Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A PROPOSED VETERINARY MEDICINAL PRODUCT

Felimazole 5 mg/ml Oral Solution

Date Created: May 2024

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Felimazole 5 mg/ml Oral Solution, Oral solution
Applicant	Dechra Limited, Snaygill Industrial Estate, Keighley Road, Skipton, North Yorkshire, BD23 2RW
Active substance	Thiamazole
ATC Vetcode	QH03BB02
Target species	Cats
Indication for use	For the stabilisation of hyperthyroidism in cats prior to surgical thyroidectomy. For the long-term treatment of feline hyperthyroidism.

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

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)

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Extension application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	08/02/2024

I. SCIENTIFIC OVERVIEW

This is an extension application submitted in accordance with Article 12(3).

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 Thiamazole and the excipients methyl parahydroxybenzoate, propyl parahydroxybenzoate, glycerol, maltitol solution/liquid, disodium Hydrogen Phosphate Dihydrate, Sodium Dihydrogen Phosphate Dihydrate, Saccharin Sodium, Citric Acid, Anhydrous and Purified Water.

The container/closure system consists of PET amber bottles with a LDPE plug and HDPE closure and is supplied with a PE/PP measuring syringe. 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.

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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. The manufacturing method consists of: Compounding, stirring, filtration and bottling.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

II.C. Control of Starting Materials

The active substance is thiamazole is an established active substance described in the European Pharmacopoeia. 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.

The excipients and packaging materials comply with the relevant monographs.

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 for: appearance, identification of impurities,, pH, Viscosity, Density, Identification and assay of active substance, identification and assay of excipients, microbiological quality.

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II.F. Stability

Stability data on the active substance has been provided in accordance with applicable European 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: 2 years
No special storage conditions

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Not required due to this is an extension application where a new pharmaceutical form is proposed however, the dose, dosing frequency and posology are unchanged.

Toxicological Studies

Not applicable

Observations in Humans

Heidari et al., 2015 paper shows the active substance thiamazole can be hepatotoxic. Also, in high doses it can cause congenital malformations in humans and laboratory animals as shown in (**Agrawal *et al*., 2022; Akmal & Kung, 2014; Iwaki *et a*l., 2021; PRAC, 2019; Romeo & Običan, 2020**). Thiamazole exposure has been recognised to cause irriversable consequences on cognitive development in young children written in **Gilbert *et al*., 2020; Mayerl *et a*l., 2020; Stagi *et a*l., 2022**). The most common treatment related adverse events are skin rashes and haematological abnormalities, (**Kim *et a*l., 2015; Lee *et a*l., 2021; Song *et al*., 2021; Yasuda et al., 2017.)**

Microbiological Studies

Not required due to this application being an extension application where a new pharmaceutical form is proposed however, the dose, dosing frequency and posology are unchanged.

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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:

- Replace the cap immediately after filling the syringe and wash hands after use.
- Following administration of the product, any residual product remaining on the tip of the dosing syringe should be wiped clean with a tissue. The contaminated tissue should be immediately disposed of.
- The used syringe should be stored with the product in the original carton.
- In the case of accidental ingestion, seek medical advice immediately and show the package insert or the label to the physician.
- This product may cause eye irritation. Avoid eye contact including hand-to-eye contact. In case of accidental eye contact, rinse eyes immediately with clean running water. If irritation develops, seek medical advice immediately and show the package insert or the label to the physician.
- Thiamazole may cause vomiting, epigastric distress, headache, fever, arthralgia (joint pain), pruritus (itching) and pancytopaenia (decrease in blood cells and platelets). Treatment is symptomatic.
- Wash hands with soap and water after handling the vomit of or used litter of treated animals.
- Do not eat, drink or smoke while handling the product, vomit or used litter of treated animals.
- Do not handle this product if you are allergic to thiamazole or one of the excipients. If allergic symptoms develop, such as a skin rash, swelling of the face, lips or eyes or difficulty in breathing, you should seek medical attention immediately and show the package insert or the label to the physician.
- As thiamazole is a suspected human teratogen and has the potential to bioaccumulate in the breast milk, women of child-bearing age, lactating women and pregnant women should wear non-permeable, single-use gloves when handling the product, vomit or used litter of treated animals.
- Prevent children from playing with or having access to the used litter of treated animals.

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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. Thiamazole is unlikely to be bioaccumulative and/or persistent in the environment.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

No pharmacological studies have been concluded due to this being an extension application where a new pharmaceutical form is proposed however, the dose, dosing frequency and posology are unchanged.

Tolerance in the Target Species

The applicant has conducted two bioequivalence studies where 40 cats received the test product as a single dose of 5mg thiamazole per cat per day (Study Numbers: D18030 and D21015). In study D21015 no serious or non-serious adverse events were reported throughout the course of the study. In D18030 the only adverse event classified to be in relation to the administration of the test or reference product was hypersalivation.

IV.II. Clinical Documentation

Laboratory Trials

The applicant has claimed bioequivalence has been demonstrated between the test product and the reference product. Therefore, documentation on safety and efficacy is not required. The applicant has not provided any new clinical studies

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.

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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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