IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Mepidor 20 mg/ml solution for injection for horses

PRODUCT SUMMARY

EU Procedure Number	IE/V/0425/001/DC (formerly UK/V/0649/001/DC)
Name, Strength, Pharmaceutical Form	Mepidor 20 mg/ml solution for injection for horses
Active Substances(s)	Mepivacaine hydrochloride
Applicant	VetViva Richter GmbH Durisolstrasse 14 4600 Wels Germany
Legal Basis of Application	Hybrid application (Article 13(3) of Directive No 2001/82/EC)
Target Species	Horses
Indication For Use	Mepivacaine is indicated for intra-articular and epidural anaesthesia in horses.
ATC Code	QN01BB03
Date of conclusion of the decentralised procedure	18 October 2017 (UK) 05 January 2018 (IE)
Date product first authorised in the Reference Member State (MRP only)	Not Applicable
Concerned Member States for original procedure	Austria, Denmark, Estonia, Finland, France, Germany, Ireland, Netherlands, Spain, Sweden. UK added via transfer of RMS

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 determined a generic 'hybrid' application because changes to the indications with regard to the reference medicinal product have been made. The reference product is Intra-Epicaine 20 mg/ml Solution for Injection, authorised in the UK since December 1990.
The product is indicated for intra-articular and epidural anaesthesia in horses.
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 reactions observed are indicated in the SPC.[1] 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 [2] 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] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II. QUALITY ASPECTS

II.A. Composition

The product contains 20 mg Mepivacaine hydrochloride and the excipients sodium chloride, sodium hydroxide, hydrochloric acid and water for Injections.

The container system consists of clear glass vials type I, bromobutyl rubber stopper or bromobutyl stopper with a fluorinated polymer coating and aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence 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 process of addition of the active and excipient to water for injection, followed by pH adjustment, filtration and filling into pre-sterilised vials.

II.C. Control of Starting Materials

The active substance is mepivacaine hydrochloride, an established active substance described in the European Pharmacopoeia (Ph. Eur). 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. An acceptable certificate of suitability was provided, along with the applicants specification reflecting the additional requirements as detailed in the certificate of suitability.

Each of the excipients are monographed in the Ph. Eur. Packaging components for the product conforms to Ph. Eur. monographs.

II.C.4. Substances of Biological Origin

The applicant has submitted a statement confirming that all starting materials and manufacture are in compliance with the requirements of the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (EMA/410/01 Rev 03).

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 appearance, clarity, colour, pH, density, identity, filling volume, impurities 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. The retest period of 60 months when stored in double polyethylene bags within a carton drum.

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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
This product does not contain an antimicrobial preservative. Use the vial on one occasion only. Discard any unused material. Keep the vial in the outer carton in order to protect from light.

This veterinary medicinal product does not require any special temperature storage conditions.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

No pharmacological or toxicological data were provided other than that submitted to support the user risk assessment (URA). This was considered acceptable for a locally acting product as it is considered that; any differences in composition of the product compared to the reference product are not expected to alter the nature of the active substance, the proposed routes of administration are included within those of the reference product and the proposed product will be administered at the same dose of the reference product. An environmental risk assessment (ERA) was submitted.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the routes of exposure of most concern are skin exposure and accidental injection.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. The proposed warnings are the same as those of the reference product and include a warning for pregnant women to avoid using the product. Therefore the following applicant's user recommendations are appropriate:

- People with known hypersensitivity to mepivacaine or other local anaesthetics of the amide group should avoid contact with the veterinary medicinal product.
- This product may be an irritant to the skin and eyes.
- Avoid contact with the skin and eyes. Wash any splashes from skin and eyes immediately with plenty of water. Seek medical advice if irritation persists.
- Adverse effects on the foetus cannot be excluded. Pregnant women should avoid handling the product.
- Accidental self-injection may result in cardiorespiratory and/or CNS effects. Care should be taken to avoid accidental self-injection. In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician. Do not drive.
- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The product will be used to treat a small number of animals in a flock or herd and as such environmental exposure will be low. A Phase II ERA was not required.

III.B.2 Residues documentation

The reference product is restricted to horses not intended for human consumption and no withdrawal period has been set. Therefore, for the establishment of withdrawal periods data available in the public domain were presented. No residues depletion studies were provided. The active substance is listed in Table 1 of the Annex of Commission Regulation (EU) 37/2010 as 'No MRL required'.
In line with the opinion of the CVMP[1], horses are unlikely to be sent for slaughter during, or straight after, treatment. Therefore, a precautionary withdrawal period of 3 days in meat and 72 hours in milk is considered acceptable to ensure consumer safety.

Withdrawal Periods

Based on the data provided, a withdrawal period of 3 days for meat/offal in horses and 72 hours for milk are justified.
[1] Committee for Medicinal Products for Veterinary Use.

IV. CLINICAL ASSESSMENT

IV.I. Pre-Clinical Studies

No pharmacological or toxicological data were provided. This was considered acceptable for a locally acting product as it is considered that; any differences in composition of the product compared to the reference product are not expected to alter

the nature of the active substance, the proposed routes of administration are included within those of the reference product and the proposed product will be administered at the same dose of the reference product.

IV.II. Clinical Documentation

No pharmacological or toxicological data were provided. This was considered acceptable for a locally acting product as it is considered that; any differences in composition of the product compared to the reference product are not expected to alter the nature of the active substance, the proposed routes of administration are included within those of the reference product and the proposed product will be administered at the same dose of the reference product.

V. OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the products are used in accordance with the Summary of Product Characteristics the benefit/risk profile of the products is favourable.