Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Cronyxin 50 mg/g oral paste for horses

Bimeda Animal Health Ltd

Date: 19 December 2018

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0178/001/DC
Name, strength and pharmaceutical form	Cronyxin 50 mg/g Oral paste for horses (DE, AT, BE, EE, ES, FR, IE, IT, NL, PL, UK) Cronyxin vet 50 mg/g Oral paste for horses (SE) Cronyxin vet (DK)
Applicant	Bimeda Animal Health Limited
Name and Address of Applicant	Bimeda Animal Health Limited 2, 3, 4 Airton Close Airton Road, Tallaght Dublin 24 D24 E032 Ireland
ATC Vetcode	QM01AG90
Target species	Horse
Indication for use	Treatment of acute inflammatory musculoskeletal disorders in horses

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MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	26 September 2018
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure	AT, BE, DK, EE, ES, FR, IE, IT, NL, PL, SE and UK

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I. SCIENTIFIC OVERVIEW

'Cronyxin 50 mg/g Oral paste 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 horse; slight reactions observed are indicated in the SPC[1].

'Cronyxin 50 mg/g Oral paste 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.

'Cronyxin 50 mg/g Oral paste for horses' is a generic to the German reference product Finadyne Paste 50 mg/g oral paste for horses of Intervet Deutschland GmbH (MA No. 4586.00.01), which has been authorised in June 1986 on the basis of a complete dossier. Bioequivalence of 'Cronyxin 50 mg/g Oral paste for horses' with the reference product was demonstrated. Therefore, the safety and efficacy of the 'Cronyxin 50 mg/g Oral paste for horses' is identical to the reference product. The initial application for the reference product was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 50 mg flunixin (as flunixin meglumine, 83 mg) and the excipients silica, colloidal anhydrous; propylene glycol; titanium dioxide (E171); xanthan gum; aluminium magnesium silicate; sorbitol, liquid (crystallising); apple flavour FL02791 and purified water.

The container/closure system is a white HDPE syringe barrel and dial-a-dose plunger with LDPE cap, containing 33 grams of paste. The plunger is graduated to give set doses corresponding to 100 kg bodyweight per graduation.

The choice of the formulation and the absence of a 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

[1] Summary of Product Characteristics

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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 flunixin meglumine, an established substance described in the European Pharmacopoeia. 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.

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 and/or certificates of suitability issued by the EDQM 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.

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The claim of a 3-months stability after broaching is based on the demonstration of stability for a batch broached and stored 3 months.

G. Other Information

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC and bioequivalence with a reference product has been demonstrated, safety studies are not required. The safety claims for this product are equivalent to those of the reference product.

Nevertheless in addition to the warning phrase regarding the skin sensitization potential added into the SPC of the reference product in 2001 under section 4.5 *Special precautions to be taken by the person administering the medicinal product to the animals* of the SPC further safety phrases were added to minimize the risks for children and to be in line with similar products in the EU.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the initial predicted environmental concentration in soil (PECsoil, initial = 28.5 µg/kg) is less than 100 µg/kg.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because this is a decentralised procedure according to Article 13(1) of Council Directive 2001/82/EC as amended and bioequivalence with the reference product has been demonstrated.

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MRLs

The active substance is listed in Table 1 of the Annex of Commission Regulation (EU) No 37/2010

Pharmacologically active Substance	Marker residue	Animal Species	MRL	Target Tissues	Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)	Therapeutic Classification
Flunixin	Flunixin	Bovine	20 µg/kg 30 µg/kg 300 µg/kg 100 µg/kg	Muscle Fat Liver Kidney	NO ENTRY	Anti-inflammatory agents/Nonsteroidal anti-inflammatory agents
		Porcine	50 µg/kg 10 µg/kg 200 µg/kg 30 µg/kg	Muscle Skin and fat Liver Kidney		
		Equidae	10 µg/kg 20 µg/kg 100 µg/kg 200 µg/kg	Muscle Fat Liver Kidney		
	5-Hydroxyflunixin	Bovine	40 µg/kg	Milk		

Withdrawal Periods

Based on the data provided above, a withdrawal period of 15 days for meat in horses is justified. The product is not authorised for use in animals producing milk for human consumption.

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IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC and bioequivalence with a reference product has been demonstrated, pre-clinical and clinical studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

The applicant provided a bioequivalence study that has been conducted with the test product Flunazine Paste (Cronyxin 5% w/w Oral Paste) and the reference medicinal product 'Finadyne Paste 50mg/g' authorized in Germany. The active ingredients of Flunazine and Finadyne pastes is flunixin meglumine. Blood samples were collected from all the horses at appropriate intervals throughout the study and the amount of flunixin in these samples was measured using a validated analytical method. The 90% confidence limits for AUC[2] and Cmax[3] ratios of the test and reference product were within the stipulated range of 80-125%.Thus, bioequivalence for reference and test product were accepted.

Tolerance in the Target Species of Animals

As this application has been submitted in accordance with Art. 13 (1) of Directive 2001/82/EC, as amended and bioequivalence with the reference product has been demonstrated, a difference in tolerance profile is not to be expected. Thus, data on tolerance in the target species are not required.

IV.B Clinical Studies

This application has been submitted in accordance with Art. 13 (1) of Directive 2001/82/EC, as amended and bioequivalence with the reference product has been demonstrated, clinical efficacy studies are not required and have not been provided. The efficacy claims for this product are the same as for the authorized reference product**.**

[2] Area under the curve
[3] Maximum plasma concentration

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

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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 Heads of Veterinary Medicinal 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>

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