College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
3531 AH Utrecht
The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Carofertin 10 mg/ml emulsion for injection for cattle and pigs

Created: December 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0194/001/DC
Name, strength and pharmaceutical form	Carofertin 10 mg/ml emulsion for injection
Applicant	ALVETRA u. WERFFT GmbH Boltzmanngasse 11 1090 Vienna Austria
Active substance(s)	Beta-carotene
ATC Vetcode	QA11CA02
Target species	Cattle (cows/heifers), pig (sows)
Indication for use	For the prevention and treatment of betacarotene deficiency and beta-carotene deficiency related fertility disorders, which can arise during phases of insufficient nutritional supply.

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	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	10 June 2015
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	RO
Concerned Member States for Repeat Use procedure	BE, DK, ES, FR, HR, IE, IT, 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.

Carofertin is a generic application. The reference product is Carofertin, (Zul .Nr. 400196.00.00) of marketing authorisation holder ALVETRA GmbH, which is registered in the Germany since 29 July October 1998. The initial application for Carofertin in Germany was assessed before there was a requirement to have a public assessment report; therefore no details in this section are available.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 10 mg/ml betacarotene and the excipients ascorbyl palmitate, all-racα-tocopherol, benzyl alcohol, macrogol 15 hydroxystearate (Solutol HS 15), isopropyl myristate and water for injections. Benzyl alcohol is used in the formulation as solubilizer.

The drug product is packed in Ph.Eur. Type II brown glass vials with Ph.Eur. Type I bromobutyl rubber stoppers and an aluminium cap and is available in a fill volume of 100 ml. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and presence and antioxidants 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 betacarotene, 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 adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided. For the active substance a CEP has been provided, i.e. CEP No. R0-CEP 2010-383-Rev 01 by DSM Nutritional Products Ltd.

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

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are 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, are not acceptable yet. The validation report for the method for isomers determination need to be submitted.

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, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product packed in 100 ml bottles 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 claimed shelf-life and storage conditions are justified.

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years
Shelf-life after first opening the immediate packaging: use immediately; do not store.

G. Other Information

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmaco-toxicological tests are not required. The pharmaco-toxicological aspects of this product is/are identical to the reference product.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline. Warnings and precautions listed on the product literature are:
"Care should be taken to avoid accidental self_injection.
In case of accidental self_injection, seek medical advice immediately and show the package leaflet or the label to the physician.
People with known hypersensitivity to betacarotene or to any of the excipients should administer the veterinary medicinal product with caution.
Wash hands after use."
These warnings and precautions 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 active substance is a natural substance, the use of which will not alter the concentration or distribution of the substance in the environment and the initial predicted environmental concentration in soil (PECsoil, initial = 5.8 µg/kg for dairy cows and 1.9 µg/kg for sows) is less than 100 µg/kg.

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.

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.

Carofertin10 mg/ml emulsion for injection for cattle and pigs	NL/V/0194/001/DC
ALVETRA u. WERFFT GmbH	DCP
	Publicly available assessment report

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**
Repeat Use procedure CMS: BE, DK, ES, FR, Hr, IE, IT, UK (NL/V/0194/001/E/001)	Module 3	17 December 2015
Change name of medicinal product from: Betacarotene 10 mg/ml to: Carofertin 10 mg/ml (NL/V/0194/001/DC)	Module 1	7 January 2016
Changes to the SPC for RO after Repeat Use procedure (NL/V/0194/001/II/002)	N/A	15 March 2016
A typing error in the authorised release specification is corrected Updated Ph. Eur. certificate of suitability from an already approved manufacturer (NL/V/0194/IA/003/G)	N/A	3 November 2017
Renewal (NL/V/0194/001/R/001)	N/A	Pending