College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
3531 AH Utrecht
The Netherlands

REFERENCE MEMBER STATE:
THE NETHERLANDS

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Presedine 10 mg/ml solution for injection for horses and cattle

NL/V/0385/001/DC

Created January 2024

PRODUCT SUMMARY

EU procedure number	NL/V/0385/001/DC
Name, strength and pharmaceutical form	Presedine 10 mg/ml solution for injection for horses and cattle
Applicant	Alfasan Nederland BV Kuipersweg 9 3449 JA Woerden The Netherlands
Active substance(s)	Detomidine hydrochloride
ATC vetcode	QN05CM90
Target species	Horses and cattle
Indication for use	A sedative intended for use in horses and cattle in: - Examinations for diagnostic purposes, such as endoscopy and X-rays; - Treatment of wounds, horse shoeing and change of bandages; - Minor surgical procedures, such as castration and excision of tumours.

Presedine 10 mg/ml solution for injection for horses and cattle	NL/V/0385/001DC
Alfasan Nederland B.V.	DCP
Publicly available assessment report	

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Generic application in accordance with Article 18 of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Domosedan 10 mg/ml oplossing voor injectie voor paarden en runderen
Marketing authorisation holder	Orion Corporation
MS where the RP is or has been authorised	The Netherlands
Marketing authorisation number	REG NL 2973
Date of authorisation	04 August 1998
Date of completion of the original decentralised procedure	03 May 2023
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(NI).
Concerned Member States for subsequent recognition procedure	Not applicable.
Withdrawn CMS during original decentralised procedure	Not applicable.

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the 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 VMP was demonstrated according to the claims made in the SPC.

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

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP Presedine 10 mg/ml solution for injection for horses and cattle contains Detomidine as hydrochloride (10 mg/mL). The excipients are Methyl parahydroxybenzoate, Sodium chloride, Hydrochloric acid diluted, Sodium hydroxide and Water for injections.

The container/closure system is a 10 or 20 mL sized, colourless, type I glass vial, which is closed by a grey type I rubber stopper and sealed by an aluminium cap.

The choice of the formulation and presence of preservative are justified. The type of preservative (Methyl parahydroxybenzoate) and its concentration are the same as per reference product.

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

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

Process validation data on the VMP have been presented in accordance with the relevant European guidelines.

The VMP is manufactured including standard manufacturing techniques. Suitable validation results on two production-scale batches have been provided. The information on the proposed holding time and the sterilization of the rubber stoppers has been clarified. No further information is required.

C. Production and control of starting materials

The active substance is Detomidine hydrochloride, an established active substance described in the European Pharmacopeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The ASMF procedure is used for the Detomidine hydrochloride drug substance.

The active substance specification is considered adequate to control the quality of the API. Batch analytical data demonstrating compliance with this specification have been provided on three batches of the active substance.

The excipients are in conformity with the Ph.Eur. requirements.

None of the starting materials used are affected by the Note for Guidance on TSE/BSE.

D. Control tests carried out on isolated intermediates during the manufacturing process

Not applicable.

E. Control tests on the finished product

The finished product specification adequately controls the relevant parameters for the pharmaceutical form. The specification limits at release and shelf life are acceptable.

The analytical methods of the drug product specification have been adequately described and validated. Compliance at release has been demonstrated on two batches of the finished product.

F. Stability tests

The stability data from the active substance manufacturer are provided in the corresponding ASMF of Detomidine hydrochloride.

Stability data have been provided on two batches of the proposed veterinary medicinal product for 18 months under long-term stability condition and for six months under accelerated stability condition. Also the stability results of the inverted product have been provided up to six months under long-term stability condition. All results are within the proposed specification limits. The proposed shelf-life of 30 months without any special storage condition is acceptable as per decision tree of the VICH GL51 in view of the data presented.

The claim of a 28 days in-use stability after first opening is based on the demonstration of stability for a batch broached and stored 28 days at +30°C at the beginning of shelf life. The applicant commits to provide data on an additional batch as per NfG on in-use stability testing of veterinary medicinal products. At least one of the batches used will be approaching the end of the shelf life. The preservative effect of Methyl parahydroxybenzoate has been demonstrated up to 28 days. The proposed in-use shelf life of 28 days is accepted.

The product has also been demonstrated to be photostable.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of pharmacological and toxicological tests are not required.

The safety aspects of this VMP are identical to the reference VMP.

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

A. Safety tests

Pharmacological studies

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of pharmacological tests are not required.

Toxicological studies

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of toxicological tests are not required.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows risks of skin and eye irritation, uterine contractions and decreased foetal blood pressure in pregnant women, as well as clinical effects of detomidine.

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

Environmental Risk Assessment

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP will be used to treat a small number of animals in a flock or herd.

B. Residues documentation

Residue tests

Bioequivalence has been demonstrated. The withdrawal periods as applicable for the reference product, can therefore be adopted for this generic application.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been accepted, efficacy studies are not required. The efficacy claims for this VMP are equivalent to those of the reference VMP.

A. Pre-Clinical Studies

No pre-clinical studies were performed.

Bioequivalence with the reference product has been accepted, because the candidate product and the reference product are solutions for injections which contain identical active substances. Bioequivalence studies were waived for both the intravenous and the intramuscular route of administration.

B. Clinical trials

No clinical trials were performed.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP 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 VMP for humans and the environment is acceptable.

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. The current SPC is available in the Union Product Database (UPD).

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 VMP.

None.