Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Meloxaid 1.5 mg/ml Oral Suspension for Dogs

Date Created: April 2016

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Meloxaid 1.5 mg/ml Oral Solution for Dogs
Applicant	Norbrook Laboratories Limited Station Works Camlough Road Newry Co. Down BT35 6JP
Active substance	Meloxicam
ATC Vetcode	QM01AC06
Target species	Dogs
Indication for use	Alleviation of inflammation and pain in both acute and chronic musculo-skeletal disorders in dogs.

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.

I. SCIENTIFIC OVERVIEW

Meloxaid 1.5 mg/ml Oral Suspension for Dogs has been developed as a generic of Metacam 1.5 mg/ml Oral Suspension for Dogs which has been centrally authorised since 1998. Bioequivalence with the reference product has been shown through an *in vivo* bioequivalence study.

The product is indicated for alleviation of pain and inflammation in acute and chronic musculo-skeletal disorders in dogs. The product is contraindicated in pregnant and lactating dogs, dogs less than 6 weeks of age and in dogs suffering from gastrointestinal disorders, impaired hepatic, cardiac or renal function and haemorrhagic disorders.

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.[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.

II. QUALITATIVE AND QUANTITIATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 1.5 mg/ml meloxicam and the excipients sodium benzoate, glycerol, povidone K30, xanthum gum, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate, citric acid anhydrous, simethicone emulsion and purified water.

The container/closure system consists of a polyethylene terephthalate screw bottle closed with HDPE/LDPE child resistant cap. The bottles are presented as 10 ml, 32 ml,100 ml 2 x 100 ml or 200 ml products and are supplied with a 1 ml and a 5 ml measuring syringe. The particulars of the containers and controls performed are provided and conform to the regulation.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

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 mixing the active substance with excipients until completely dissolved, adjusting the pH of the solution as necessary, before filling into the bottles. 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 meloxicam, an established active substance described in the European Pharmacopoeia (Ph. Eur.). Data on the active substance were provided in the form of a Ph. Eur. Certificate of Suitability. 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.

The excipients are all described in a pharmacopoeia and comply with their respective monographs. Certificates of analysis have been provided.

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. Control tests on the finished product include identification and assay of the active substance, viscosity, resuspendability, dissolution, pH and microbiological contamination.

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.

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 3 years is specified by the Ph. Eur. Certificate of Suitability.

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.

In-use stability studies were also performed for several presentations, which provided acceptable data.

G. Other Information

Shelf life of the finished product as packaged for sale is 18 months.
Shelf life after first opening the immediate packaging is 6 months.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with a reference product has been demonstrated, 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 which considers the risk following accidental spillage onto skin and accidental ingestion by a child. These risks have been mitigated by adequate warnings on the product literature and the use of child resistant packaging. The risks to the user are considered to be the same as those for the reference product. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

- People with known hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) should avoid contact with the veterinary medicinal product.
- In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
- Wash any splashes from skin immediately with water.

Environmental Safety

An Environmental Risk Assessment (ERA) has been supplied. The ERA was conducted in accordance with VICH and CVMP guidelines.

Phase I:
The product will only be used in non-food animals and as a result environmental exposure will be low. Therefore, a Phase II ERA was not required.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

An *in vivo* bioequivalence study has been provided to compare the test product with the reference product. Healthy dogs were randomly divided into 2 groups of 9 and administered both products according to the two period, two sequence cross-over study. A dose of 0.2 mg meloxicam/kg was given orally and a 35 day washout period was included between treatments. Blood samples were taken prior to administration of the product and at regular intervals up to 120 hours post-treatment.

Blood samples were analysed to determine the key pharmacokinetic parameters for each product. These were AUC[3] and C_{max}[4], which were compared with ANOVA using the log transformed data. The 90% confidence intervals (CI) were calculated for both parameters and limits, 80-125% for AUC and 70-143% for C_{max}, were set.

The results showed that the concentration curves for both products were similar. AUC was found to be 21.2 (±6.6 SD) µg.h/ml for the test product and 18.6 (±5.8 SD) µg.h/ml for the reference product. The C_{max} was shown to be 0.67 (±0.17 SD) µg/ml and 0.60 (±0.08 SD) µg/ml for the test and reference products respectively. The ratios of the population means for specific parameters fell within the predefined acceptance limits for both parameters. Therefore, bioequivalence to the reference product was demonstrated.

Tolerance in the Target Species

The applicant has conducted a controlled target animal tolerance study using multiple doses in the target species. Healthy dogs were randomly assigned into treatment groups of 5 dogs. Group A received 0.2 mg/ kg of the test product once, followed by daily administration of 0.01 mg/kg for 12 days. Group B received 0.6 m/kg meloxicam twice, 24 hours apart, followed by a daily dose of 0.3 mg/kg for 11 days. Group C was the control group and received a placebo at a dose of 1 ml/ 7.5 kg once, followed by 1 ml/15 kg per day for 12 days.
Clinical examinations were performed at regular intervals following administration of the product. Blood and faecal samples were taken for

[3] AUC – Area under the curve
[4] C_{max} – Maximum plasma concentration

biochemistry and haematology and animals were weighed before and on day 19 after treatment. A repeated measures ANOVA was performed for all clinical, biochemical and haematological parameters.

Several animals vomited or had diarrhoea during the study, but these adverse reactions are commonly observed with this type of product. The SPC carries a suitable warning. No dose-related effect was observed during study and the product is considered to be safe for the target species.

IV.II. Clinical Documentation

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC as amended, and bioequivalence with a reference product has been demonstrated, clinical studies are 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(s) is favourable

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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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