IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Felimazole 5 mg/ml oral solution for cats

PRODUCT SUMMARY

EU Procedure number	IE/V/0505/004/X/001
Name, strength and pharmaceutical form	Felimazole 5 mg/ml oral solution for cats
Active substance(s)	Thiamazole
Applicant	Dechra Regulatory B.V. Handelsweg 25, 5531 AE Bladel, Netherlands
Legal basis of application	Application in accordance with Article 62 of Regulation (EU) 2019/6 (Variation requiring assessment)
Date of completion of procedure	06/07/2023
Target species	Cats
Indication for use	For the stabilisation of hyperthyroidism prior to surgical thyroidectomy. For the long-term treatment of feline hyperthyroidism.
ATC vet code	QH03BB02
Concerned Member States	AT, BE, BG, HR, CZ, DK, FI, FR, DE, EL, HU, IT, LU, NL, MO, PL, PT, RO, SK, SI, ES, SE, UK(NI)

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in the relevant articles of Regulation (EU) 2019/6. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

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; the reactions observed are indicated in the SPC.
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 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. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars
The product contains 5 mg/ml thiamazole and the excipients methyl parapropylbenzoate (E218), propyl parahydroxybenzoate, citric acid, glycerol, maltitol liquid, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate, saccharin sodium, honey powder flavour, caramel brown colour and purified water.
The container/closure system consists of polyethylene terephthalate (PET) amber bottles of 30 ml or 100 ml, closed with a low density polyethylene (LDPE) plug and a high density polyethylene (HDPE) closure. The veterinary medicinal product is supplied with a 1 ml polyethylene (PE) / polypropylene (PP) measuring syringe for administration of the solution to the animal. The

syringe is graduated in 0.25 mg increments up to 5 mg. Each closed bottle and accompanying syringe is contained in a cardboard carton.
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product
The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.
Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials
The active substance is thiamazole an an established 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 has been provided.
There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

D. Control on Intermediate Products
Not applicable.

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 has been provided.
Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

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 has 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
Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This is an application for an I.II.1.d variation requiring assessment for the addition of a new pharmaceutical form (oral solution) based on the approved marketing authorisation for the veterinary medicinal product Felimazole 5 mg coated tablets for cats' (VPA22622/009/002) which was first authorised in 2002 (based on a full dossier application).
The applicant has demonstrated bioequivalence of the candidate oral solution product with the tablet formulation of Felimazole used for the initial approval procedure.
As bioequivalence with a suitable authorised comparator product has been demonstrated, results of safety and efficacy tests are not required.
The safety and efficacy aspects of this product are identical to the authorised comparator product.
Warnings and precautions as listed on the product literature are largely the same as those of the authorised comparator product and are adequate to ensure safety of the product to users and the environment.

III. SAFETY ASSESSMENT

Pharmacological Studies
The applicant conducted two (1 pilot and 1 pivotal) *in vivo* bioequivalence studies in which bioavailability of the candidate product was compared to the authorised comparator product, Felimazole 5mg coated tablets for cats.
The test article used in the pivotal *in vivo* bioequivalence study was selected based on the results of the pilot *in vivo* bioequivalence study. The pivotal *in vivo* bioequivalence study was conducted to GLP-standard and in accordance with relevant guidance. In this two-period two-sequence single dose cross-over study, 5 mg of the test or reference article was administered

to 24 cats, 14 days apart. The test article was well-tolerated. The evaluation of bioequivalence was based upon validated measurement of the active substance, thiamazole, in plasma. Calculated lower and upper confidence limits for the ratio of the geometric means for AUC_t and C_{max} fell between the pre-specified acceptance criteria of 80 and 125%. As such, bioequivalence between the candidate and comparator product was accepted.

Toxicological Studies
No toxicological data were provided as the candidate and authorised comparator products contain the same active substance, thiamazole. The omission of these data was accepted based on the demonstration of bioequivalence between the candidate product and a suitable comparator product.

User Safety
The applicant provided a user safety assessment broadly in compliance with the relevant guideline. The proposed user safety warnings incorporate those approved for the authorised comparator product, and warnings specific to the new pharmaceutical form (oral solution).
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product, as follows:

- As thiamazole is a suspected human teratogen and it is excreted in the breast milk, women of child-bearing age and lactating women must wear non-permeable single use gloves when handling the veterinary medicinal product, vomit or used litter of treated animals. If you are pregnant, think you may be pregnant or are attempting to conceive, you should not administer the veterinary medicinal product or handle the litter/vomit of treated cats.
- This veterinary medicinal product can cause allergic reactions after dermal contact. Do not handle this veterinary medicinal 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.
- This veterinary medicinal product may cause skin and eye irritation. Avoid skin and eye contact including hand-to-eye contact. In case of accidental skin and/or eye contact, rinse exposed skin and/or 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). Avoid oral exposure including hand-to-mouth contact, especially by children.
- Do not leave filled syringes unattended.
- Replace the cap immediately after filling the syringe.
- 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 veterinary medicinal product, vomit or used litter of treated animals.
- Following administration of the veterinary medicinal product, any residual veterinary medicinal product remaining on the tip of the dosing syringe should be wiped off with a tissue. The contaminated tissue should be immediately disposed of. The used syringe should be stored with the veterinary medicinal 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.
- Wash hands after use.

Environmental Risk Assessment
Phase I
The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the candidate product will be used only in a non-food producing target animal species, that is, cats.
Conclusion
Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT

As bioequivalence with a suitable authorised comparator product has been demonstrated, target animal tolerance and efficacy studies are not required.

IV.A Pre-Clinical Studies
Tolerance in the Target Species of Animals

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies
The efficacy claims for this product are equivalent to those of the comparator product.

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 for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.