SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Trilocur 50 mg/ml oral suspension for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Trilostane 50 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Sorbitol liquid (non-crystallising)	
Glycerol	
Water purified	
Xanthan gum	
Sodium benzoate	1.5 mg
Saccharin sodium	
Xylitol	
Sodium dihydrogen phosphate dihydrate	
Citric acid	
Silica colloidal anhydrous	
Vanillin	

White to off-white suspension

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) in dogs.

3.3 Contraindications

Do not use in animals suffering from primary hepatic disease and/or renal insufficiency.
Do not use where there is suspected 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 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 anaemias as further reductions in packed-cell volume and haemoglobin may occur. Regular monitoring should be undertaken.

The veterinary medicinal product contains the excipient xylitol which may be a cause of adverse effects if administered at high doses. Administration of Trilocur 50 mg/ml oral suspension for dogs at doses in excess of 10 mg trilostane/kg bodyweight has the potential to result in xylitol toxicity. In dogs requiring doses higher than 10 mg trilostane/kg, use an alternative trilostane product.

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 not handle this product.

The content of the product may cause skin and eye irritation and sensitisation. Take care to avoid accidental contact with the skin and eyes. In case of accidental skin contact, wash the affected area with soap and water. In case of accidental contact with the eyes, immediately rinse with plenty of water.
If skin or eye irritation persists, seek medical advice.
People with known hypersensitivity to trilostane, vanillin, or sodium benzoate should avoid contact with the veterinary medicinal product.
Accidental ingestion may cause harmful effects, including nausea, vomiting, and diarrhoea. Care should be taken to avoid accidental ingestion, especially by a child. Keep filled syringes away from children and store used syringes out of the sight and reach of children. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands with soap and water after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Uncommon (1 to 10 animals / 1,000 animals treated):	Lethargy[2], anorexia[2], vomiting[2], diarrhoea[2]
Rare (1 to 10 animals / 10,000 animals treated):	hypoadrenocorticism, hypersalivation. Bloated, ataxia, muscle tremor, skin disorders, renal insufficiency[3] and arthritis[3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Weakness[2], adrenal necrosis[1] and sudden death
Undetermined frequency (Cannot be estimated from the available data):	Acute Addisonian crisis (collapse)

[1] May result in hypoadrenocorticism.

[2] These signs associated with iatrogenic hypoadrenocorticism may occur, particularly if monitoring is not adequate (see section 4.9). Signs are generally reversible within a variable period following withdrawal of treatment.
Lethargy, vomiting, diarrhoea and anorexia have been seen in dogs treated with trilostane in the absence of evidence of hypoadrenocorticism.

[3] May be unmasked by treatment with the product. Treatment may unmask arthritis due to a reduction in endogenous corticosteroid levels.

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 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 inhibitors (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

Administer orally, once daily with food. The starting dose for treatment is approximately 2 mg/kg. Titrate the dose according to individual response as determined by monitoring (see below). If a dose increase is required, slowly increase the once daily dose. 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 cases an alternative trilostane product should be used (see section 3.5 Special precautions for safe use in target species). In these situations appropriate additional monitoring should be implemented.
The dose can be calculated as follows:

$$Volume\ (ml) = \frac{\text{Daily dose } \left(\frac{\text{mg}}{\text{kg}}\right) \text{x body weight (kg)}}{10\ \left(\frac{\text{mg}}{\text{ml}}\right)}$$

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.
Shake well before use.

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 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.

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, AUC ranged from 52 to 281 micrograms/ml/min in fed dogs., and from 16 to 175 micrograms/ml/min in 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.
Trilostane has been demonstrated to be excreted primarily in the faeces of the rat, indicating biliary excretion as the major metabolic pathway. In the monkey, trilostane is excreted in equal amounts in the faeces and urine. Results have shown that trilostane is rapidly and well absorbed from the gastrointestinal tract in both the rat and monkey and that it accumulates in the adrenal glands of the rat.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 6 months.

5.3 Special precautions for storage

Do not freeze.

5.4 Nature and composition of immediate packaging

High density polyethylene bottle with child resistant polypropylene/high density polyethylene stoppers and a polyethylene plug in a cardboard box.
To each package a 1 ml and 5ml polypropylene measuring syringe is added.

Pack sizes:
Cardboard box containing one bottle of 10 ml, and a 1-ml and a 5-ml polypropylene measuring
syringe
Cardboard box containing one bottle of 25 ml, and a 1-ml and a 5-ml polypropylene measuring
syringe
Cardboard box containing one bottle of 36 ml, and a 1-ml and a 5-ml polypropylene measuring
syringe
Cardboard box containing one bottle of 50 ml, and a 1-ml and a 5-ml polypropylene measuring
syringe
Cardboard box containing one bottle of 72 ml, and a 1-ml and a 5-ml polypropylene measuring
syringe
Cardboard box containing one bottle of 100 ml, and a 1-ml and a 5-ml polypropylene measuring
syringe
Not all pack sizes may be marketed.

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.

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

Emdoka bvba
John Lijsentraat 16
B-2321 Hoogstraten
Belgium

7. MARKETING AUTHORISATION NUMBER

Vm 34534/5006

8. DATE OF FIRST AUTHORISATION

August 2024

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

August 2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the ‘Product Information Database’ on www.gov.uk.

Gavin Hall

Approved: 21 August 2024