SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetoryl 5 mg hard capsules for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Active substance:
Trilostane 5 mg

Excipients:

Qualitative composition of excipients and other constituents
Titanium dioxide (E171)
Ferric oxide (yellow) (E172)
Ferric oxide (black) (E172)
Gelatin
Maize starch
Lactose monohydrate
Magnesium stearate

Hard gelatin capsules with an ivory body and a black cap, printed “VETORYL 5 mg”.

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 dogs weighing less than 3 kg.
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 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. Regular monitoring should be undertaken.

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 capsules.
Wash hands with soap and water following accidental exposure and after use.
The content of the capsules may cause skin and eye irritation and sensitisation. Do not divide or open capsules: in the event of accidental breakage of the capsules and contact of the granules with eyes or skin, wash immediately with plenty of water. If irritation persists, seek medical advice and show the package leaflet/label to the physician.
People with known hypersensitivity to trilostane or any of the excipients should avoid contact with the veterinary medicinal product.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or label to the physician.

3.6 Adverse events

Dogs:

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 any animals intended for breeding.

3.8 Interactions 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

For oral use.
The starting dose for treatment is approximately 2 mg/kg, based on available combinations of capsule sizes. 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 combinations of capsule sizes to slowly increase the once daily dose. A wide range of capsule 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.
Do not divide or open capsules.
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 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 32 mg/kg to healthy dogs, however mortalities did occur after repeated administration of higher doses (40–67 mg/kg/day) to healthy dogs.

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 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. In a pharmacokinetic study in laboratory beagles administered a single Vetoryl 60 mg hard capsule, AUC ranged from 52 to 281 micrograms·minute/mlin fed dogs, and from 16 to 175 micrograms·minute/mlin fasted dogs. 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

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

5.4 Nature and composition of immediate packaging

PVC/PVdC/aluminium foil blisters in a cardboard box. Each blister contains 10 capsules.
Pack size: 30 capsules.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Vm 50406/3017

8. DATE OF FIRST AUTHORISATION

19 February 2021

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

January 2025

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).

Gavin Hall
Approved: 05 February 2025