



**Veterinary
Medicines
Directorate**

**United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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NATIONAL PROCEDURE

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT**

Vetoryl 20 mg Hard Capsules for Dogs

Date Created: March 2025

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Vetoryl 20 mg Hard Capsules for Dogs
Applicant	Dechra Limited, Snaygill Industrial Estate, Keighley Road, Skipton, North Yorkshire, BD23 2RW
Active substance	Trilostane
ATC Vetcode	QJ01DB01
Target species	Dogs
Indication for use	For the treatment of pituitary-dependent and adrenal-dependent hyperadrenocorticism (Cushing's disease and syndrome).

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	Full application in accordance with VMRs 2013 (Schedule 1, Part 1) as amended.
Date of conclusion of the procedure	09/12/2024

I. SCIENTIFIC OVERVIEW

This is a full application for the Vetoryl capsule product range to extend the authorised product range to 20 mg capsules.

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 lactose monohydrate, maize starch, magnesium stearate, titanium dioxide (E171), ferric oxide (yellow) (E172), ferric oxide (black) (E172) and gelatin.

The container/closure system consists of capsules packaged in PVC-PVDC / aluminium blisters. The particulars of the containers and controls performed are provided and conform to the regulation.

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

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

II.C.4. Substances of Biological Origin

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

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

The tests performed during production are described and the results of three consecutive runs, conforming to the specifications, are provided.

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.

II.F. Stability

Stability data on the active substance has 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 European 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:
3-years.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACOTOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Studies have been conducted which show that trilostane acts by selectively and reversibly inhibiting 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.

Data shows that dogs treated with trilostane demonstrate large inter-individual variability. In a pharmacokinetic study in laboratory beagles administered a single Vetoryl 60 mg hard capsule, AUC ranged from 52 to 281 micrograms·minute/ml in fed dogs, and from 16 to 175 micrograms·minute/ml 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.

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 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 and show the package leaflet/label to the physician

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

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

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

Pharmacology

The applicant has provided a dissolution study where the 20 mg capsule was compared to the 10 mg capsule. In this study the dissolution was evaluated over 4 time points at three pH values of 1.2, 4.5 and 8.0.

At pH 1.2 and 4.5 more than 85% of the 10 mg and 20 mg capsules were not dissolved at the 15 minute time point. This satisfied the criteria set out in the study.

At pH 8.0 more than 85% of the active substance was not dissolved for both the 10 mg and 20 mg at 10 minutes therefore, in accordance with the bioequivalence guideline, where more than 85% of the drug is dissolved within 15 minutes, dissolution profiles may be accepted as similar based on this single timepoint.

Tolerance in the Target Species

Tolerance studies were not required because this is an extension of the existing Veteryl product range.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics 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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