Veterinary Medicines Directorate

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Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dugnixon 50 mg/ml Solution for Injection for Cattle, Pigs and Horses

Date Created: December 2017

PuAR correct as of 03/05/2018 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0640/001/DC
Name, strength and pharmaceutical form	Dugnixon 50 mg/ml Solution for Injection for Cattle, Pigs and Horses
Applicant	GLOBAL VET HEALTH SL C/Capçanes, nº12-bajos. Polígono Agro-Reus. REUS 43206 Tarragona SPAIN
Active substance	Flunixin
ATC Vetcode	QM01AG90
Target species	Cattle, pigs and horses
Indication for use	**Cattle** For the control of acute inflammation associated with respiratory disease. The product has also been shown to have some benefit in the treatment of experimental acute bovine pulmonary emphysema (Fog Fever). The product may be used as adjunctive therapy in the treatment of acute mastitis. **Horses** For the alleviation of inflammation and pain associated with musculo-skeletal disorders. For the alleviation of visceral pain associated with colic in the horse. **Pigs** For use as an adjunctive therapy in the treatment of swine respiratory diseases.

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)

As the product was refused a marketing authorisation, a Summary of Product Characteristics was not approved for this product.

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 conclusion of the decentralised procedure	20th September 2017.
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Ireland

I. SCIENTIFIC OVERVIEW

This is an application for a generic product, Dugnixon 50 mg/ml Solution for Injection for Cattle, Pigs and Horses, in in accordance with Article 13 (1) of Directive 2001/82/EC, as amended. The reference product is Finadyne 50 mg/ml solution for injection authorised in the UK since 1987. The proposed product was considered to be qualitatively and quantitatively the same as the reference product. Minor differences in quantity of the excipients is not expected to have any impact on efficacy.

In cattle, the product is indicated for the control of acute inflammation associated with respiratory disease. The product has also been shown to have some benefit in the treatment of experimental acute bovine pulmonary emphysema (Fog Fever), and may be used as adjunctive therapy in the treatment of acute mastitis.

In horses, the product is indicated for the alleviation of inflammation and pain associated with musculo-skeletal disorders and for the alleviation of visceral pain associated with colic in the horse.

In Pigs, the product is indicated for use as an adjunctive therapy in the treatment of swine respiratory diseases.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto 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, the

[1] SPC – Summary of product Characteristics.

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 [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 QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains 50 mg/ml flunixin as flunixin meglumine and the excipients phenol, diethanolamine, propylene glycol, disodium edetate, sodium formaldehyde sulfoxylate dehydrate and water for injections.

The container/closure system consists of 50 ml and 100 ml sterile and translucent polypropylene vials with a grey butyl rubber cap, grey aluminium cap and a flip-off seal. The product may also be presented in 250 ml sterile and translucent polypropylene vials with a pink butyl rubber cap, grey aluminium cap and a flip-off seal.

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.

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 a simple process of mixing the active substance and excipients to water under nitrogen. Suitable sterilisation is performed, prior to the packaging of the product.

II.C. Control of Starting Materials

The active substance is flunixin, 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

[2] Efficacy – The production of a desired or intended result.

specification have been provided. Acceptable certificates of Suitability were noted. The excipients and packing materials are monographed in the Ph. Eur.

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. 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: appearance, clarity, colour, odour, apparent homogeneity, relative density, refractive index, pH, extractable volume, watertightness/airtightness, labelling, identity, assay, sterility and related substances/impurities.

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.

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. Data were provided for nine batches stored in commercial packaging, three batches stored in each proposed vial size at 25ºC/60% RH for up to 24 months, at 30ºC/65% RH for up to 12 months, and at 40oC/75% RH for up to 6 months. In-use stability data were also provided.

G. Other Information

Based on stability testing results, the following storage precautions appear in the SPC:

- Store below 25ºC
- Keep the vial in the outer container in order to protect from light.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

No pharmacological or toxicological data were required to be submitted for this application.

Toxicological Studies

The applicant is claiming exemption from the requirement for *in vivo* bioequivalence studies in accordance with exemptions 7.1.a) and b) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2). In this instance, it is acceptable that no pharmacological or toxicological data have been provided.

User Safety

A user risk assessment was provided. Warnings and precautions as listed on the product literature, updated to be in line with the CVMP[3] guidance are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- Flunixin meglumine is a non-steroidal anti-inflammatory drug (NSAID).
- The product may cause an allergic reaction in people sensitised to NSAIDs.
- People with known hypersensitivity to NSAIDs should avoid contact with the product. Hypersensitivity reactions may be serious.
- This product may cause skin and eye irritation.
- Avoid contact with skin or eyes.
- In case of skin or eye contact, wash exposed area with plenty of clean water. If symptoms persist, seek medical advice.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- Do not eat or drink when using the product.
- Wash hands after use.

[3] CVMP – Committee for Medicinal Products for Veterinary Use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

A Phase I ernvironmental risk assessment was performed. The product will be used to treat a small number of animals in a flock or herd and as such environmental exposure will be low. A Phase II ERA was not required.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because exemption from provision of bioequivalence studies can be accepted, in accordance with bio-waiver 7.1(a) and (b) of the CVMP guideline on the conduct of bioequivalence studies for VMPs (EMA/CVMP/016/00-Rev.2).

MRLs

The following table shows the maximum residue limits (MRL) for the active substance and excipients.

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
Flunixin	Flunixin	Bovine	20 30 300 100	Muscle Fat Liver Kidney	
	5-Hydroxy flunixin		40	Milk	
	Flunixin	Porcine	50 10 200 30	Muscle Skin+fat Liver Kidney	
		Equidae	10 20 100 200	Muscle Fat Liver Kidney	
Diethanolamine		All species	OOS	All tissues	
Phenol			NMR		
Disodium edetate			NMR		
Propylene glycol			NMR		
Sodium formaldehyde sulfoxylate			NMR		
Hydrochloric acid			NMR		
Purified water			OOS		
NMR = No MRL Required; OOS = Out of scope.					

Withdrawal Periods

Based on the withdrawal periods specified for the reference product, the following withdrawal periods were defined:

Cattle (meat and offal):	5 days
Cattle (milk)	24 hours
Horses (meat and offal):	7 days
Pigs (meat and offal):	22 days

IV CLINICAL DOCUMENTATION

In accordance with the legal basis of the application, it is acceptable that no pre-clinical or clinical data have been provided.

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 is favourable.

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.

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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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