(agentschap College ter Beoordeling van Geneesmiddelen)

Medicines Evaluation Board agency
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REFERENCE MEMBER STATE: THE NETHERLANDS

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dexdormostart 0.5 mg/ml solution for injection for dogs and cats

NL/V/0400/001/DC

Created: November 2023

PRODUCT SUMMARY

EU procedure number	NL/V/0400/001/DC
Name, strength and pharmaceutical form	Dexdormostart 0.5 mg/ml solution for injection
Applicant	Alfasan Nederland B.V. Kuipersweg 9 3449 JA Woerden The Netherlands
Active substance(s)	Dexmedetomidine hydrochloride
ATC vetcode	QN05CM18
Target species	Dogs, cats
Indication for use	Non-invasive, mildly to moderately painful, procedures and examinations which require restraint, sedation and analgesia in dogs and cats. Deep sedation and analgesia in dogs in concomitant use with butorphanol for medical and minor surgical procedures. Premedication in dogs and cats before induction and maintenance of general anaesthesia.

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)	Dexdomitor
Marketing authorisation holder	Orion Corporation
Marketing authorisation number EU procedure number	EU/2/09/033
Date of authorisation	30 August 2002
Date of completion of the original decentralised procedure	20 September 2023
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, HR, 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Withdrawn CMS during original decentralised procedure	Not applicable.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, 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 veterinary medicinal Dexdormostart solution for injection for dogs and cats contains Dexmedetomidine as hydrochloride (0.5 mg/mL). The excipients are Methyl parahydroxybenzoate, Propyl parahydroxybenzoate, Sodium chloride, Hydrochloric acid diluted (for pH control), Sodium hydroxide (for pH control) 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 preservatives are justified. The type of preservatives (Methyl parahydroxybenzoate and Propyl parahydroxybenzoate) and their concentrations are the same as for the reference product. A Bioequivalence study is not necessary from a quality point of view as per sections 7.1.a,b of the EMA Guideline on the conduct of bioequivalence studies for veterinary medicinal products.

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

Process validation data on the product have been presented for batches of the lower batch size in accordance with the relevant European guidelines. The applicant commits to validate an additional batch of the larger batch size. The validation protocol is in line with the requirements of the Annex I to the EMA Guideline on Process Validation.

The product is manufactured including standard manufacturing techniques. The holding time prior to terminal sterilisation is acceptable.

C. Production and control of starting materials

The active substance is Dexmedetomidine hydrochloride, an active substance described in the USP but not described in the European Veterinary Pharmacopoeia or in the British Pharmacopoeia. The active substance is in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the API. Compliance with the proposed specification has been demonstrated 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 controls the relevant parameters for the pharmaceutical form. In general, the specification limits at release and shelf life are acceptable.

In general, the analytical methods of the drug product specification have been adequately described and validated. The analytical method for related substances has been demonstrated to be stability-indicating.

F. Stability tests

The stability data from the active substance manufacturer has been provided.

Stability data have been provided on two batches of the proposed veterinary medicinal product for 18 months under long-term stability condition and for 6 months under accelerated stability condition. Also the stability results of the inverted product have been provided up to 6 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 and in line with the decision tree of the VICH GL51.

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 well as to repeat the in-use shelf life when the end of the shelf life is approaching, as per NfG on in-use stability testing of veterinary medicinal products.

The preservative effect of Methyl parahydroxybenzoate and Propyl parahydroxybenzoate has been demonstrated up to 28 days. 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 and the environment.

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.

Observations in humans

Dexmedetomidine is an alpha-2 adrenergic agonist. Primary pharmacodynamic effects are sedation and relaxation. The applicant has provided information, which shows that dexmedetomidine is authorized for use in human patients in the European Union as well as several other countries worldwide, for the indication of sedation in an intensive care setting. Reported adverse reactions following use of dexmedetomidine include hypotension, hypertension, bradycardia and sinus arrest.

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 and hypersensitivity reactions, as well as clinical effects of dexmedetomidine.

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

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 VMP will only be used in non-food animals (cats and dogs).

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 demonstrated, 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 was demonstrated, 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.