College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Metaxx 15 mg/ml oral suspension for horses

NL/V/0377/001/DC

Date:
June 2023

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0377/001/DC
Name, strength and pharmaceutical form	Metaxx 15 mg/ml oral suspension for horses
Applicant	Alfasan Nederland BV Kuipersweg 9 3449 JA Woerden The Netherlands
Active substance(s)	meloxicam
ATC Vetcode	QM01AC06
Target species	horses
Indication for use	Alleviation of inflammation and relief of pain in both acute and chronic musculo-skeletal disorders in horses.

Metaxx 15 mg/ml oral suspension for horses	NL/V/0377/001/DC
Alfasan Nederland BV	DCP
	Publicly available assessment report

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://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	21 December 2022
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK(NI)

I. SCIENTIFIC OVERVIEW

Metaxx 15 mg/ml oral suspension for horses 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 reactions observed are indicated in the SPC.
Metaxx 15 mg/ml oral suspension for horses 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 demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

The quality / safety / efficacy aspects of Metaxx 15 mg/ml oral suspension for horses is based on bioequivalence with the (EU) Reference Product Metacam 15 mg/ml oral suspension for horses (Centralised procedure; REG NL 10180).
Warnings statements and precautions are adopted from the (EU) Reference Product.
Additional statements have been added, based on increased knowledge and the current state of science. Adverse events and contraindications are indicated in the SPC.

II. QUALITY ASPECTS

A. Composition

The proposed product concerns a yellow oral suspension for horses and is a generic veterinary medicinal product. It contains the active substance meloxicam (15 mg/mL) and the excipients sodium benzoate (preservative), liquid sorbitol, glycerol, saccharin sodium, xylitol, sodium dihydrogen phosphate dihydrate, colloidal anhydrous silica, xanthan gum, citric acid, Honey aroma and Purified water or water for injections.

The product is to be packed in HDPE bottles containing 125 ml or 336 ml with a HDPE tamper-proof child-resistant screw cap. A 24 ml PP measuring syringe is included.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

The same antimicrobial preservative, i.e. sodium benzoate, in the same concentration (1.5 mg/mL) as present in the reference product is included in the proposed formulation.
The applicant has developed a preparation which is almost identical to the reference product but which contains xanthan gum instead of hydroxyethylcellulose as suspending agent. The applicant has adequately investigated the influence of the replacement.

Results of the test for efficacy of antimicrobial preservation performed at the lower preservative limit in the end of shelf life specifications are provided.

No drug substance overage is included for the proposed medicinal product.

B. Method of Preparation of the Product

The manufacturing formulae for batch sizes of the proposed range of batch sizes are presented. In view of the data generated with the pilot batch size (100 L), the proposed maximum batch size of 500 L is acceptable The manufacturing process is considered a standard process since the drug product is an oral suspension that is manufactured by subsequent adding and stirring of ingredients and checking for homogeneity after each addition. Besides, the dosage form manufacturer is known to have much experience with the manufacture of essentially similar products or processes.

Process validation is presented for three pilot batches which were then filled into all the proposed bottle sizes.

C. Control of Starting Materials

The active substance is meloxicam, an established substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

For the active substance a CEP is used. A copy of the currently valid version of the CEP, with a signed declaration of access, has been provided. Batch analytical data demonstrating compliance with this specification is provided.

Each of the excipients complies with the relevant Ph. Eur. monograph, except for Honey aroma for which a suitable in-house specification is included.

It is confirmed that 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 release and shelf life specifications control the relevant parameters for the pharmaceutical form. The tests in the specification and their limits 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 one of the two proposed production sites have been provided demonstrating compliance with the specification.

F. Stability

The retest period and packaging of the drug substance as stated on the CEP are adopted.

Stability data on three pilot batches of the finished product in the two bottle sizes have been provided in accordance with applicable European guidelines, which were stored at 25 °C/60%RH (36 months) and also under accelerated conditions (6 months). The data were considered acceptable to support the 36 months with no special storage conditions required. It should be committed that the first three production batches will be placed on long term stability studies through the proposed shelf life and on accelerated studies for six months.

An in-use stability study was performed for all three batches and two bottle sizes referred to above. The study was continued for 6 months. All physico-chemical test results were within specification.

G. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological, pharmacological and clinical 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 / the environment / consumers. Additional statements have been added, based on increased knowledge and the current state of science. Adverse events, warnings and contraindications are indicated in the SPC.

III.A Safety Testing

User Safety

Being a generic procedure the applicant refers to the reference product for information on this section.

Additionally, the applicant has provided a user safety assessment in compliance with the relevant guideline. Combined with increased knowledge and the current state of science, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the VICH Guideline on Environmental Impact Assessment (EIAs) for Veterinary Medicinal Products-Phase I (CVMP /VICH/592/98-FINAL) and the supporting CVMP technical guidance document (EMA/CVMP/ERA/418282/2005-Rev.1- Corr.) which showed that no further assessment is required.

The environmental risk assessment can stop in Phase I because this product is intended for use in horses, in individual animals, and a Phase II assessment is not deemed necessary.

Metaxx 15 mg/ml oral suspension for horses	NL/V/0377/001/DC
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The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

III.B Residues documentation

Residue Studies

Being a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, results of residue studies are not required.

MRLs

Meloxicam is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Target tissues	**Equidae**
Muscle	20 µg/kg
Liver	65 µg/kg
Milk	65 µg/kg

Withdrawal Periods

Based on the data provided above, being a generic application submitted according to Article 13(1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, the following is justified: a withdrawal period of 3 days for meat and offal in horses and ‘not authorised for use in horses producing milk for human consumption’.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

Additionally to the above, based on increased knowledge and the current state of science, warning statements and precautions have been added to the product literature ensuring safety to the target animals. Adverse events, warnings and contraindications are indicated in the SPC.

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when Metaxx 15 mg/ml oral suspension for horses is used in accordance with the Summary of Product Characteristics, the risk benefit profile 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 Heads of Veterinary Medicines Agencies website (www.HMA.eu).

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.

None

Summary of change (Application number)	**Section updated**	**Approval date**
<Example: Change to active substance specification> (MS/V/XXX/X/IB/XX)	N/A	