The format of this leaflet has been determined by the Ministry of Health, and its content has been checked and approved in January 2019

Consumer leaflet for a Veterinary Product

This medicine is marketed according to a veterinarian's prescription only.

For animal use only

1. **Name of the veterinary medicine, form and strength**

Vetoryl 30 mg, veterinary

Vetoryl 60 mg, veterinary

Capsules for dogs

2. Active ingredient and its contents per dose unit:

Each capsule of Vetoryl 30 mg veterinary includes: Trilostane 30 mg

Each capsule of Vetoryl 60 mg veterinary includes: Trilostane 60 mg

List of excipients: See Section 13

3. What is the medicine intended for

In dogs: For the treatment of Cushing's disease and Cushing syndrome (increased secretion of cortisone due to hyperactivity of the pituitary gland or the adrenal gland - hyperadrenocorticism)

Therapeutic group: Antiadrenal preparations

4. Contraindications

Do not use in animals suffering from primary hepatic disease and/or renal insufficiency.

Vetoryl 30 mg veterinary must not be used in dogs weighing less than 3 kg.

Vetoryl 60 mg veterinary must not be used in dogs weighing less than 10 kg.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

5. Side effects

Signs associated with hypoadrenocorticism, including weakness, lethargy, anorexia, vomiting and diarrhea may occur, particularly if monitoring is not adequate. Signs are generally reversible within a variable period following withdrawal of treatment.

Acute Addisonian crisis (collapse) may also occur. Lethargy, vomiting, diarrhoea and anorexia have been seen in dogs treated with trilostane in the absence of evidence of hypoadrenocorticism .

There have been occasional isolated reports of adrenal necrosis in treated dogs which may result in hypoadrenocorticism.

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

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

A small number of reports have been received of sudden death during trilostane treatment.

Other mild, rare, adverse effects include ataxia, hypersalivation, bloating, muscle tremors and skin changes.

Side effects can be reported to the Ministry of Health by clicking on the link "Adverse Drug Reactions Repot" that appears on the home page of the Ministry of Health web site (www.health.gov.il), which leads to an online form for reporting side effects. Alternatively you can use the following link:

https://sideeffects.health.gov.il/

6. Target animals

Dogs

7. Route of administration and dosage

For oral administration, once daily with food.

The dosage will be determined by the treating veterinarian.

The initial dose is usually 2 mg /kg, based on available combinations of capsules of different strengths.

The dose should be adapted to the individual response of the dog.

Monitoring and follow-up:

The veterinarian will take samples for biochemical assays (including electrolytes) and will perform an ACTH stimulation test prior to the initiation of treatment and then at 10 days, 4 weeks, 12 weeks, and thereafter every 3 months following initial diagnosis and after each dose adjustment.

The ACTH stimulation test must be performed 4 - 6 hours post dosing to enable an accurate interpretation of results. It is recommended to administer the dose in the morning, since this will enable your veterinarian to perform monitoring tests 4 - 6

hours after dosing. 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.

Your dog should be monitored at regular intervals for primary hepatic disease, renal disease, and for diabetes mellitus.

8. How to use the product

See instructions in Section 7.

9. Withdrawal time

Not relevant.

10. Warnings

- Special warnings for use in dogs

The treating veterinarian must make an accurate diagnosis of the increased cortisone excretion (hyperadrenocorticism).

Where there is no apparent response to treatment, the diagnosis should be re-evaluated. Dose increases may be necessary.

The veterinarian should be aware that dogs with hyperadrenocorticism are at increased risk of pancreatitis. This risk may not diminish following treatment with trilostane.

- Special warnings for safe use of the medicine in animals

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.

Close medical monitoring is required during treatment, especially for liver enzymes levels, electrolytes, urea and creatinine.

In cases that the dogs suffer from diabetes in addition to increased cortisone excretion (hyperadrenocorticism), specific monitoring is required.

If the dog was previously 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.

Use very cautiously in dogs with anemia, because additional reduction of red blood cells and hemoglobin may occur. Regular monitoring is essential.

- Special warnings regarding the safety of the person administering the product

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

Pregnant women or women who intend to become pregnant should avoid contact with the product.

Wash hands with water and soap after accidental exposure to the product or after using the product.

The contents of the capsule 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 its content with eyes or skin, wash immediately with plenty of water. If irritation persists, seek medical advice.

People with known hypersensitivity to trilostane or any of the excipients should avoid contact with the product.

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

- Pregnancy and lactation

Not to be used in pregnant or lactating bitches or in dogs intended for mating.

- Interactions with other drugs and other forms of interactions

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.

- Overdose

Overdose may lead to signs of hypoadrenocorticism (lethargy, anorexia, vomiting, diarrhea, cardiovascular symptoms, collapse). There were no mortalities following chronic administration at 36 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 should be given, including corticosteroids, correction of electrolyte imbalances and fluid therapy, 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.

11. Storage instructions

- Avoid poisoning! This medicine, and any other medicine, must be kept in a closed place out of the reach and sight of children and/or infants to prevent accidental poisoning.
- Do not use the medicine after its expiration date (exp. date) as it appears on the package. The expiration date refers to the last day of the stated month.
- Storage conditions: Do not store above 25^0C. Store in the blister pack and in the outer carton.

12. Instructions for disposing of the product / remaining product at the end of its use

Any unused veterinary medical product or any waste remaining after using the veterinary medical product must be disposed of as toxic waste; do not throw into the sewage system.

13. Additional information

- In addition to the active ingredient, the medicine also contains:

Lactose, Maize Starch, Magnesium Stearate, Gelatin, Water Purified, Titanium Oxide, Yellow iron oxide, Black iron oxide, Capsule Ink 10A1 Black [Shellac **Glaze-45%(20-% Esterfield) in ethanol **, Iron oxide black, Propylene Glycol, Ammonium hydroxide 28%], Capsule Ink 10A2 Black (Shellac, Propylene Glycol, Strong Ammonia Solution, Potassium hydroxide, Black iron oxide), Capsule Ink 09A1 Grey (Shellac, Titanium dioxide, Iron oxide black, Strong Ammonia Solution, Potassium hydroxide, Propylene Glycol), Capsule Ink 09A2 Grey [Shellac**Glaze-45%(20-% Esterfield) in ethanol **, Titanium dioxide, Iron oxide black, Propylene Glycol, Ammonium hydroxide 28%, Simethicone].

- What the medicine looks like and the contents of the package

Hard gelatin capsules of ivory color (body) with a black cap. The capsule strength printed on the body of the capsule.

- Package size: 30 capsules (each pack contains 3 blisters of 10 capsules each).

License holder: VETMARKET LTD., 23 HACHORESH WAY, INDUSTRIAL PARK MODI'IN REGION

Manufacturer: Dales Pharmaceuticals, Snaygill Industrial Estate Keighley Road Skipton North Yorkshire BD23 2RW United Kingdom

For

Dechra Limited, Snaygill Industrial Estate, Keighley Road, Skipton, North Yorkshire, BD23 2RW, United Kingdom

This leaflet was checked and approved by the Ministry of Health in: January 2019

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Vetoryl **30 mg veterinary: 161-54-35189**

Vetoryl **60 mg veterinary: 161-55-35214**