College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Metomotyl 2.5 mg/ml solution for injection for cats and dogs
Metomotyl 5 mg/ml solution for injection for cats and dogs

Date: 25 June 2014

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0182/001-002/DC
Name, strength and pharmaceutical form	Metomotyl 2.5 mg/ml solution for injection for cats and dogs Metomotyl 5 mg/ml solution for injection for cats and dogs
Applicant	Le Vet Beheer B.V. Wilgenweg 7 3421 TV Oudewater The Netherlands
Active substance(s)	Metoclopramide hydrochloride
ATC Vetcode	QA03FA01
Target species	Cats and Dogs
Indication for use	Symptomatic treatment of vomiting and reduced gastro-intestinal motility associated with gastritis, pyloric spasm, chronic nephritis and digestive intolerance to some drugs. Prevention of vomiting after surgery.

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MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://mri.medagencies.org/veterinary/.

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	2,5 mg/ml: Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended. 5 mg/ml: Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	21th of May 2014
Concerned Member States for original procedure	AT, BE, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SK, UK

I. SCIENTIFIC OVERVIEW

The VMP 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 VMP can be safely used in the target species; the slight reactions observed are indicated in the SPC.
The VMP is safe for the user, the consumer of foodstuffs from treated animals 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 the VMP are based on bioequivalence with the reference product Primperid solution for injection, REG NL 1947.
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. Adverse events and contraindications are indicated in the SPC.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains metoclopramide HCl 5 mg/ml as metoclopramide hydrochloride monohydrate. The excipients are metacresol, sodium chloride and water for injections.

The container/closure system consists of clear colourless type I glass bottles filled with 5, 10, 20, 25, 30 and 50 ml, fitted with red chlorobutyl 20 mm stoppers and aluminium 20 mm caps. The vials are packed in an outer carton in order to protect from light. The particulars of the containers and controls performed are provided and conform to the regulation. The stoppers comply with the Ph.Eur. test for fragmentation and self-sealing up to 20 punctures.

The choice of the formulation and of the presence of preservative metacresol are justified.

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.

Process validation data on the smallest commercial scaled batch size of the product have been presented in accordance with the relevant European guidelines.

Process validation for full-scale batches will be performed post-authorisation.

C. Control of Starting Materials

The active substance, metoclopramide hydrochloride, is 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 have been provided. A valid CEP for the drug substance 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

No intermediate product is formed.

E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form i.e. appearance, colour, visible particles, pH, identification of metoclopramide and metacresol, assay of metoclopramide and metacresol, related substances and sterility. 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 retest of the active substance of 5 years if stored in an inner LDPE bag and outer black LDPE bag place in a HDPE drum or fibre drum has been included on the CEP.

Stability data (18 months long term and 6 months accelerated) on the finished product have been provided on two batches of each strength packed in the smallest and the largest pack size.

Based on the 18 months real time and 6 months stability data a tentative shelf life of 30 months can be granted. This has been updated in December 2017 to 36 months (see Module 4).

The claim of a 28 day stability after broaching is based on the demonstration of stability for a batch broached and stored 28 days below 25°C.

A photostability study demonstrated that the drug product is light sensitive. Therefore the drug product should be packed in the outer carton in order to protect from light.

G. Other Information

Not applicable

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic/hybrid application according to Article 13, and bioequivalence with a reference product has been demonstrated, toxicological, pharmacological and clinical tests are not required. The safety claims for this product are essentially equivalent to those of the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users / the environment / consumers.

III.A Safety Testing

User Safety

Being a generic/hybrid procedure the applicant refers to the reference product for information on this section.

Additionally, the applicant has provided a user safety assessment in compliance with the relevant guideline. Combined with increased knowledge and the current state of science, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

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Environmental Risk Assessment

Phase I

The environmental risk assessment can stop in Phase I because this product is intended for use in cats and dogs and a Phase II assessment is not deemed necessary.

The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic/hybrid 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.

Tolerance in the Target Species of Animals

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

However, an extensive overview of tolerance data presented in public literature has been provided by the applicant. Additionally, based on increased knowledge and the current state of science, warning statements and precautions have been added to the product literature ensuring safety to the target animals.

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.

December 2017	Type IB: B.II.f.1. change in the shelf life or storage conditions of the finished product; b) Extension of the shelf life of finished product; 1. As packaged for sale The shelf life is increased from 30 months to 36 months, based on real time stability data.
August 2019	Renewal procedure End of Procedure 2 August 2019 CRD 21 May 2019.
February 2022	Update CEP of the active substance metoclopramide hydrochloride monohydrate to R1-CEP 2004-075-Rev 04
November 2023	VRA G.I.18 QRD template v9 update