Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Trilocur 50 mg/ml Oral Suspension for Dogs

Date Created: November 2024

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Trilocur 50 mg/ml Oral Suspension for Dogs
Applicant	Emdoka bvba, John Lijsentraat 16, B-2321 Hoogstraten, B-2321, Belgium
Active substance	Trilostane
ATC Vetcode	QH02CA01
Target species	Dogs
Indication for use	For the treatment of pituitary-dependent and adrenal-dependent hyperadrenocorticism (Cushing's disease and syndrome) in dogs.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic hybrid application in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10a) as amended.
Date of conclusion of the procedure	21/08/24

I. SCIENTIFIC OVERVIEW

This is a generic hybrid application owing to the different pharmaceutical form and difference in strengths compared to the reference product. The reference product is Vetoryl 30 mg hard capsules which have been authorised in the UK since 2005.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC.[1] The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy[2] of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains trilostane and the excipients sorbitol liquid (non-crystallising), glycerol, purified water, xanthan gum, sodium benzoate, saccharin sodium, xylitol, sodium dihydrogen phosphate dihydrate, citric acid, silica colloidal anhydrous and vanillin.

The container/closure system consists of HDPE bottles closed with HDPE screw caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

Process validation data on the product have been presented in accordance with the relevant regulatory guidelines.

II.C. Control of Starting Materials

The active substance is trilostane an established active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

All excipients comply with Ph. Eur.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product are those suitable for this pharmaceutical form.

II.F. Stability

Stability data on the active substance have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 6 months.
Do not freeze.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Bibliographical data has been provided which show that 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.

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.

Bioequivalence studies were conducted and bioequivalence was established in regards to the reference product.

Toxicological Studies

Not required due to the legal basis of the application.

User Safety

A user risk assessment was provided in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:,

- 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.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Not required due to the legal basis of the application.

IV.II. Clinical Documentation

Not required due to the legal basis of the application.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that the benefit/risk profile of the product is favourable.

MODULE 4

POST- AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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