ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Animeloxan 20 mg/ml Solution for Injection for Cattle, Pigs and Horses

PuAR correct as of 22/08/2018 when RMS was transferred to DE. Please contact the RMS for future updates

Updated: December 2017

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0377/002/DC
Name, strength and pharmaceutical form	Animeloxan 20 mg/ml Solution for Injection for Cattle, Pigs and Horses
Applicant	aniMedica GmbH Im Suedfeld 9 48308 Senden-Boesensell Germany
Active substance(s)	Meloxicam
ATC Vetcode	QM01AC06
Target species	Cattle, pigs and horses
Indication for use	Cattle: For use in acute respiratory infection with appropriate antibiotic therapy to reduce clinical signs in cattle. For use in diarrhoea in combination with oral re-hydration therapy to reduce clinical signs in calves of over one week of age and young, non-lactating cattle. For adjunctive therapy in the treatment of acute mastitis, in combination with antibiotic therapy. For the relief of post-operative pain following dehorning in calves. Pigs: For use in non-infectious locomotor disorders to reduce the symptoms of lameness and inflammation. For adjunctive therapy in the treatment of puerperal septicaemia and toxaemia (mastitis-metritis-agalactia syndrome) with appropriate antibiotic therapy Horses: For use in the alleviation of inflammation and relief of pain in both acute and chronic musculo-skeletal disorders. For the relief of pain associated with equine colic.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

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 completion of the original decentralised procedure	26th October 2011.
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Germany, Poland

I. SCIENTIFIC OVERVIEW

This was a decentralised application for a generic product, submitted in accordance with article 13 (1) of Directive 2001/82/EC, as amended. The reference product is Metacam 20 mg/ml Solution for Injection for Cattle Pigs and Horses, authorised in 2001 for cattle. The additional species were subsequently added in 2003 and 2005 respectively. In cattle, the indication is for use in acute respiratory infection with appropriate antibiotic therapy to reduce clinical signs, for use in diarrhoea in combination with oral re-hydration therapy to reduce clinical signs in calves of over one week of age and young, non-lactating cattle. Additionally for adjunctive therapy in the treatment of acute mastitis, in combination with antibiotic therapy. In pigs, the indication is for use in non-infectious locomotor disorders to reduce the symptoms of lameness and inflammation, and for adjunctive therapy in the treatment of puerperal septicaemia and toxaemia (mastitis-metritis-agalactia syndrome) with appropriate antibiotic therapy. In horses, the product is indicated for the treatment of the alleviation of inflammation and relief of pain in both acute and chronic musculo-skeletal disorders and for the relief of pain associated with equine colic.

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.[1]

The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy of the product was

[1] SPC – Summary of product Characteristics,

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. Composition

The product contains 20mg/ml meloxicam and excipients N-methyl 2-pyrrolidone, ethanol, anhydrous sodium hydroxide, hydrochloric acid, dilute and water for injection.

The container/closure system consists of clear glass (Type I) bottles of 50 ml and 100 ml, closed with bromobutyl rubber stoppers and aluminium /PP caps. The product is available in boxes containing 1 x 50 ml or 12 x 50 ml and 1 x 100 ml or 12 x 100 ml, not all pack sizes may be marketed.. 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.

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 meloxicam, 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. All excipients comply with appropriate Ph. Eur monographs.

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

Not applicable.

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. Control tests on the finished product include those for visual analysis, identification of active substance, extractable volume, pH, sterility and related substances.

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. Long term, intermediate and accelerated studies demonstrated the appropriateness of the product to retain a two year shelf-life.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf-life of the product as stored for sale: 3 years.
Shelf-life of the product after first opening: 28 days.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, (CVMP[2] EMEA/CVMP/543/03-Final), citing that only professionals (veterinarians, farmers) will use the product, and that the main route of exposure is the dermal route. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:-

[2] CVMP – The Committee for Medicinal Products for Veterinary Use.

- Accidental self-injection may give rise to pain. People with known hypersensitivity to NSAIDs should avoid contact with the veterinary medicinal product.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- If accidental skin contact occurs, wash the affected area thoroughly.
- Wash hands after use.
- In view of the risk of accidental self-injection and the known adverse class-effects of NSAIDs and other prostaglandin inhibitors on pregnancy and/or embryofoetal development, the veterinary medicinal product should not be administered by pregnant women or women attempting to conceive.

Ecotoxicity

The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that environmental exposure will not be large, as only a small number of animals will be treated at one time.

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

III.B Residues documentation

Residue Studies

The applicant conducted residue depletion studies for a new route of administration in order to accommodate the addition of the subcutaneous route for cattle, and in order to retain pigs as a target species, administration performed via the intramuscular route. (The formulation of the product was slightly different to that of the reference product). All data were satisfactory.

Withdrawal Periods

Based on the data provided above, withdrawal periods were designated as follows:-

Cattle:	
Meat and offal:	15 days
Milk:	5 days
Pigs:	
Meat and offal:	8 days
Horses:	
Meat and offal:	5 days

IV CLINICAL ASSESSMENT (EFFICACY)

Although this was a generic product, bioequivalence and tolerance studies were required in order to permit the use of the product via the subcutaneous route (cattle) and the intramuscular route (pigs).

IV.A Pre-Clinical Studies

Pharmacology

A study was presented in cattle that investigated bioequivalence between Animeloxan 20 mg/ml Solution for Injection for Cattle Pigs and Horses and Metacam 20 mg/ml Solution for Injection for Cattle Pigs and Horses. A suitable number of animals were recruited into a 2 x 2 cross-over trial with two treatment periods. There was a wash-out period of 14 days. The products were delivered via subcutaneous injection at 0.5 mg meloxicam /kg bodyweight, and blood samples were analysed at appropriate timepoints. C_{max}[3] and AUC[4] confidence intervals of the test product were within the parameters of the reference product, and Animeloxan 20 mg/ml Solution for Injection for Cattle Pigs and Horses was therefore considered to be bioequivalent to the reference product for this species and route of administration. A similar assay in pigs (intramuscular route, 0.4 mg meloxicam/kg bodyweight), confirmed that the product could also be used as appropriate in this species.

Tolerance in the Target Species of Animals

Suitable studies showed that the product was generally well-tolerated in the target species (cattle, pigs). Any possible adverse effects are cited in the SPC and product literature.

IV.B Clinical Studies

Laboratory Trials

As this was a generic application submitted under Article 13 (10 of Directive 2001/82/EC as amended, and a reference product was already established, no data were required for this section.

Field Trials

As this was a generic application submitted under Article 13 (10 of Directive 2001/82/EC as amended, n and a reference product was already established, o data were required for this section.

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

[3] C_{max} – maximum plasma concentration of the active substance.
[4] AUC – Area under the curve.

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

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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