College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vigophos 100/0.05 mg/ml Solution for Injection for Cattle

Updated: 26 February 2024

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0426/001/DC
Name, strength and pharmaceutical form	Vigophos 100 mg / ml + 0.05 mg / ml solution for injection for cattle (AT, BE, CZ, DE, DK, ES, HU, IE, IT, NL, PL, PT, RO, SI, SK, UK) Vigophos vet 100 mg / ml + 0.05 mg / ml solution for injection for cattle (SE)
Applicant	Livisto Int'l, S.L. Avenida Universitat Autonoma 29 E-08290 Cerdanyola del Valles (Barcelona) Spain
Active substance(s)	Butafosfan Cyanocobalamin
ATC Vetcode	QA12CX91
Target species	Cattle
Indication for use	For the supportive treatment of secondary ketosis (e.g in abomasal displacement).

MODULE 2

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	31 January 2018
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure	AT, BE, CZ, DK, HU, IE, IT, NL, PL, PT, RO, SI, SK, ES, SE, and UK (DE was the former RMS, procedure number DE/V/0172/001)

I. SCIENTIFIC OVERVIEW

The Vigophos 100/0.05 mg/ml solution for injection for cattle 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.

Vigophos 100/0.05 mg/ml solution for injection for cattle 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 safety and efficacy aspects of this product is identical to the German reference product Catosal 100/0.05 mg/ml solution for injection for cattle, Bayer Vital GmbH (authorisation number: 6294349.00.00). 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 butafosfan 100.0 mg/ml, cyanocobalamin 0.05 mg/ml and the excipients benzyl alcohol, sodium hydroxide and water for injections.

The container/closure system are brown glass flasks of hydrolytic class type II closed with coated bromobutyl or chlorobutyl rubber stoppers and aluminium caps.

The choice of the preservative is fully 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 in accordance with the principles of good manufacturing practice at licensed manufacturing sites.

The product is manufactured using conventional manufacturing techniques. Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substances butafosfan and cyanocobalamin are established active substances and cyanocobalamin is described in the European Pharmacopoeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

Scientific data for butafosfan and certificates of suitability for cyanocobalamin issued by the EDQM have been provided.

The active substances specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with the specifications 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 sites 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.

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 and stored 28 days at +25°C/60% RH.

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 a reference product has been demonstrated, safety studies are not necessary.

The pharmacology and toxicology aspects of this product are identical to the reference product, with the exception of the substitution of the excipient 1-butanol with benzyl alcohol. The pharmacology and toxicology aspects of benzyl alcohol, which is commonly used as a preservative in many injectable drugs and solutions, have been evaluated.

User Safety

The applicant has provided and updated a user safety assessment in compliance with the relevant guideline which shows all potential routes of accidental administration

and confirms that the product is not expected to pose a risk for users when used as recommended. The following warnings and precautions as listed in the product literature are adequate to ensure safety to users of the product:

People with known hypersensitivity to any of the ingredients should avoid contact with the product.

The product might be mildly irritating to the skin and the eye. Dermal and ocular exposure should therefore be avoided. In case of exposure rinse the skin and/or the eye with water.

Environmental Risk Assessment

A 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 because this is a generic application submitted in accordance to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with the reference product can be assumed.

MRLs

The active substances are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmaco-logically active substance	Marker residue	Animal Species	MRL	Target tissues	Other pro-vision	Thera-peutic Classi-fication
Butafosfan	NOT APPLICABLE	All mammalian food producing species	No MRL required	NOT APPLICABLE	NO ENTRY	Alimentary tract and metabolism/mineral supplements
Vitamin B12	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	NO ENTRY	NO ENTRY

Withdrawal Periods

Based on the data provided above, a withdrawal period of zero 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, results of toxicological, pharmacological and clinical tests are not required. The efficacy claim for this product is equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

This is an application for a generic product. Both products are identical in terms of quality and quantity of the active substances. Furthermore, Vigophos 100/0.05 mg/ml solution for injection for cattle and Catosal 100/0.05 mg/ml solution for injection for cattle show similar impurity profiles of both active substances. Systemic and local

tolerance has been justified. Studies have not been provided. There is no impact expected neither from the active substances nor the excipients.

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.

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
Change in the shelflife or storage conditions of the finished product (DE/V/0172/001/IB/001)	N/A	13/04/2018
B.II.f.1.b.1 Change in the shelf-life or storage conditions of the finished product - Extension of the shelf life of the finished product as packaged for sale (supported by real time data) (DE/V/0172/001/IB/003)	N/A	17/12/2021
RMS change from DE/V/0172/001 to NL/V/0426/001	Admin. info	26/02/2024