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

Relaquine 35 mg/ml Oral Gel for Horses

NL/V/0303/001, formerly UK/V/0465/001

Updated: January 2023

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0303/001
Name, strength and pharmaceutical form	Relaquine 35 mg/ml Oral Gel for Horses
Applicant	Floris Holding BV Kempenlandstraat 33 5626 GK Vught The Netherlands
Active substance	Acepromazine 35.00 mg (as Acepromazine maleate) (47.50 mg)
ATC Vetcode	QN05AA04
Target species	Horses
Indication for use	For sedation of horses.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the dutch registered veterinary medicinal products database:

https://www.diergeneesmiddeleninformatiebank.nl/nl/

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 mutual recognition procedure	21st of December 2012
Date product first authorised in the Reference Member State (MRP only)	26th February 2013
Concerned Member States for original procedure	AT, BE, DE, DK, FR, NO, SE, UK

I. SCIENTIFIC OVERVIEW

Relaquine 35 mg/ml Oral Gel for Horses is authorised for use in horses for sedation. The product is intended for oral administration and contains acepromazine (as acepromazine maleate). The product is presented in an oral dosing syringe which is graduated at 1 ml intervals. The recommended dosage rate is 0.15 mg acepromazine per kg bodyweight. The dose may be varied to administer between 0.5 and 1.5 times the above recommendation depending on the level of sedation required, i.e. for mild sedation, administer half the recommended dose and for deeper sedation, administer 1½ times the recommended dose. The product should only be used in horses of less than 200 kg body weight in accordance with a benefit/risk assessment by the responsible veterinarian. Do not use in neonates.

This application for a national MA for a generic product was submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended by 2004/28/EC. Bioequivalence is claimed with the reference product, Sedalin 35 mg/ml Oral Gel, which was authorised in the UK in March 1996. The applicant has claimed exemption from bioequivalence studies in accordance with exemption 4.e) of the Guidelines for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products.

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[1]. The product is safe for the user,

[1] Summary of Product Characteristics

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

II. QUALITY ASPECTS

A. Composition

The active substance is acepromazine (as acepromazine maleate), and the excipients are methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), sodium acetate trihydrate, sodium cyclamate (E952), hydroxyethylcellulose, glycerol (E422) and purified water.

The container/closure system consists of a white, high-density polyethylene syringe barrel, and white, low-density polyethylene syringe plunger. The product is fitted with a white, high-density polyethylene, push-fit cap and contains 10 ml of gel. The product is presented in an oral dosing syringe which is graduated at 1ml intervals.

The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation is 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 in accordance with the European Pharmacopoeia and relevant European guidelines.

During the routine manufacture of the product, sodium acetate, sodium cyclamate and acepromazine maleate are dissolved in the required volume of purified water with continuous stirring. To this solution, a solution of methyl and propyl parahydroxybenzoate is added. After mixing to uniformity, hydroxyethylcellulose is added and dissolved using prolonged stirring. The gel formed is filled into the dosing syringes, which are closed with their designated caps.

The manufacturing formula, method of manufacture and in-process controls were considered appropriately described.

C. Control of Starting Materials

Active substance

The active substance, acepromazine maleate, is an established substance monographed in the BP (Vet) and United States Pharmacopoeia. It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

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.

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

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

E. Control on intermediate products

Not applicable.

F. 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.

G. Stability

Active substance

Data have been provided which indicate that the active substance is stable when stored in the appropriate container under appropriate conditions. The retest interval of 4 years is justified.

Finished Product

Data have been provided which indicate that the finished product is stable for 2 years when stored at a below 25°C.

In-Use

An in-use shelf life of 28 days is justified.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years
Shelf-life after first opening the immediate packaging: 28 days.

Do not store above 25°C.
Protect from frost.
Protect from light.
After use, replace cap on syringe. Keep the broached syringe in the original carton and store in a dry place.

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 were not required. Bioequivalence was claimed with the reference product, Sedalin 35 mg/ml oral gel.

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 and the environment.

III.A Safety Testing

User Safety

The applicant submitted an environmental risk assessment that adequately considered the inherent toxicity of the active ingredient and final product, dermal and ocular exposure, accidental ingestion and risk management.

The following warnings and precautions as listed on the product literature and SPC are adequate to ensure safety to users of the product. These are essentially the same as those stated for the reference product, Sedalin 35 mg/ml oral gel.

- Wash hands and exposed skin thoroughly after use.
- Persons with sensitive skin or in continuous contact with the product are advised to wear impermeable gloves.
- Avoid contact with eyes.

- If accidental eye contact occurs, flush gently with running water for 15 minutes and seek medical advice if any irritation persists.
- In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician but, DO NOT DRIVE as sedation can occur.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guidelines. The assessment ended at phase I based on use in individual horses only. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

The product is not to be used in horses intended for human consumption, and treated horses may never be used for human consumption. The animal must be declared as not intended for human consumption under the national horse passport legislation. A withdrawal period is therefore not required.

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.

IV.A Pre-Clinical Studies

This application was made in accordance with Article 13.1 of Directive 2001/82/EC as amended by Directive 2004/28/EC and Directive 2009/9/EC and therefore the results of pre-clinical, target safety or clinical field studies were not required. Bioequivalence was claimed with the reference product, Sedalin 35 mg/ml oral gel.

Tolerance in the Target Species of Animals

This application was made in accordance with Article 13.1 of Directive 2001/82/EC as amended by Directive 2004/28/EC and Directive 2009/9/EC and therefore the results of tolerance in the target species were not required. Bioequivalence was claimed with the reference product, Sedalin 35 mg/ml oral gel.

Resistance

This application was made in accordance with Article 13.1 of Directive 2001/82/EC as amended by Directive 2004/28/EC and Directive 2009/9/EC and therefore the results relating to resistance were not required. Bioequivalence was claimed with the reference product, Sedalin 35 mg/ml oral gel.

IV.B Clinical Studies

This application was made in accordance with Article 13.1 of Directive 2001/82/EC as amended by Directive 2004/28/EC and Directive 2009/9/EC and therefore the results of pre-clinical, target safety or clinical field studies were not required. Bioequivalence was claimed with the reference product, Sedalin 35 mg/ml oral gel.

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 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 Variations

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 Product Information Database of the Medicines Evaluation Board website.

https://www.diergeneesmiddeleninformatiebank.nl/nl/

Post Authorisation Variations

Relaquine

Procedure No.	Date of approval	Description of change
VNRA	28 December 2022	Change in the batch size of the finished product.
VNRA	05 October 2022	Introduction of a summary of the PSMF.
VNRA	15 August 2022	Change to quality testing (replacement) for a finished product.
NL/V/0303/001/IA/005	04 July 2021	Addition of a device which is not an integrated part of the primary packaging.
NL/V/0303/001/E/001	24 July 2020	Repeat use, addition of CMS: AT, BE, DK, NO
NL/V/0303/IB/004/G	02 January 2020	Addition new container, Pack size change – 15 ml syringe, Up to 10-fold increase in batch size, Extension of shelf life after first opening.
	22 January 2019	RMS change
UK/V/XXXX/IA/180/G	13 December 2018	Change in QPPV
UK/V/0465/001/IB/003	23 August 2018	To add wording to the SPC and QRD regarding how to use the syringe.
UK/V/XXXX/IA/138/G	17 July 2017	Replacement of a site where batch control/testing takes place
00425/2015	08 July 2015	Changes to the labelling, or the package leaflet, which are not connected with the SPC.
UK/V/0465/001/IB/001	23 April 2015	Changes to veterinary medicinal product – to update the wording

		for withdrawal period and to change the product name in Sweden.
UK/V/0465/001/MR	21 December 2012	New MRP: DE, FR, SE, UK
01823/2011	14 March 2012	Addition of a new specification parameter to the specification with its corresponding test method
01823/2011	14 March 2012	Change in test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance