MINISTERIO DE SANIDAD Y CONSUMO
agencia española de medicamentos y productos sanitarios

SUBDIRECCIÓN GENERAL
DE MEDICAMENTOS
DE USO VETERINARIO

Agencia Española de Medicamentos y Productos Sanitarios

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28022 – Madrid
España
(Reference Member State)

MUTUAL RECOGNITION PROCEDURE

DRAFT PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

NORFLUNIX 50 mg/ml
Solution for Injection for pigs

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0121/001/MR
Name, strength and pharmaceutical form	Norflunix 50 mg/ml solution for injection for pigs
Applicant	Norbrook Laboratories Ltd., Station Works, Camlough Road, Newry, Co. Down, BT35 6JP Northern Ireland
Active substance(s)	Flunixin (as meglumine)
ATC Vet code	ATC vet code: QM01AG90
Target species	Pigs
Indication for use	This product is indicated for the alleviation of inflammation and pain associated with MMA syndrome (mastitis, metritis and agalactia) in pigs.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (http://www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Mutual Recognition application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	Day 90: 30/07/2008
Date product first authorised in the Reference Member State (MRP only)	15/04/2003
Concerned Member States for original procedure	BE, EL, IT

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

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 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 demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains Flunixin (50 mg) (equivalent to 82.9 mg of Flunixin meglumine)

Excipients are: sodium formaldehide sulphoxylate dihydrate, disodium edetate dihydrate, phenol, propylene glycol, diethanolamine, hydrochloric acid and water for injections.

The container is type I clear colourless glass vial, closed with bromobutyl bung and aluminium cap.

The particulars of the containers and controls performed are provided and conform to the regulation.

The presence of phenol as preservative is 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, using conventional manufacturing techniques. A flow chart is enclosed in the dossier. The manufacturing process is detailed.

Process validation data on the product have been presented in accordance with the relevant European guidelines. Analysis certificates of three full-scale batches also support the suitability of the process to obtain a product with a consistent quality.

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 practices.

The active substance specifications are considered adequate to control the quality of the material. Certificates of analysis of three batches demonstrating compliance with these specifications have been provided.

The excipients Disodium edetate dihydrate, phenol, propylene glycol, hydrochloric acid and water for injections comply with their corresponding monograph of European Pharmacopeia.
Sodium formaldehide sulphoxylate dihydrate and Diethanolamine comply with the requirements of the monograph of the US NF.
Certificates of analysis for all the excipients are submitted.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Declaration of compliance with the Annex to Commission Directive 1999/104/EC issued by the manufacturer have been provided. None of the raw material used in the manufacture of this product is from animal origin.

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.

G. Stability

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 (24 months) when stored under the approved conditions.

The claim of a 28 days stability after broaching is based on the demonstration of stability for a batch broached and stored one months at +25°C.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL) *(for pharmaceuticals only)*

For generics, insert in the relevant sections as appropriate:

As this is a generic application according to Article 13 of Directive 2001/82/EC based on the essential similarity of Norflunix Injection and the reference product Finadyne 5% Solution Injection, 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 / the environment / consumers.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the formulation and presentation of the product means that the most likely route of exposure is through the skin or by deliberate ingestion, but when the product is used in accordance with label recommendations, the product is unlikely to result in toxicity.

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

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. No warnings regarding flunixin are therefore required. The SPC contains a standard phrase in section 6.6 as required.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because this is a generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended based on the essential similarity of the reference product Finadyne 5% Solution Injection.

MRLs

Flunixin is listed in Annex I of Council Regulation 2377/90 (Council Regulation 2728/1999 O.J. L328; 22.12.99 and Council Regulation 2908/2000 OJ L336; 30.12.2000). The marker substance is flunixin in tissues and, 5-Hydroxiyflunixin in milk.

MRLs are listed below:

	Bovine	Porcine	Equidae
Muscle	20 µg/kg	50 µg/kg	10 µg/kg
Liver	300 µg/kg	200 µg/kg	100 µg/kg
Kidney	100 µg/kg	30 µg/kg	200 µg/kg
Fat / skin	30 µg/kg	10 µg/kg	20 µg/kg
Milk	40 µg/kg		

Withdrawal Periods

Based on the identical composition and the same parenteral administration between the generic and the reference product a withdrawal period of 21 days for meat and offal was set.

IV. CLINICAL ASSESSMENT (EFFICACY)

For generics, insert in the relevant sections as appropriate:

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC as amended, based on the bioequivalence of NORFLUNIX 50 mg/ml solution for injection for pigs and the reference product FINADYNE SOLUTION INJECTION efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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.

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 veterinary Heads of 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