Veterinary
Medicines
Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

AceSedate 10 mg/ml Solution for Injection for Horses

Date Created: February 2019

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	AceSedate 10 mg/ml Solution for Injection for Horses
Applicant	Jurox (UK) Limited Second Floor, Richmond House 105 High Street, Crawley West Sussex RH10 1DD United Kingdom
Active substance	Acepromazine 10 mg (as acepromazine maleate) 13.55 mg
ATC Vetcode	QN05AA04
Target species	Horses
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. At low doses, acepromazine reduces anxiety which is beneficial for use in horses prior to shoeing or transportation. Sedation: At higher dose rates acepromazine is an effective sedative, as an adjunct to, or replacement for, physical restraint e.g. dentistry, handling and shoeing. The relaxant effects aid examination of the penis in horses and the treatment of tetanus and choke.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

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 conclusion of the procedure	21st February 2019

I. SCIENTIFIC OVERVIEW

This is an application for a generic product, AceSedate 10 mg/ml Solution for Injection for horses. The reference product was ACP Injection 10 mg/ml Solution for Injection, authorised in the UK from 30 June 1992 until 10 October 2017. The applicant for the proposed product claimed exemption from the requirement for bioequivalence studies in accordance with exemption 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 horses, as an anaesthetic premedication, a tranquilser and for use in sedation as described in the Summary of Product Characteristics (SPC). The product is administered by intramuscular injection at 0.03 - 0.10 mg per kg bodyweight. This is approximately equivalent to 0.15 - 0.5 ml of 10 mg/ml injection per 50 kg (approx. 1 cwt) bodyweight. The product may also be administered by intravenous injection at the same dose rate as that recommended for intramuscular use, except that it is recommended the injection is made slowly.

Normally, single doses of acepromazine are administered. Long term use is not recommended. On the rare occasions that repeat dosing is required, the dosing interval should be 36 - 48 hours.

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, any reactions observed are indicated in the SPC. The product is safe for the user and for the environment, when used as recommended. Not authorised for use in horses intended for human consumption. 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. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 10 mg/ml Acepromazine (as acepromazine maleate 13.55 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 amber glass (Type I) vial or 50 ml amber glass (Type II) vial, closed with a grey chlorobutyl rubber bung and aluminium crimped seal with plastic flip-cap. 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 a simple mixing, heating and cooling process, with suitable pH adjustment and addition of the filtered product into sterilised vials.

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 active substance described in the British Veterinary Pharmacopoeia and United States Pharmacopoeia. 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. Suitable Certificates of analysis were provided.

All excipients are monographed in the European Pharmacopoeia (Ph. Eur). Where appropriate, Ph. Eur monographs were adhered to for packaging.

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.

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 are those for: appearance, clarity, acepromazine and phenol identification, degradation products, pH and sterility.

II.F. Stability

Stability data on the active substance and product as packaged for sale have been provided in accordance with applicable guidelines, demonstrating the stability of the active substance when stored under the agreed approved conditions. The retest period for the active substance is 4 years when stored in tightly closed containers below 25ºC. Suitable in-use and photostability tests were performed. The SPC and product literature carry acceptable instructions for storage and use of the product.

G. Other Information

Do not store above 25°C.
Following withdrawal of the first dose, use remainder of the product within 28 days. Discard unused material.
Keep the vial in the outer carton in order to protect from light.
Do not freeze.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline. The addition of a larger pack size than that approved for the reference product was accepted, as no increased exposure is expected for a product used by professionals only.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- This product contains a potent sedative; care should be taken when handling and administering this product to avoid accidental self-exposure. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician but DO NOT DRIVE as sedation may occur. Symptomatic treatment may be required.

- This product may cause irritation of skin and eyes. Avoid contact with skin and 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 Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

The applicant followed the VICH decision tree and stopped at question 3 based on use of the product in non-food producing horses only. Exposure of the environment is expected to be limited based on the indications, use in individual animals only and the presentation of the product as an injectable solution. No Phase II assessment was required. The disposal advice on the SPC and product literature was considered acceptable.

III.B.2 Residues documentation

No residue depletion studies were conducted because the product is only permitted for use in non-food producing horses.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

Due to the nature of the application, no pharmacodynamic or pharmacokinetic studies were required.

Pharmacodynamics

Acepromazine is a phenothiazine. It is a central nervous system depressant with associated activity on the autonomic system. The active substance possesses anti-emetic, hypothermic, hypotensive and anti-spasmodic properties and shows a marked potentiating effect on barbiturate anaesthesia.

Pharmacokinetics

The length of action of acepromazine appears to be prolonged and to be dose dependent.

Tolerance in the Target Species

Tolerance studies were not required because of the nature of the application. Adverse reactions are as cited in the SPC. Accidental intracarotid injection in horses can produce clinical signs ranging from disorientation to convulsive seizures and death.

IV.II. Clinical Documentation

It was established that the proposed and reference products were quantitatively and qualitatively the same in terms of the active substance, and can be considered bioequivalent. Therefore, in accordance with the legal base, clinical studies were not required.

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 is favourable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

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 Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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