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

Ziapam 5 mg/ml solution for injection for cats and dogs

Created: January 2020

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0180/001/DC
Name, strength and pharmaceutical form	Ziapam 5 mg/ml solution for injection for cats and dogs
Applicant	LABORATOIRE TVM 57 rue des Bardines 63370 Lempdes France
Active substance(s)	Diazepam
ATC Vetcode	QN05BA01
Target species	Cats and dogs
Indication for use	For the short term management of convulsive disorders and skeletal muscle spasms of central and peripheral origin. As part of a pre-anaesthetic or sedation protocol.

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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).

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	29 January 2014
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	AT, BE, DE, ES, FR, IT, PL, PT, UK

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 claims for this product are equivalent to those of the reference product.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

Ziapam is a generic application. The reference product is DIAZEPAM 0.5%, solution for injection. The marketing authorisation for DIAZEPAM 0.5%, solution for injection was granted in Italy in 1993 under MA no. 100372010 of the Marketing Authorisation Holder (MAH) Intervet Productions S.r.l.. The initial application for DIAZEPAM 0.5%, solution for injection 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 product is a solution for injection, containing 5.00 mg/ml diazepam and the following excipients; propylene glycol, ethanol, benzylalcohol, benzoic acid, sodium benzoate, sodium hydroxyde and water for injection.

The product is packed in a glass ampoule type I containing 2.0 ml of the solution.

The primary material is in conformity with the Ph.Eur. requirements.

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

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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 for full-scale batches is completed.
The tests performed during production are described.

C. Control of Starting Materials

The active substance is diazepam, 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 manufacturers have been granted a certificate of suitability for the active substance.

The excipients are in conformity with compendial requirements.

The packaging materials are in conformity with the Ph.Eur. requirements.

D. Control on intermediate products

Not applicable.

E. Control Tests on the Finished Product

The finished products 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.

F. Stability

The certificates of suitability states retest periods of the active substance when stored under the approved conditions and the approved packaging.

Stability data on the finished products 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

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There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

III. 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 pharmacological and toxicological tests are not required.

III.A Safety Testing

User Safety

The applicant has provided warnings in the product literature which were not mentioned in the product literature of the reference product. The additional warnings were proposed because the active substance and some of the excipients are skin sensitizers and may cause irritation to eyes and skin.
The warnings listed on the product literature are:
"People with known sensitivity to diazepam or the excipients should avoid contact with the veterinary medicinal product.
The product can cause skin irritation. Avoid contact with skin.
In the case of contact with skin, wash with soap and water. If irritation persists, seek medical advice.
Wash hands after use.
The product can cause eye irritation. Avoid contact with eyes. If the product comes into contact with the eyes, rinse the eyes immediately with plenty of water and seek medical attention if irritation persists.
This product is a CNS depressant. Avoid accidental self-injection. If accidental self-injection occurs, seek medical advice immediately and show the package leaflet or the label to the physician. Do not drive, as sedation may occur.
Diazepam may be harmful for the foetus and unborn child. Diazepam and its metabolites are secreted into milk, thereby exerting a pharmacological effect on the nursing neonate. As such, women of child-bearing potential and nursing mothers should not handle this product."

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

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)

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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.

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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 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.

Summary of change	**Section updated**	**Approval date**
Extension of the shelf life of the veterinary medicinal product as packaged for sale from 3 years to 4 years. (NL/V/0180/001/IB/001)	N/A	15 March 2018
Renewal (NL/V/0180/001/R/001)	N/A	7 January 2019

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