IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Acecare 2 mg/ml Solution for Injection for Dogs and Cats

PRODUCT SUMMARY

EU Procedure Number	IE/V/0459/001 (formerly UK/V/0591/001)
Name, Strength, Pharmaceutical Form	Acecare 2 mg/ml Solution for Injection for Dogs and Cats
Active Substances(s)	Acepromazine
Applicant	Ecuphar NV Legeweg 157-I 8020 Oostkamp Belgium
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Cats, Dogs
Indication For Use	Anaesthetic Premedication: Following acepromazine administration, the amount of anaesthetic necessary to induce anaesthesia is considerably reduced. This reduction is approximately one-third of a suitable induction agent. Tranquilisation: Acepromazine tranquilisation (ataraxy) involves a modification of temperament which is not associated with hypnosis, narcosis or marked sedation. This is achieved with low doses of acepromazine. Sedation: At higher dose rates acepromazine is a sedative.
ATC Code	QN05AA04
Date of completion of the original decentralised procedure	16 May 2016 (UK) 15 July 2017 (IE)
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	UK(NI)

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 was an application for a generic product, submitted in accordance with Article 13 (1) 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. Exemption was claimed from the requirement for bioequivalence studies in accordance with 7.1.a) and 7.1.b) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2).

The product is indicated for use in cats and dogs as an anaesthetic, tranquiliser, or sedative. For premedication, 0.03 – 0.125 mg/kg bodyweight may be administered by intramuscular, subcutaneous, or slow intravenous injection. For other uses, the

product is administered by intramuscular or subcutaneous injection at 0.0625 – 0.125 mg/kg bodyweight. This is equivalent to 0.625 – 1.25ml of 2 mg/ml injection per 20 kg bodyweight. The product may be used in this respect by intravenous injection, but it is recommended that the injection is made slowly. The maximum dose to be provided is 4 mg acepromazine per animal. Under normal circumstances, single doses of acepromazine are provided. Refer to section 4.3 of the Summary of Product Characteristics (SPC) for further information.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species. Any adverse 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 [1] 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.
[1] Efficacy – The production of a desired or intended result.

II. QUALITY ASPECTS

II.A. Composition
The product contains acepromazine 2mg/ml, as acepromazine maleate 2.71 mg/ml, and the excipients phenol, sodium hydroxide (for pH adjustment), maleic acid (for pH adjustment) and water for injections.
The container/closure system consists of 20 ml clear glass vials (Type II), closed with a bromobutyl-coated rubber bung and an aluminium crimped seal. 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 solubilisation of the components, followed by filling and sterilisation. Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials
The active substance is acepromazine, an established substance described in the British Veterinary Pharmacopoeia, and specific in-house methods. 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 ASMF[1] data were provided.
All excipients are monographed within the European Pharmacopoeia. 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. Signed declarations were provided.

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 include those for pH, relative density, refractive index, extractable volume, appearance, colour, visible particles, identification and assay of acepromazine, identification and assay of phenol, related substances and sterility.

II.F. 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. A retest period of 4 years was agreed. Stability data on the finished product were provided for three batches of finished product and one batch of reference product stored under VICH[2] conditions, stored for up to 36 months at 25°C/60%RH and 40°C/75%RH. In-use stability test data were also provided, from three batches tested after 3, 12 and 36 months when stored at 25°C/60%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.
- Do not store above 25^{o}C.
- Keep the vial in the outer carton in order to protect from light.
- Following withdrawal of the first dose, use remainder of the product within 28 days.
- Discard unused material.

[1] ASMF – Active Substance Master File.
[2] VICH - International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (1), 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. 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 Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:

- Care should be taken when handling and administering this product to avoid exposure.
- Take precautions to avoid accidental injection or self- administration of this potent drug. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Symptomatic treatment may be required.
- Avoid contact with eyes. 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 wash the contaminated area 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 product will be used in a small number of non-food animals, therefore, the product is not expected to pose a risk to the environment when used as recommended. The risk assessment stops at Phase I of the VICH decision tree. A Phase II assessment was not required.

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13(1) 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(s) is favourable.