IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

SEDATOR, 1.0 mg/ml, solution for injection for cats and dogs

PRODUCT SUMMARY

EU Procedure Number	IE/V/0476/001 (formerly UK/V/0326/001)
Name, Strength, Pharmaceutical Form	SEDATOR, 1.0 mg/ml, solution for injection for cats and dogs
Active Substances(s)	Medetomidine hydrochloride
Applicant	Eurovet Animal Health B.V. Handelsweg 25 5531 AE Bladel Netherlands
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Cats,Dogs
Indication For Use	Dogs: for restraint, sedation and analgesia associated with clinical examinations and procedures, minor surgery, pre-anaesthesia and as a premedication before thiopentone-halothane general anaesthesia and as a premedicant before general anaesthesia with propofol. In combination with butorphanol for sedation, analgesia and as a premedicant to thiopentone anaesthesia. Cats: for restraint and sedation. In combination with ketamine for induction of general anaesthesia prior to surgical procedures in the cat. In combination with butorphanol for sedation and analgesia, and combined with both butorphanol and ketamine for general anaesthesia. As a premedication before alphaxalone/alphadolone for general anaesthesia.
ATC Code	QN05CM91
Date of completion of the original mutual recognition procedure	30 July 2008 (UK) 26 September 2008 (IE)
Date product first authorised in the Reference Member State (MRP only)	21 March 2007
Concerned	IE (now RMS)

Member States for original procedure	UK added via RMS change

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.
The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

This product is authorised as generic product submitted according to Article 13(1) of the Directive 2001/82/EC as amended by 2004/28/EC. The reference product is Domitor (Pfizer/Orion), which has been authorised in the UK since 31 October 1988.
Sedator contains the active substance medetomidine hydrochloride 1mg/ml. This is a sedative, which acts as an α_2-adrenoreceptor[1] agonist[2]. The product is intended for intravenous, intramuscular and subcutaneous administration in the dog and for intramuscular and subcutaneous administration in the cat. Doses depend on the level of sedation required and on specific combinations with other 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. The product 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 product was demonstrated according to the claims made in the SPC. The overall risk/benefit analysis is in favour of granting a marketing authorisation.
[1] Adrenoreceptor is a binding site on a cell
[2] Agonists bind to a specific receptor triggering a response in the cell

II. QUALITY ASPECTS

A. Composition

The product contains the active substance medetomidine hydrochloride and excipients methyl parahydroxybenzoate (E 218), propyl parahydroxybenzoate (E 216), sodium chloride, sodium hydroxide, hydrochloric acid and water for injections.

The container/closure system comprises clear colourless, sterile aqueous solution and presented in a Type I (Ph. Eur.) clear glass vials of 5, 10 and 20 ml capacity. Vials are fitted with a teflon coated halogenated rubber stopper and sealed with an aluminium cap. 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 fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

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

C. Control of Starting Materials

The active substance is well established and supporting data have been provided in the form of a European Drug Master File (EDMF)[1]. It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

The excipients are all materials described in the European Pharmacopoeia.

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

There are no intermediate products.

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

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

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. The product has a shelf life of 2 years with the vial kept in the carton.

A study was conducted demonstrating that the product remains stable for 28 days after a dose has been removed from the vial. A 28 day in-use shelf life is justified.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

The supporting data submitted by the company demonstrate that the product is suitably formulated and quality–controlled. A shelf life of 2 years is justified, subject to the following storage warnings: Keep vial in carton.
[1] European **Drug Master File** or E**DMF** is a confidential document prepared by a manufacturer and contains detailed information about a substance.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, data on pharmacodynamics and pharmacokinetics are not required. The data submitted are in accordance with the requirements of the applicable European bioequivalence guideline.

Toxicological Studies

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, this information is not required.

User Safety

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. These are the same as the reference product. These are included on the SPC as follows:

- In the case of accidental oral intake or self-injection, seek medical advice immediately and show the package leaflet to the doctor, but DO NOT DRIVE as sedation and changes in blood pressure may occur.
- Avoid skin, eye or mucosal contact.
- Immediately after exposure, wash the exposed skin with large amounts of fresh water.
- In the case of accidental contact of the product with eyes, rinse with large amounts of fresh water. If symptoms occur, seek the advice of a doctor.
- If pregnant women handle the product, special caution should be observed not to self inject as uterine contractions and decreased foetal blood pressure may occur after accidental systemic exposure.
- Advice to doctors: Medetomidine is an alpha2-adrenoreceptor agonist. Symptoms after absorption may involve clinical effects including dose-dependent sedation, respiratory depression, bradycardia, hypotension, a dry mouth, and hyperglycaemia. Ventricular arrhythmias have also been reported. Respiratory and haemodynamic symptoms should be treated symptomatically.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that:

- Sedator is a generic product of the reference product Domitor Injection.
- The same environmental warnings and disposal advice used for Domitor Injection will be included in the SPC and product literature for Sedator.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.
The SPC states:

Any unused product or waste material should be disposed of in accordance with national requirements.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, pharmacological studies are not required.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, target species tolerance studies are not required.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, clinical 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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.