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

Temprace 0.5 mg/ml Solution for Injection for Dogs and Cats (AT, BE, BG, CY, CZ, EL, ES, FR, HR, HU, IE, IT, LU, NL, PT, RO, SI, SK, UK)

Temprace Vet 0.5 mg/ml solution for injection for dogs and cats (DK, EE, FI, IS, LT, LV, NO, PL, SE)

Date Created: April 2018

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0321/001/DC
Name, strength and pharmaceutical form	Temprace 0.5 mg/ml Solution for Injection for Dogs and Cats
Applicant	Le Vet Beheer B.V. Wilgenweg 7 3241 TV Oudewater The Netherlands
Active substance	Acepromazine 0.5 mg (equivalent to 0.678 mg acepromazine maleate)
ATC Vetcode	QN05AA04
Target species	Dogs and Cats
Indication for use	For anaesthetic premedication, tranquilisation and sedation.

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	Generic hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedure	20th December 2017
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, and Sweden.

I. SCIENTIFIC OVERVIEW

This was an application for a generic hybrid product, submitted in accordance with Article 13 (3) of Directive 2001/82/EC as amended. The reference product is ACP injection 2 mg/ml Solution for Injection, marketed in the UK since June 1992.This was determined a generic 'hybrid' application because changes to the strength of the active substance with regard to the reference medicinal product have been made.

The product is indicated for the use in dogs and cats as an anaesthetic, tranquiliser or sedative for intravenous injection only. For premedication, 0.03-0.125 mg acepromazine per kg bodyweight, corresponding to 0.6-2.5 ml product per 10 kg bodyweight. For other uses, 0.0625-0.125 mg acepromazine per kg bodyweight, corresponding to 1.25-2.5 ml product per 10 kg bodyweight. It is recommended that the injection is made slowly. The maximum dose that should be given is 4 mg acepromazine per animal. Normally single doses of acepromazine are administered; refer to section 4.5 of the Summary of Product Characteristics (SPC) for further information.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTIUENTS

II.A. Composition

The product contains acepromazine 0.5 mg, equivalent to 0.678 mg acepromazine maleate and the excipients phenol, sodium chloride, sodium hydroxide (for PH adjustment), maleic acid (for pH adjustment) and water for injections.

The container/closure system consists of 10, 20 and 100 ml clear glass vials (Type I), closed with a coated bromobutyl rubber stopper and aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

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

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

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of mixing followed by filling and terminal sterilisation.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

II.C. Control of Starting Materials

The active substance is acepromazine, an established active substance described in the British Veterinary 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. Appropriate Active Substance Master File (ASMF) data were provided.

All the excipients are supplied in accordance with the relevant Ph. Eur monographs and acceptable certificates of analysis were provided. Packaging was suitably verified for use.

II.C.4. Substances of Biological Origin

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

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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 have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product include those for appearance, relative density, volume, pH, identification and assay of acepromazine, identification and assay of phenol, related substances and sterility.

II.F. Stability

Stability data on the finished product 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.
A retest period of 4 years was agreed. Stability data on the finished product were provided for four production-scale batches, and the full 5 year, long term (25±2˚C/60±5%RH). Results from these data dictated the agreed shelf-life and storage precautions as cited in the SPC.

G. Other Information

- Shelf life of the veterinary medicinal product as packaged for sale: 30 months
- Shelf life after opening of the immediate packaging: 28 days.
- Keep the vial in the outer carton in order to protect from light.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (3), and a biowaiver absolving the applicant from the need to provide bioequivalence tests with a reference product on the basis of essential similarity was accepted, the results of pharmacological and toxicological tests are not required. The product contains a

lower concentration of acepromazine (0.05 mg/ml) than the reference product (2 mg/ml) so approximately 4 times the volume of solution would be injected compared to the reference product.

III.A Safety Documentation

Observations in Humans

Bibliographical data were provided which show the likely effects in humans which are:

- Hypertension and epilepsy at oral doses of 200 mg/day daily for 6 weeks
- CNS and respiratory depression along with hypertension at doses of 950 mg and 1250 mg acepromazine (adult suicide attempts)
- Sedation, tachycardia and evidence of poor perfusion after a dose of 6.25-8.3 mg/kg orally (accidental ingestion by a child)

User Safety

A user risk assessment was provided in compliance with the relevant guideline which contained summaries of the effects in humans and the toxicity of acepromazine and also of the excipients. At the concentrations in the product and amounts likely to be accidentally injected, none are of toxicological concern.

The applicant has updated user safety information on the SPC compared to that of the reference product.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- This product contains a potent sedative; care should be taken, when handling and administering the product, to avoid accidental self-exposure.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician but DO NOT DRIVE as sedation may occur. Symptomatic treatment may be required.
- If accidental eye contact occurs, flush gently with fresh running water for 15 minutes and seek medical advice if any irritation persists.
- In the event of accidental skin contact, contaminated clothing should be removed and the area washed with large amounts of soap and water. Medical advice should be sought if irritation persists.
- Wash hands and exposed skin thoroughly after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The VICH decision tree provided correctly concludes that the environmental assessment stops in Phase I. The disposal advice in the SPC and product literature is satisfactory and the product is not expected to pose a risk for the environment when used as recommended.
The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

IV CLINICAL DOCUMENTATION

As this is a generic application according to Article 13(3) and bioequivalence with a reference product has been accepted on the basis of essential similarity, 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 benefit/risk profile of the product is favourable.

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 **(Application number)**	**Approval date**
Introduction of a new Pharmacovigilance system which has been assessed by the EMA for another product of the same MAH NL/V/xxxx/WS/021	12 July 2019
RMS change from UK to NL	21 March 2019