Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

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

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

CALIERCORTIN 4 mg/ml solution for injection

Date: 09 April 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0179/001/DC
Name, strength and pharmaceutical form	CALIERCORTIN 4 mg/ml, solution for injection for cattle, pigs, horses, dogs and cats
Applicant	Laboratorios Calier S.A.
Active substance(s)	Dexamethasone (as sodium phosphate)
ATC Vetcode	QH02AB02
Target species	Cattle, Horse, Pig, Dog and Cat
Indication for use	For palliative (supportive) treatment of the following diseases in cattle, horses, pigs, dogs, and cats: - primary ketoses, - acute, non-infectious arthritis, tendovaginitis and bursitis - non-infectious inflammatory or allergic skin diseases. When using dexamethasone, the indication should always be carefully checked.

MODULE 2

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

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	21 Nov 2018
Date product first authorised in the Reference Member State	n.a.
Concerned Member States for original procedure	AT, BG, CY, EL, ES, HR, IT, PL, PT, RO

I. SCIENTIFIC OVERVIEW

Caliercortin 4 mg/ml solution for injection for cattle, pigs, horses, dogs and cats 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 cattle, pigs, horses, dogs and cats; the slight reactions observed are indicated in the SPC.

Caliercortin 4 mg/ml solution for injection for cattle, pigs, horses, dogs and cats 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.

Caliercortin 4 mg/ml solution for injection for cattle, pigs, horses, dogs and cats is a generic to the German reference product Dexamethason 4 mg/ml solution for injection for cattle, horses, pigs, dogs, and cats of Bela-Pharm GmbH & Co.KG (MA No. 6933074.00.00), which has been authorised in December 2005.

The test and reference product, have the same concentration of the active substance and contain the same excipients in similar quantity. Both products can be considered as bioequivalent in line with the bioequivalence guideline (EMA/CVMP/016/00-Rev.2, 2011).
Therefore, the safety and efficacy of Caliercortin 4 mg/ml solution for injection for cattle, pigs, horses, dogs and cats 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 4.0 mg dexamethasone as dexamethasone sodium phosphate and the excipients benzyl alcohol, propylene glycol, sodium citrate dehydrate, potassium dihydrogen phosphate and water for injection.

The product is packaged in 10 ml amber coloured glass vials (Ph.Eur. type I) and 50 ml amber coloured glass vials (Ph.Eur. type II). The vials are closed with grey chlorobutyl rubber stoppers with a teflon layer and sealed with blue aluminium flip off ring.

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.

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. Scientific data and/or certificates of suitability issued by the EDQM 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.

The claim of a 7 days stability after broaching is based on the demonstration of stability for a batch broached and stored 7 days at +5°C ± 3°C.

G. Other Information

None.

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).

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.

Warnings and precautions as listed on the product literature are in line with 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

A user risk assessment was provided in compliance with the relevant guideline. 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.

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will be used to treat a small number of animals in a flock or herd.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because Caliercortin 4 mg/ml Solution for Injection for Bovine, Porcine, Equine, Dogs and Cats is a generic product. The reference product is authorised with the same withdrawal periods as claimed for Dexacalier 4 mg/ml Solution for Injection for Bovine, Porcine, Equine, Dogs and Cats.

MRLs

Dexamethasone is listed in Table 1 of Commission Regulation (EU) No 37/2010 with the following entry:

Pharmacologically active substance(s)	Marker residue	Animal Species	MRLs	Target tissues	Other provisions
Dexamethasone	Dexamethasone	Bovine, porcine, *Equidae*	0.75 µg/kg 2.0 µg/kg 0.75 µg/kg	Muscle Liver Kidney	
		Bovine	0.3 µg/kg	Milk	

Withdrawal Periods

Based on the MRLs for the active substance and on the established withdrawal periods for the reference product, the following withdrawal periods were set:

Cattle:	Meat and offal:	16 days
	Milk:	4 days
Pigs:	Meat and offal:	4 days
Horses:	Meat and offal.	16 days

Not authorized for use in mares producing milk for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

This is a generic application according to Article 13 (1) of the Directive 2001/82/EC, as amended. The test and the reference product have the same concentration of the active substance and contain the same excipients in similar quantity. Both products can be considered as bioequivalent.

Therefore, pre-clinical and clinical tests are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

As this is a generic application 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.

Possible adverse effects are adequately described in the product literature.

IV.B Clinical Studies

Since this is a generic application 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.

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 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.

28.02.2019	Repeat use procedure to add Spain

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
Extension of the shelf life of the finished product as packaged for sale (supported by real time data) from 18 months to 2 years (DE/V/0179/001/IB/001)	N/A	11.03.2021