ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Adrestan 30 mg
Hard capsules
Trilostane

2. STATEMENT OF ACTIVE SUBSTANCES

1 capsule contains:
Active substance:
Trilostane 30 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. The starting dose for treatment is approximately 2 mg/kg, based on available combinations of capsule sizes. Titrate the dose according to individual response, as determined by monitoring.

8. WITHDRAWAL PERIOD

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

Do not store above 25°C.
Keep the blister strips in the carton.

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

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

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
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

Vm 10434/4088

17. MANUFACTURER'S BATCH NUMBER

Lot:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Adrestan 30 mg
Hard capsules
1 capsule contains 30 mg 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 oral administration to dogs

For animal treatment only

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

Adrestan 30 mg hard capsules
Trilostane

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDERS RESPONSIBLE FOR BATCH RELEASE

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

Manufacturers responsible for batch release:
Genera Inc.
Svetonedeljska cesta 2
Kalinovica
10436 Rakov Potok
Croatia

Dales Pharmaceuticals Limited
Snaygill Industrial Estate
Keighley Road
Skipton
North Yorkshire
BD23 2RW
United Kingdom

Penn Pharmaceutical Services Ltd
23/24 Tafarnaubach Industrial Estate
Tredegar
South Wales
NP22 3AA
United Kingdom

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Adrestan 30 mg hard capsules
Trilostane

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

Hard gelatin capsules (ivory body/black cap) containing 30 mg of trilostane.
The ivory body is printed with the strength of the capsule.

4. INDICATION(S)

For the treatment of pituitary-dependent and adrenal-dependent hyperadrenocorticism in dogs.

5. CONTRAINDICATION(S)

Do not use in dogs weighing less than 3 kg.
Do not use in animals suffering from primary hepatic disease and/or renal insufficiency.
Do not use in known cases of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTION(S)

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.
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.

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

7. TARGET SPECIES

Dogs.

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

Oral use, once daily, with food.
The starting dose for treatment is approximately 2 mg/kg , based on available combinations of capsule sizes.
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

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

Not applicable.

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not store above 25°C.

Keep the blister strips in the carton.
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 WARNINGS

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:
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.
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.
Subsequent close monitoring during treatment should be carried out. Particular attention should be paid to liver enzymes, electrolytes, urea and creatinine.
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.

User Warnings:
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.
In the event of accidental ingestion, seek medical advice immediately and show the package leaflet or 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):
Overdose may lead to signs of hypoadrenocorticism. Treatment should be withdrawn and supportive therapy, including corticosteroids, correction of electrolyte imbalances and fluid therapy may be indicated depending on the clinical signs.
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.
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. Symptomatic treatment or appropriate replacement therapy should be initiated. 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 from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

January 2021

15. OTHER INFORMATION

For animal treatment only. To be supplied only on veterinary prescription.
Symptomatic treatment of hypocortisolaemia may be required.
Only complete blister strips should be dispensed.

Packaged in 3 blisters of 10 capsules. For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

Approved: 22/02/21

D Austin