College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Acticarp 50 mg/ml Solution for Injection for Cattle

NL/V/0156/001/DC

Created: October 2020

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0156/001/DC
Name, strength and pharmaceutical form	Acticarp 50 mg/ml Solution for Injection for Cattle
Applicant	Ecuphar NV Legeweg 157-i 8020 Oostkamp Belgium
Active substance(s)	Carprofen
ATC Vetcode	QM01AE91
Target species	Cattle
Indication for use	The product is indicated as an adjunct to antimicrobial therapy to reduce clinical signs in acute infectious respiratory disease and acute mastitis in cattle.

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) and on the Medicines Evaluation Board – Veterinary Medicinal Products Unit website (https://www.diergeneesmiddeleninformatiebank.nl/nl).

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 completion of the original decentralised procedure	25 January 2012
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	AT, BE, CZ, DE, EE, ES, FR, IT, LT, LU, LV, PL, PT, SK, UK

I. SCIENTIFIC OVERVIEW

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 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 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.

Acticarp is authorized by means of a generic application. The reference product is RIMADYL CATTLE 50 mg/ml Oplossing voor injectie, authorized under marketing authorization number REG NL 10078 and marketed by Zoetis B.V.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 50 mg carprofen and the following excipients; ethanol, macrogol 400, poloxamer 188, ethanolamine and water for injection

The product is packed in amber type I glass bottles of 50 ml, fitted with grey type I fluorotec rubber stoppers and aluminium caps. The glass vials and stoppers are in conformity with the Ph.Eur. requirements

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

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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.

The product is manufactured using conventional manufacturing techniques. Process validation for three full-scale batches will be fulfilled post-authorisation.

The tests performed during production are described.

C. Control of Starting Materials

The active substance is carprofen, an established active substance described in the European/British Veterinary 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.

The excipients are in conformity with compendial requirements
The glass vials and stoppers are in conformity with the Ph.Eur. requirements.

D. Control on intermediate products

Adequate in-process specifications of bulk solution for Carprofen Injection before filtration has been provided.

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 have been provided in accordance with applicable European guidelines, confirming the retest period 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 of 3 years when stored under the approved conditions.

G. Other Information

None.

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III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

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

III.A Safety documentation

User Safety

Warnings and precautions as listed on the product literature are identical to those of the reference product. These 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 bioequivalence with the reference product is claimed.

However, as the product is also intended to be administered by the subcutaneous route, an injection site residue depletion study in cattle was performed with the final product at the recommended dose. The marker residue, sum of carprofen and carprofen glucuronide was measured at the injection site. The results demonstrated that residue levels are below muscle MRL (500 µg/kg) at 12 days post injection. These data confirm that the proposed withdrawal period of 21 days for meat of cattle is sufficient.

MRLs

Carprofen is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Marker residue	Animal Species	MRL (µg/kg)	Target Tissues
Sum of carprofen and carprofen glucuronide conjugate	Bovine, Equidae Bovine	500 1000 1000 1000 No MRL required	Muscle Fat Liver Kidney Milk

For all excipients, no MRL is required.

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Withdrawal Periods

Based on the data provided above, a withdrawal period of 21 days for meat in cattle and zero hours for milk are justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Since the product can also be administered subcutaneously, a local tolerance study was carried out. Within 48 hours after administration, 8 animals out of 18 showed swelling at the site of injection. None of the animals showed signs of irritation or any signs of deviation in general health condition which would have been caused by the injection. Swellings decreased in size with time and required 17 to 19 days to become unnoticeable. This adverse reaction is adequately described in the product literature.

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.

Summary of change	**Section updated**	**Approval date**
Change of the name in Spain (NL/V/0156/001/IB/001)	N/A	30 August 2012
Change in the manufacturing process of the finished product (NL/V/0156/001/IB/002)	N/A	10 October 2012
Change in the shelf life of the finished product as packaged for sale (NL/V/0156/001/IB/003)	Module 3, section 2.F SPC	3 March 2012
Addition of two sites for batch control/testing arrangements (NL/V/xxxx/IA/012/G)	N/A	26 February 2015
Renewal (NL/V/0156/001/R/001)	N/A	8 August 2016
Update DDPS (NL/V/xxxx/IA/021/G)	N/A	11 January 2017
Minor change in the manufacturing process (NL/V/0156/001/IA/005)	N/A	23 March 2017
Update DDPS: change in QPPV (NL/V/xxxx/IA/027/G)	N/A	11 October 2018