College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
3531 AH Utrecht
The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Kelevo 200 µg tablets for dogs and cats,
Kelevo 400 µg tablets for dogs and cats,
Kelevo 800 µg tablets for dogs

NL/V/0349/001-003/DC

Created: April 2021

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0349/001-003/DC
Name, strength and pharmaceutical form	Kelevo 200 µg tablets for dogs and cats; Kelevo 400 µg tablets for dogs and cats; Kelevo 800 µg tablets for dogs
Applicant	LIVISTO Int'l, S.L. Av. Universitat Autònoma, 29 08290 Cerdanyola del Vallès (Barcelona), Spain
Active substance(s)	Levothyroxine sodium
ATC Vetcode	QH03AA01
Target species	Cats, dogs
Indication for use	Treatment of primary and secondary hypothyroidism.

Product name: Kelevo	NL/V/0349/001-003/DC
Applicant: LIVISTO Int'l, S.L.	DCP
	Publicly available assessment report

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with: - article 13(1) of Directive 2001/82/EC (generic application) for Kelevo 200 µg tablets for dogs and cats - article 13(3) of Directive 2001/82/EC (hybrid application) for Kelevo 400 µg for dogs and cats and Kelevo 800 µg tablets for dogs
Date of completion of the original decentralised procedure	3 March 2021
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	AT, DE, EE, EL, ES, HU, IE, IT, LT, LV, PL, PT, SI.

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 slight 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 risk/benefit analysis is in favour of granting a marketing authorisation.

Kelevo 200 µg, 400 µg and 800 µg are generic products. The reference product for the Kelevo 200 µg tablet, is Levothyroxine LIVISTO 200 mcg tabletten voor honden en katten (MA.-No.: REG NL 124859), which is registered in the Netherlands since 15.05.2019. Kelevo 400 µg and Kelevo 800 µg are a hybrid applications (additional strengths) that also cite the LIVISTO 200 mcg tabletten voor honden en katten as the reference product.

The reference veterinary medicinal product for data protection is L-Thyroxine tablets, 200 µg (REG NL 9049), registered since 2002 by Aesculaap B.V., The Netherlands.

The initial application for L-Thyroxine tablets, 200 µg (REG NL 9049) was assessed before there was a requirement to have a public assessment report; therefore no details in this section are available.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The tablets contain 200 µg, 400 µg and 800 µg Levothyroxine sodium and the following core excipients: Calcium hydrogen phosphate dihydrate, Croscarmellose sodium, Magnesium stearate, Microcrystalline cellulose and Yeast flavour.
The tablet is cross scored and meant to be broken into equal halves or quarters.
The products are packed in Al-PVC/PE-PVDC blisters, each containing 10 or 25 tablets.

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 from a licensed manufacturing site.
The product is manufactured using conventional manufacturing techniques. Process validation data on the product have been presented in accordance with the relevant European guidelines.
The tests performed during production are described.

C. Control of Starting Materials

The active substance is Levothyroxine sodium is an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice. A CEP procedure has been employed.
The active substance specification is considered adequate to control the quality of the material from the supplier. Batch analytical data demonstrating compliance with this specification have been provided.
All excipients are in conformity with the Ph.Eur. requirements with the exception of Yeast flavour which have been adequately specified.
The packaging is conformity with the Ph. Eur. and EU Food Directive.

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies.

The Magnesium stearate and Yeast flavour are of vegetable origin.

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. Relevant 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.

F. Stability

Stability data on the active substance have 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. According to the stability results provided the claimed shelf life of 24 months can be granted for the 200 µg and 400 µg tablet strengths and 18 months for the 800 µg tablet strength.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This is a generic application in accordance with article 13.1 and hybrid application in accordance with article 13.3 of Directive 2001/82/EC, as amended by Directive 2004/28/EC. Bioequivalence with the reference product has been demonstrated and the product is therefore deemed essentially similar to the reference product. Consequently, as details on toxicological studies have been sufficiently described in the file of the reference product, no results of pharmacological and/or toxicological tests are required. For user risk assessment publicly available data were provided.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that:
This product contains a high concentration of L-thyroxine sodium and may be harmful when ingested, particularly for children. Any unused tablet portion(s) should be returned to the open blister, inserted back into the outer packaging and stored out of the sight and reach of children and always be used at the next administration. In the case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after handling the tablets.

These warnings and precautions are adequate to ensure safety to users of the product.

A warning with respect to pregnant women has been included by the applicant however has not been substantiated by any data and based on the currently available data no risk for pregnant women has been identified.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines. The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will only be used in non-food animals.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference 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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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 Heads of Veterinary Medicines Agencies website (www.HMA.eu).

This section 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.

None