ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetoryl 5 mg
Hard capsules for dogs
Trilostane

2. STATEMENT OF ACTIVE SUBSTANCES

1 capsule contains:
Active substance: Trilostane 5 mg

3. PHARMACEUTICAL FORM

[Hard capsules.]

4. PACKAGE SIZE

30 capsules

5. TARGET SPECIES

[Dogs]

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Administer orally, once daily, with food.
Do not divide or open capsules.

8. WITHDRAWAL PERIOD

[Not Applicable.]

9. SPECIAL WARNING(S), IF NECESSARY

[Read the package leaflet before use.]

Do not use in animals suffering from primary hepatic disease and/or renal insufficiency.
Do not use in pregnant or lactating bitches or in any animals intended for breeding.
User warnings: Women who are pregnant or are intending to become pregnant should avoid handling the capsules.

10. EXPIRY DATE

EXP:

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

16. MARKETING AUTHORISATION NUMBER(S)

Vm 10434/4084

17. MANUFACTURER'S BATCH NUMBER

Lot:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetoryl 5 mg
Hard capsules for dogs
Trilostane

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Dechra Limited, UK

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Vetoryl 5 mg hard capsules for dogs
Trilostane

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Dechra Limited
Snaygill Industrial Estate
Keighley Road
Skipton
North Yorkshire
BD23 2RW

Manufacturer responsible for batch release:
Dales Pharmaceuticals Limited
Snaygill Industrial Estate
Keighley Road
Skipton
North Yorkshire
BD23 2RW
United Kingdom

Genera Inc.
Svetonedeljska cesta 2
Kalinovica
10436 Rakov Potok
Croatia

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetoryl 5 mg hard capsules for dogs
Trilostane

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

1 capsule contains:
Active substance: Trilostane 5 mg.
Hard gelatin capsules (ivory body/black cap).
The ivory body is printed with the strength of the capsule.

4. INDICATION(S)

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

5. 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 known cases of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

If your dog becomes lethargic, develops vomiting or diarrhoea, or has a depressed appetite, stop
treatment and consult your veterinary surgeon.
Corticosteroid withdrawal syndrome or hypocortisolaemia should be distinguished from hypoadrenocorticism by evaluation of serum electrolytes.
Signs associated with iatrogenic hypoadrenocorticism, including weakness, lethargy, anorexia, vomiting and diarrhoea 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.

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

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

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

9. ADVICE ON CORRECT ADMINISTRATION

Do not divide or open capsules.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store in the original package in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the blister after EXP.
The expiry date refers to the last day of that month

12. SPECIAL WARNING(S)

If your dog is being treated with any other medications advise your veterinary surgeon prior to the use of Vetoryl.
Tell your veterinary surgeon if your dog is suffering from concurrent illnesses, especially liver disease, kidney disease, anaemia or diabetes mellitus.
Tell your veterinary surgeon if you intend to breed from your dog or your dog is pregnant or nursing.

Special warnings for each target species:
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.

Special precautions for use in animals:
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.
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.
Dogs should be monitored at regular intervals for diabetes mellitus. 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 one 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.
Close monitoring during treatment should be carried out. Particular attention should be paid to liver enzymes, electrolytes, urea and creatinine.

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 trying 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 the eyes or skin, wash immediately with plenty of water. If irritation persists, seek medical advice.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. People with known hypersensitivity to trilostane or any of the excipients should avoid contact with the product.

Use during pregnancy, lactation:
Do not use in pregnant or lactating bitches or in any animals intended for breeding.

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.

Overdose (symptoms, emergency procedures, antidotes):
If an overdose of the product is given consult your veterinary surgeon immediately. Overdose may lead to signs of hypoadrenocorticism (lethargy, anorexia, vomiting, diarrhoea, cardiovascular signs, 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, including corticosteroids, correction of electrolyte imbalances and fluid therapy may be indicated depending on 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.

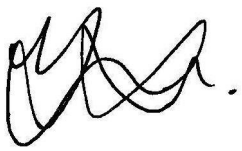
13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

For animal treatment only.
Symptomatic treatment of hypocortisolaemia may be required.
Only complete blister strips should be dispensed.
30 hard capsules.



Approved: 19 February 2021