Irish Medicines Board

(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dexa-ject 2mg/ml solution for injection for cattle, horses, pigs, dogs and cats

MODULE 1

PRODUCT SUMMARY

EU Procedure number	IE/V/0293/001/DC
Name, strength and pharmaceutical form	Dexa-ject 2 mg/ml solution for injection for cattle, horses, pigs, dogs and cats
Applicant	Dopharma Research BV Zalmweg 24 4941 VX Raamsdonksveer Netherlands
Active substance(s)	Dexamethasone sodium phosphate
ATC Vetcode	QH02AB02
Target species	Cattle, horses, pigs, dogs and cats.
Indication for use	Horses, cattle, pigs, dogs and cats: Treatment of inflammatory or allergic conditions. Cattle: Induction of parturition. Treatment of primary ketosis (acetonaemia). Horses: Treatment of arthritis, bursitis or tenosynovitis.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Article 13(1) of Directive 2001/82/EC, as amended
Date of completion of the original decentralised procedure	28/06/2012
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	BE, DE, DK, EE, ES, FR, HU, IS, IT, LT, LV, NL, PL, RO, SE and UK.

I. SCIENTIFIC OVERVIEW

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

This was a generic type application submitted via the decentralised procedure by Dopharma Research B.V. in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The application was submitted in 17 Member States (including the RMS). The concerned Member States for this procedure were BE, DE, DK, EE, ES, FR, HU, IS, IT, LT, LV, NL, PL, RO, SE and UK.

The application is for Dexa-ject 2 mg/ml solution for injection for cattle, horses, pigs, dogs and cats with dexamethasone as active substance. The reference product cited by the applicant is Dexadreson 2 mg/ml Solution for Injection (VPA 10996/27/1, Intervet Ireland Ltd.). Dexadreson 2 mg/ml Solution for Injection was first authorised in the RMS in October 1989.

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 adverse 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 efficacy of the product was demonstrated according to the claims made in the SPC by way of demonstrating bioequivalence to the reference product.

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

II. QUALITY ASPECTS

A. Composition

The product contains dexamethasone 2 mg/ml (as dexamethasone sodium phosphate) as the active substance and the excipients benzyl alcohol, citric acid anhydrous, sodium chloride, sodium citrate, sodium hydroxide and water for injections.

The container/closure system consists of colourless Type I glass vials of 50 ml or 100 ml which are closed with bromobutyl rubber stoppers and sealed with aluminium caps.

B. Method of Preparation of the Product

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 dexamethasone sodium phosphate, 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.

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

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 active substance has 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.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

The application has been submitted in accordance with article 13.1 of Directive 2001/82/EC, as amended (a generic application). The applicant has justified the omission of pharmacological data on the grounds that the product:

- has the same qualitative and quantitative composition in terms of the active substance as the reference product
- has the same pharmaceutical form as the reference product
- can be considered bioequivalent to the reference product.

Justification was provided for the absence of bioequivalence studies on the grounds that:

- the product is to be parenterally administered as a solution for injection and contains the same active substance and the same excipients in nearly the same concentration as the reference product
- the excipients do not affect absorption or in-vivo stability of the active substance
- minor differences in composition in respect of the excipients will not affect the bioavailability of dexamethasone

It was accepted that the candidate formulation and reference product are qualitatively and quantitatively identical in respect of the active substance dexamethasone and that the candidate formulation was qualitatively the same as the reference product in terms of the excipients included in the formulation.

The applicant conducted a comparative analysis of the reference product. Based upon the information available in the SPC of the reference product and the results of the comparative analysis performed by the applicant on the reference product, it could be concluded that the proposed formulation for Dexa-ject is essentially similar to that of the reference product.

Warnings and precautions as listed on the product literature are in line with those of the reference product and other similar products recently authorised via European procedures and considered adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing

Pharmacological Studies

No data presented. Given the legal basis of the application (Article 13.1 – a generic application), the omission of pharmacological studies could be accepted.

Toxicological Studies

No data presented. Given the legal basis of the application (Article 13.1 – a generic application), the omission of toxicological studies could be accepted.

User Safety

The applicant demonstrated essential similarity in formulation between the candidate formulation and the reference product. It was therefore accepted that the safety for the user can be assumed based upon extrapolation of the acceptable safety profile of the reference product. The risk to the user is expected to be the same as any posed by the authorised reference product.

User safety advice in the SPC is in line with that approved for the reference product and other similar products recently authorised via European procedures.

The user safety advice and warnings were considered adequate and appropriate to ensure safe use 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 was required. The assessment concluded that as the product would only be used for the treatment of 'a small number of animals', the environmental impact assessment could end in phase I.

Warnings and precautions as listed on the product literature are considered adequate to ensure safety of the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

No data provided. For generic veterinary medicinal products intended to be administered by intramuscular, subcutaneous or transdermal routes, evidence to demonstrate equivalent or differing depletion of residues from the administration site is normally required. However, in this instance, the applicant satisfactorily demonstrated essential similarity in formulation between the candidate and reference products to justify the omission of specific injection site depletion studies.

MRLs

The active substance dexamethasone is included in table 1 of Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	Marker residue	Animal species	MRL	Target tissues
Dexamethasone	Dexamethasone	Bovine, caprine, porcine, Equidae	0.75 µg/kg 2 µg/kg 0.75 µg/kg	Muscle Liver Kidney
		Bovine, caprine	0.3 µg/kg	Milk

Withdrawal Periods

Based on the data provided, and the withdrawal periods approved for the reference product in various Member States, the following withdrawal periods could be accepted:

Cattle:	Meat and offal:	8 days
Milk:		72 hours
Pigs:	Meat and offal:	2 days
Horses:	Meat and offal:	12 days

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13.1, and essential similarity with a reference product has been demonstrated, efficacy studies were not required. The efficacy claims for this product are in line with those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

No data presented. Given the legal basis of the application (Article 13.1 – a generic application), the omission of pharmacological data could be accepted.

Tolerance in the Target Species of Animals

No data provided. For generic veterinary medicinal products intended to be administered by intramuscular, subcutaneous or transdermal routes, evidence to demonstrate target animal tolerance at the administration site is normally required.

However, in this application, the applicant satisfactorily demonstrated essential similarity between the candidate formulation and the reference product i.e. the product includes the same active substance and the same excipients as the reference product and their concentrations have been shown to be essentially similar.

Given that essential similarity between candidate and reference products has been satisfactorily demonstrated it was accepted that the use of the product as recommended in the proposed SPC will not present an unacceptable risk in terms of target animal tolerance.

Resistance

No data provided. Given the nature of the active substance (corticosteroid) no information in respect of resistance was considered necessary.

IV.B Clinical Studies

Laboratory Trials
Field Trials

No data provided**.** The application has been submitted in accordance with article 13.1 of Directive 2001/82/EC, as amended (a generic application). The applicant satsifactorily justified the omission of clinical studies on the grounds that the product:

- has the same qualitative and quantitative composition in terms of the active substance as the reference product
- has the same pharmaceutical form as the reference product
- can be considered bioequivalent to the reference product.

Justification was provided for the absence of bioequivalence studies on the grounds that:

- the product is to be parenterally administered as a solution for injection and contains the same active substance and the same excipients in nearly the same concentration as the reference product
- the excipients do not affect absorption or in-vivo stability of the active substance
- minor differences in composition in respect of the excipients will not affect the bioavailability of dexamethasone

It was accepted that the candidate and reference products are qualitatively and quantitatively identical in respect of the active substance dexamethasone and that the candidate formulation was qualitatively the same as the reference product in terms of the excipients included in the formulation.

The applicant conducted a comparative analysis of the reference product. Based upon the information available in the SPC of the reference product and the results of the comparative analysis performed by the applicant on the reference product, it could be concluded that the proposed formulation for Dexa-ject is essentially similar to that of the reference product. No clinical studies were therefore considered necessary.

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.