IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Morphasol 10 mg/ml solution for injection for horses

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

PRODUCT SUMMARY

EU Procedure number	IE/V/0246/001/DC
Name, strength and pharmaceutical form	Morphasol 10 mg/ml solution for injection for horses
Active substance(s)	Butorphanol (as Butorphanol tartrate)
Marketing Authorisation Holder	aniMedica GmbH Im Südfeld 9 48308 Senden-Bösensell Germany
Legal basis of application	Application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of procedure	29th October 2010
Target species	Horses
Indication for use	For short term relief of pain associated with colic of gastrointestinal tract origin. For sedation in combination with certain 2-adrenoceptor agonists
ATCvet code	QN02AF01
Method of Sale and Supply	Prescription Only Medicine
Concerned Member States	AT, BE, DE, ES, FI, FR, HU, IS, LU, NL, NO, PL, SE, UK

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

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 potential 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 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.

II QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains 10 mg/ml butorphanol (as butorphanol tartrate) as the active substance and the excipients benzethonium chloride, citric acid monohydrate, sodium citrate, sodium chloride and water for injections.

The container/closure system is a 20 ml multidose clear Type I glass vial with a grey butyl rubber stopper and an aluminium cap.

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 at 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 butorphanol (as butorphanol tartrate), an established active substance. 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.

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.

D. Control on Intermediate Products

Not applicable.

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.

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.

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 Not

applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This application has been submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended (that is, a so called "hybrid" application). The reference product is Torbugesic 1% Solution for Injection (VPA 10861/065/001) which has been authorised in the RMS for not less than 10 years. Given that:

both Morphasol and the reference product are similar in terms of active substance content (the same qualitative and quantitative composition, 10 mg butorphanol/ml),
both are solutions for injection, both are intended for intravenous administration only, and both are to be administered at the same mg/kg dose

it can be accepted that the bioavailability of butorphanol following administration will be similar for both products. In accordance with paragraph 4a of the current bioequivalence guideline such products can be considered bioequivalent without the need for *in vivo* bioequivalence studies. Given that bioequivalence is assumed, it is accepted that the safety and efficacy profile will be similar for both products.

Based on the information presented in the dossier, the product, when used in accordance with label recommendations, is not expected to be an unacceptable risk to the user. The following user safety statements apply to the product: Direct contact with skin or eye of the user should be avoided since the product might induce irritation and sensitization. Accidental spillage on the skin should be washed immediately with soap and water. When the product comes into contact with the eyes, rinse immediately with plenty of water.
Care should be taken when handling the product to avoid self-injection. In case of accidental self-injection, seek medical advice immediately and show the package insert or the label to the physician, and do not drive, since drowsiness, nausea and dizziness may occur. Effects can be reversed by the administration of an opioid antagonist.

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

The proposed 'zero day' withdrawal period is in line with the authorised withdrawal period of the reference product in the RMS and can be accepted.

IV CLINICAL ASSESSMENT (EFFICACY)

This application has been submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended (that is, a so called "hybrid" application). The reference product is Torbugesic 1% Solution for Injection (VPA 10861/065/001) which has been authorised in the RMS for not less than 10 years. <?xml:namespace prefix = "o" ns = "urn:schemasmicrosoft-com:office:office" />

Given that: both Morphasol and the reference product are similar in terms of active substance content (the same qualitative and quantitative composition, 10 mg butorphanol/ml), both are solutions for injection, both are intended for intravenous administration only, and both are to be administered at the same mg/kg dose.

It can be accepted that the bioavailability of butorphanol following administration will be similar for both products. In accordance with paragraph 4a of the current bioequivalence guideline such products can be considered bioequivalent without the need for in vivo bioequivalence studies. Given that bioequivalence is assumed, it is accepted that the efficacy profile will be similar for both products. Consequently, the indication for analgesia and sedation in combination with detomidine and romifidine (as authorised for the reference product) can be accepted. The additional sedative combination (butorphanol-xylazine) is supported by a clinical study conducted by the applicant. Based on the results presented, it is clear that the Morphasol-xylazine combination at the doses used is effective for sedation. Data have been provided to justify the recommended dose of butorphanol to be used (25-50 microgram/kg) when administered in combination with xylazine.

With respect to target animal tolerance, no Morphasol-specific target animal safety studies were provided. The absence of these data is justified on the basis that: the safety profile of butorphanol is well known, all excipients are present in other authorised parenteral preparations and are recognised as being safe, field data suggest no evidence of unexpected treatment related adverse effects when Morphasol was administered at a dose of 0.025 mg butorphanol/kg (although it is accepted that the dose of butorphanol used in that study, and consequently the volume of Morphasol, was 25% the dose proposed for analgesia), and pharmacovigilance data from a third country provides some supporting evidence that the safety profile of Morphasol is acceptable.

The clinical particulars as detailed in Section 4 of the proposed SPC are broadly in line with those of the reference product. Based on the data presented, the following indications/dose rates have been justified:

For intravenous administration only.

For analgesia:

Dose rate: 100 µg butorphanol per kg bodyweight (BW) (equivalent to 1 ml for 100 kg BW), by intravenous injection. Butorphanol is intended for use where short duration analgesia is required. The dose may be repeated as required. The need for and timing of repeat treatment will be based on clinical response. For information on the onset and duration of analgesia see section 5.1. For cases where longer duration analgesia is likely to be required, an alternative therapeutic agent should be used.

For sedation in combination with detomidine hydrochloride:

A dose rate of 12 µg detomidine hydrochloride per kg BW should be given intravenously followed within 5 minutes by a dose rate of 25 µg butorphanol per kg BW (equivalent to 0.25 ml for 100 kg BW) intravenously.

For sedation in combination with romifidine:

A dose of 40-120 µg romifidine per kg BW followed within 5 minutes by a dose rate of 20 µg butorphanol per kg BW (equivalent to 0.2 ml for 100 kg BW) should be administered intravenously.

For sedation in combination with xylazine:

A dose rate of 500 µg xylazine per kg BW followed immediately by a dose of 25-50 µg butorphanol per kg BW (equivalent to 0.25-0.5 ml per 100 kg) should be administered intravenously.

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 for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI 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 HPRA website.

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 product.

Changes:
None.