College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Rapidexon 2 mg/ml Solution for Injection

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0284/001/MR
Name, strength and pharmaceutical form	Rapidexon 2 mg/ml Solution for Injection
Applicant	Eurovet Animal Health BV
Active substance	Dexamethasone (as dexamethasone sodium phosphate)
ATC Vetcode	QH02AB02
Target species	Horses, Cattle, Pigs, Cats, Dogs
Indication for use	In horses, cattle, pigs, dogs and cats: Dexamethasone may be used for the treatment of inflammatory or allergic conditions. In cattle: Treatment of primary ketosis (acetonaemia). Induction of parturition In horses: Treatment of arthritis, bursitis or tenosynovitis.

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	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	27 February 2008
Date product first authorised in the Reference Member State (MRP only)	21 February 2006
Concerned Member States for original procedure	Austria Belgium Czech republic Denmark Finland France Greece Hungary Ireland Lithuania The Netherlands Poland Portugal Slovak Republic Slovenia Spain Sweden

I. SCIENTIFIC OVERVIEW

Rapidxon 2 mg/ml Solution for Injection 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 slight reactions observed are indicated in the SPC. 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 overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains the active substance dexamethasone (as dexamethasone soldium phosphate) and excipients sodium chloride, sodium citrate dihydrate (E331), benzyl alcohol (E1519), citric acid monohydrate, sodium hydroxide and water for injections.

The container/closure system comprises clear, colourless, neutral glass (Type I) vials of nominal capacity 30 ml (with either a 25 or 30 ml fill), 50 ml and 100 ml. The multi-dose vials are sealed with a pierceable rubber stopper, allowing removal of the required dose volume. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and 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.

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.

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 substance dexamethasone (as dexamethasone soldium phosphate), an established active substance. Two sources of supply have been approved for use in this injection. From one source, the monograph of the European Pharmacopoeia for dexamethasone sodium phosphate has been taken as the basis for the specification for this ingredient, though additional testing is applied to ensure that potential impurities arising from the specified method of synthesis are limited in accordance with current guidelines. Details of the manufacture and control of the other source of dexamethasone sodium phosphate are presented in Active Substance Master File (ASMF). 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 appropriately controlled and comply with the tests specified in the relevant monograph of the European Pharmacopoeia.

The packaging materials comply with the tests specified in the relevant monographs of the European Pharmacopoeia for materials used for injectable products, together with additional requirements to ensure their suitability for use as containers for this product.

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

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

E. Control on intermediate products

There are no intermediate products.

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 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.

In-use stability testing was carried out on recently manufactured and older vials of the product stored under the recommended temperature conditions. To simulate normal usage, doses were removed at intervals throughout the test period and the product has been shown to remain in compliance with requirements of the shelf-life specification for 28 days.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf life
A shelf-life of 24 months for the veterinary medicinal product as packaged for sale in 50 ml and 100 ml vials was justified.
A shelf-life of 18 months for the veterinary medicinal product as packaged for sale in 25 ml vials was justified.
A 28 days shelf-life after first opening the immediate packaging was justified.

Special precautions for storage
The following warnings are included on the SPC and product literature: “Do not store above 25°C. Do not freeze. Keep vial in the outer carton.”

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological tests are not required.

The pharmacological aspects of this product are identical to the reference product.

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 and consumers.

Toxicological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

The toxicological aspects of this product are identical to the reference product.

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 and consumers.

User Safety

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. These are identical to those of the reference product. These are as follows:

In case of accidental self-injection, seek medical advice immediately and show the package leaflet to the physician.
People with known hypersensitivity to the active substance or any of the excipients should avoid contact with the veterinary medicinal product.
Pregnant women should not handle this veterinary medicinal product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

As this is a generic application according to Article 13, bioequivalence with a reference product has been demonstrated. Justification and data were submitted to support the withdrawal periods and to ensure consumer safety.

The residues aspects of this product are identical to the reference product.

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 consumers.

MRLs

Dexamethasone is listed in Annex I of Council Regulation 2377/90. The marker substance is Dexamethasone.

MRLs are listed below:

	Bovine	Porcine	*Equidae*
Muscle	0.75 µg/kg	0.75 µg/kg	0.75 µg/kg
Liver	2.0 µg/kg	2.0 µg/kg	2.0 µg/kg
Kidney	0.75 µg/kg	0.75 µg/kg	0.75 µg/kg
Milk	0.3 µg/kg	-	-

Withdrawal Periods

Based on the information provided above, a withdrawal period of 7 days for meat and offal in cattle and 72 hours for milk, a withdrawal period of 2 days for meat and offal in pigs, and a withdrawal period of 11 days for meat and offal in horses are justified.

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, pharmacological studies are not required.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, target species tolerance studies are not required.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, clinical 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 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.

•	27 February 2014	To change the distributor.
•	02 January 2014	Change of withdrawal period from 7 days for cattle and 11 days for horses to 8 days for both species for meat and offal.
•	19 April 2013	Change of QPPV and contact details for QPPV for an existing pharmacovigilance system.
•	19 August 2011	Submission of an updated certificate of suitability for the active substance.
•	14 July 2011	Renewal – UK as RMS
•	09 December 2009	Change of distributor
•	19 September 2008	New MA (MRP)
•	02 May 2007	SPC/label changes
•	13 December 2006	Change in the name of the medicinal product
•	11 October 2006	Change of distributor