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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Tralieve 20 and 80 mg chewable tablets for dogs

February 2018

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0213/001-002/DC
Name, strength and pharmaceutical form	Name: Tralieve. Strength: 20 mg and 80 mg. Pharmaceutical form: Tablet.
Applicant	Le Vet Beheer B.V. Wilgenweg 7 3421 TV Oudewater The Netherlands
Active substance(s)	Tramadol hydrochloride
ATC Vetcode	QN02AX02.
Target species	Dogs.
Indication for use	For the reduction of acute and chronic mild soft tissue and musculoskeletal pain.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website:
http://www.cbg-meb.nl/CBG/en/veterinary-medicines/database-veterinarymedicines/default.htm

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	28 February 2018.
Date product first authorised in the Reference Member State (MRP only)	-
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK.

I. SCIENTIFIC OVERVIEW

Tralieve 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.
Tralieve 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.

The safety and efficacy aspects of *Tralieve* are based on bioequivalence with the Italian reference product *Altadol 50 mg compresse solubili per cani,* which has been authorized in Italy since 9 July 2005. The marketing authorisation holder of the reference product is FORMEVET S.r.l. Warnings statements and precautions are adopted from the reference product. Additional statements have been added, based on increased knowledge and the current state of science.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The tablets contain 20 mg, 80 mg tramadol hydrochloride and the following excipients: cellulose microcrystalline, lactose monohydrate, sodium starch glycolate (type A), magnesium stearate, silica, colloidal hydrated, chicken flavour, and yeast (dried). The tablet is cross scored and meant to be broken into equal halves or quarters.

The products are packed in PVC/PE/PVDC-Al blisters.

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

A bioequivalence study was performed for the 50 mg strength and additionally a bio-waiver of strength was applied for the other strengths.

B. Method of Preparation of the Product

The product is manufactured in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

The product is manufactured using conventional manufacturing techniques. Suitable validation results on two commercial scale batches of each strength have been provided.

The tests performed during production are described, and are regarded to be acceptable.

C. Control of Starting Materials

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

The active substance is manufactured in accordance with the principles of good manufacturing practice. For the manufacture of the active substance a CEP procedure is used and a valid version of the CEP is provided.

The active substance specification is suitable to control the quality of the material. Batch analytical data demonstrating compliance with the proposed specification have been provided.

All excipients are in conformity with the Ph. Eur. requirements with the exception of the yeast and chicken flavour for which in-house specifications are used.

For the pharmacopoeial excipients, the relevance of additional functionality related characteristics is discussed and where applicable, they are included in the specification of the excipient.

The packaging is in conformity with the Ph. Eur. and EU Food Directive.

Lactose monohydrate is produced from milk which is sourced from healthy animals in the same condition as milk for human consumption and that the calf's rennet used complies with the public statement of the EMEA.

The magnesium stearate is 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. The proposed limit for dissolution of NLT 80% (Q) in 15 minutes is acceptable. Non-routine testing for dissolution is acceptable when at least six commercial batches show compliances with the specification limit for dissolution, and disintegration time is tested when dissolution is not tested. After the first six commercial batches, dissolution should be tested every 10th batch, at least once each year. Based on the batch and stability data, the limit for total impurities is tightened to 1.5% at release and 2.0% at the end of shelf-life.

Validation data for the analytical methods have been provided, as well as batch analytical data from the proposed production site, demonstrating compliance with the specification.

F. Stability

The applicant has submitted stability data on the active substance. The stability studies are performed in accordance with the European Guidelines. On the basis of the provided stability data the claimed re-test period of 5 years can be granted.

Stability data on the finished product have been provided in accordance with applicable European guidelines. The provided stability data for the finished product is sufficient to extrapolate the shelf-life to two years. A shelf life of 2 years, when stored below 30°C is justified. The product shows sensitivity to moisture and requires the storage precaution *"Store in the original package in order to protect from moisture"*.

G. Other Information

Not applicable.

3. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological, pharmacological and clinical tests tests are not required.

Warning statements and precautions as listed in the product literature are based on those of the reference product and supplemented with additional statements, based on increased knowledge and the current state of science. This information is considered adequate to ensure safety of the product to users and the environment.

3.A User Safety

User Safety

Being a generic procedure the applicant refers to the reference product for information on this section. Additionally, the applicant has provided a user safety assessment. Combined with increased knowledge and the current state of science, warning statements and precautions have been added to the product literature, ensuring safety to users of the product.

Ecotoxicity

Phase I
The environmental risk assessment can stop in Phase 1, because the product will be used only in nonfood animals.

Conclusion
Based on the data provided, the ERA can stop at Phase 1. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

4. 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 based on increased knowledge and the current state of science.

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 website:

http://www.cbg-meb.nl/CBG/en/veterinary-medicines/database-veterinarymedicines/default.htm

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.