.9); generally reversible within a variable period following withdrawal of treatment.
[b] Has been seen in dogs treated with trilostane in the absence of evidence of hypoadrenocorticism.
[c] including Acute Addisonian Crisis (collapse) (see section 3.10).
[d] mild
[e] unmasked by treatment with the product due to a reduction in endogenous corticosteroid levels.
[f] may result in hypoadrenocorticism

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

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 in pregnant or lactating bitches.

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 angiotensin converting enzyme (ACE) inhibitors. The concurrent use of such drugs should be subject to a risk-benefit analysis by the veterinary surgeon, as death (including sudden death) has been reported in dogs when treated concurrently with trilostane and an ACE inhibitor.

3.9 Administration routes and dosage

For oral use.
The starting dose for treatment is approximately 2 mg/kg.
Administer once daily, with food.

To ensure a correct dosage, body weight should be determined as accurately as possible.
Titrate the dose according to individual response, as determined by monitoring (see below). If a dose increase is required, use the appropriate tablet strength and tablet part to slowly increase the once daily

dose. A wide range of divisible tablet strengths 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.

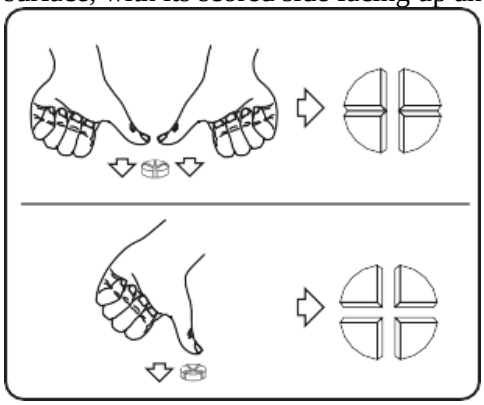
A small number of animals may require doses significantly in excess of 10 mg per kg body weight per day. In these situations, appropriate additional monitoring should be implemented.

A dose adjustment may be necessary if the dog is swapped from Vetoryl hard capsules to Vetoryl chewable tablets, or vice versa, as a strict interchangeability between the two products cannot be assured, as some dogs may respond differently to the change in pharmaceutical form.

Monitoring:
Samples should be taken for biochemistry (including electrolytes) and an adrenocorticotrophic hormone (ACTH) stimulation test pre-treatment following initial diagnosis, and then at 10 days, 4 weeks, 12 weeks, and thereafter every 3 months, for monitoring at regular intervals, after each dose adjustment, or if swapping from Vetoryl hard capsules to Vetoryl chewable tablets, or vice versa. 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.

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.

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 32 mg/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 overdosage, 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.
When used to treat hyperadrenocorticism, 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 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. In a study in fed beagle dogs, after administration of one Vetoryl 60 mg hard capsule, mean Cmax was 2820 ng/ml (range 300 to 9340 ng/ml), mean AUC was 169 (range 79 to 630 micrograms·minute/ml), and harmonic mean half-life was 2.8 hours (range 1.2 to 8.7 hours); after administration of one Vetoryl 60 mg chewable tablet, mean Cmax was 6360 ng/ml (range 962 to 8300 ng/ml), mean AUC was 218 micrograms·minute/ml (range 84 to 666 micrograms·minute/ml), and harmonic mean half-life was 2.5 hours (range 1.1 to 17.3 hours).

Generally trilostane is rapidly removed from the plasma with concentrations in the plasma reaching a maximum between 0.5 to 2.5 hours and returning almost to baseline by six to twelve hours after administration. The primary active metabolite of trilostane, ketotrilostane follows a similar pattern. Furthermore, there was no evidence that trilostane or its metabolites accumulated with time. An oral bioavailability study in dogs demonstrated that trilostane was absorbed more extensively when administered with food.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

5.3 Special precautions for storage

Tablet fractions should be stored in the original blister and outer carton and should be used at the next administration.
Do not store above 30°C.

5.4 Nature and composition of immediate packaging

Aluminium – Polyamide/Aluminium/PVC blister.
Each blister contains 10 tablets.Cardboard box of 1, 3, 5, 6 or 10 blisters.

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

Dechra Regulatory B.V.

7. MARKETING AUTHORISATION NUMBER(S)

VPA22622/023/009

8. DATE OF FIRST AUTHORISATION

02/04/2024

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).