Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vetoryl Flavoured 20 mg Tablets for Dogs
Vetoryl Flavoured 30 mg Tablets for Dogs
Vetoryl Flavoured 60 mg Tablets for Dogs
Vetoryl Flavoured 120 mg Tablets for Dogs

Date Created: November 2024

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Vetoryl Flavoured 20 mg Tablets for Dogs Vetoryl Flavoured 30 mg Tablets for Dogs Vetoryl Flavoured 60 mg Tablets for Dogs Vetoryl Flavoured 120 mg Tablets for Dogs
Applicant	Dechra Regulatory B.V., Handelsweg 25, 5531 AE Bladel, The Netherlands
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)

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 application in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10a) as amended.
Date of conclusion of the procedure	30/08/2024

I. SCIENTIFIC OVERVIEW

Vetoryl Flavoured 60 mg Tablets for Dogs have been demonstrated to be bioequivalent to the reference product Vetoryl 60 mg hard capsules. Bioequivalence of the other tablet strengths in the range was inferred through appropriate in vitro studies.

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 maize starch, monohydrate lactose, microcrystalline cellulose, sodium starch glycolate (Type A), colloidal hydrated silica, magnesium stearate, yeast (dried) and chicken flavour.

The container/closure system consists of blister packs packed into cartons. 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 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 described in a GMP certificate. 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 are described in Ph. Eur.

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

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: 3 years
Tablet fractions should be stored in the original blister and outer carton and should be used at the next administration.
Do not store above 30°C.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Bibliographical data has been provided which show that trilostane acts by 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.
The applicant also has provided bibliographical data which show inter-individual variability. In a study in fed beagle dogs, after administration of one Vetoryl 60 mg hard capsule, mean C_{max} was 2820 ng/ml (range 300 to 9340 ng/ml), mean AUC was 169 (range 79 to 630 micrograms·minute/ml), and harmonic mean half-life was 2.8 hours (range 1.2 to 8.7 hours); after administration of one Vetoryl 60 mg chewable tablet, mean C_{max} was 6360 ng/ml (range 962 to 8300 ng/ml), mean AUC was 218 micrograms·minute/ml (range 84 to 666 micrograms·minute/ml), and harmonic mean half-life was 2.5 hours (range 1.1 to 17.3 hours).
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 this product.
Wash hands after use. People with known hypersensitivity to trilostane or any of the excipients should avoid contact with this product.
Accidental ingestion may cause adverse gastrointestinal effects including vomiting and diarrhoea. To prevent children from having access to the tablets, used blister packs should be stored in the original carton out of reach and sight of children.
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 conducted studies describing the pharmacodynamic and pharmacokinetic properties of the active substance.

Tolerance in the Target Species

The applicant has conducted a target animal tolerance study using multiples of the recommended dose in the target species. An authorised reference product containing the same active substance was used as a control. All doses were administered by oral administration on 90 occasions.
Minimal adverse effects were seen following doses up to 1 times the recommended dose.

Adverse effects consisting of significant morbidity and mortality were seen following 3 times the recommended dose.

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 products are 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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