Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vitamin AD_3E pro injectione, solution for injection for horses, cattle, pigs, and dogs (DE, HR, IS, IT, LV, PT)
Vitamin AD_3E, solution for injection for horses, cattle, pigs, and dogs (AT)
Belavit AD_3E, solution for injection for horses, cattle, pigs, and dogs (CY, EL, ES, FR, IE, SL, UK)
Belavit AD_3E vet., solution for injection for horses, cattle, pigs, and dogs (NO)

Date: 03 April 2019

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0313/001/MR
Name, strength and pharmaceutical form	Vitamin AD3E pro injectione, solution for injection for horses, cattle, pigs, and dogs (DE, HR, IS, IT, LV, PT) Vitamin AD3E, solution for injection for horses, cattle, pigs, and dogs (AT) Belavit AD3E, solution for injection for horses, cattle, pigs, and dogs (CY, EL, ES, FR, IE, SL, UK) Belavit AD3E vet., solution for injection for horses, cattle, pigs, and dogs (NO)
Applicant	Bela-Pharm GmbH & Co. KG Lohner Str. 19 49377 Vechta
Active substance(s)	Retinol palmitate all-rac-alpha-Tocopherylacetate Cholecalciferol concentrate (oily form)
ATC Vetcode	ATC vet code: QA11JA
Target species	Cattle, Horses, Pigs and Dogs
Indication for use	Treatment of combined vitamin A, vitamin D, and vitamin E deficiencies.

MODULE 2

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

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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 mutual recognition procedure	03 April 2019
Date product first authorised in the Reference Member State (MRP only)	08 May 2018
Concerned Member States for original procedure	AT, HR, CY, FR, EL, IS, IE, IT, LV, NO, PT, ES, SI, UK

I. SCIENTIFIC OVERVIEW

The safety and efficacy aspects of this product are identical to the reference product "Belavit AD_3E injekcio A.D.V." authorised for cattle, horses pigs and dogs in Hungary in 2013 (reference number 3314/1/13 NEBIH ATI). The Lithuanian authorisation of "Vitamin AD_3E, injecinis tirpalas" in 2007 (reference number LT/2/94/0131/001) served as initial authorisation and reference product regarding the protection period.
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.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 176.47 mg retinol palmitate (equivalent to 300,000 I.U. Vitamin A), 50.00 mg all-rac alpha tocopheryl acetate (equivalent to 45.56 mg alpha-tocopherol), 100.00 mg oily solution of cholecalciferol (contains 2.5 mg cholecalciferol;

equivalent to 100,000 I.U. Vitamin D3) as active substances and the excipients medium-chain triglycerides and DL-alphatocopherol.

The veterinary medicinal product is marketed in 100 ml brown glass vials with bromobutyl stoppers and aluminium caps, packed in carton boxes.

The choice of the formulation is 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 substances retinol palmitate, all-rac alpha tocopheryl acetate and cholecalciferol (oily solution) are established substances described in the European Pharmacopoeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The specifications of the active substances are 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 and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

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, 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 substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances when stored under the approved conditions, or the active substance is fully tested to ensure compliance with its specification immediately prior to its use in manufacture of the product.

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 28 days stability after broaching is based on the demonstration of stability for a batch broached.

G. Other Information

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13(1) and bioequivalence with the reference product has been accepted, similar safety is assumed. Results of safety tests are not required.

Pharmacology and toxicology of this product is identical to the reference product.

Warnings and precautions as listed on the product literature are in line with current standards of the user safety guideline EMA/CVMP/543/03-Rev.1 and are adequate to ensure safety of the product to users, the environment and consumers.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline EMA/CVMP/543/03-Rev.1 which shows that all vitamins are characterized by low acute toxicity, but have the potential to cause adverse effects mainly due to prolonged exposure to high doses. Users are veterinarians or professional farmers potentially exposed to the product via skin contact, ocular exposure as well as accidental self-injection.
The most critical endpoints of vitamin A are its teratogenic potential and adverse effects on liver and bone density. The main effect of a vitamin D hypervitaminosis is hypercalcaemia with associated symptoms including organ calcification and renal and cardiovascular damage. Adverse effects of vitamin E on blood clotting, severe muscular weakness and fatigue are reported in therapeutic use. Local toxicity of the product is irritation of the skin and eyes and a skin sensitizing potential.
Taking all aspects into account suitable warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

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.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted as this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed.

MRLs

The active ingredients are listed in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as amended:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs	Target tissues	Other provisions
Vitamin A	Not applicable	All food producing species	No MRL required	Not applicable	No entry
Vitamin D	Not applicable	All food producing species	No MRL required	Not applicable	No entry
Vitamin E	Not applicable	All food producing species	No MRL required	Not applicable	No entry

All excipients are considered as not falling within the scope of Regulation (EC) No 470/2009 (EMA/CVMP/519714/2009–Rev.38) with regard to residues of veterinary medicinal products in foodstuffs of animal origin, when used as in this product.

Withdrawal Periods

Based on the data provided and comments of some CMS, the following withdrawal periods are justified.

Cattle: meat and offal: 50 days
milk: 0 hours

Horse: meat and offal: 50 days
Not authorised for use in horses producing milk for human consumption.

Pig: meat and offal: 20 days

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC as amended, and similarity 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.

IV.A Pre-Clinical Studies

As this is a generic application according to Art. 13 (1) of Directive 2001/82/EC, as amended, preclinical studies are not required.

Tolerance in the Target Species of Animals

Due to the similarity of generic and reference formulations, studies on target animal tolerance are not required. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies

As this is a generic application according to Art. 13 (1) of Directive 2001/82/EC, as amended, clinical studies are not required.

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.

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