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Czech Republic
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Catophos 100 mg/ml + 0,05 mg/ml solution for injection

MODULE 1

PRODUCT SUMMARY

EU Procedure number	CZ/V/0173/001/DC
Name, strength and pharmaceutical form	**Catophos 100 mg/ml + 0,05 mg/ml solution for injection for horses, cattle, dogs and cats**
Applicant	CP-Pharma Handelsgesellschaft, mbH Ostlandring 13 31303 Burgdorf Germany
Active substance(s)	Butafosfan 100.00 mg Cyanocobalamin (vitamin B12) 0.05 mg
ATC Vet code	QA12CX99
Target species	Cattle, horses, dogs and cats
Indication for use	As supportive treatment of metabolic or reproductive disorders, when supplementation of phosphorous and cyanocobalamin is needed. In case of peri-parturient metabolic disorders, tetany and paresis (milk fever), the product should be administered in addition to magnesium and calcium, respectively. Supporting muscle function in the presence of deficiencies of phosphorous and/or cyanocobalamin.

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	Hybrid application in accordance with Article 13.3 of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	17/04/2023
Date product first authorised in the Reference Member State (MRP only)	N.A.
Concerned Member States for original procedure	AT, BE, DE, DK, EE, ES, FI, FR, HU, IE, IT, LT, LV, NL, NO, PL, PT, SE, SK, UK(NI)

I. SCIENTIFIC OVERVIEW

This was determined a hybrid application in accordance with Article 13 (3) of Directive 2001/82/EC, as amended.

The reference product is Catosal solution for injection marketed by Bayer Animal Health GmbH, which was first authorised in Czech Republic on 09/09/1994 on the basis of full dossier in accordance with Art. 12.3 of Directive 2001/82/EC.
The proposed product is quantitatively and qualitatively the same as the reference product as regards the active substances, and contains comparable excipients in similar amounts. Biowaiver according to the section 7.1 a) and b) of the CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4) was accepted.

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; any 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 100 mg of butafosfan and 0.050 mg of cyanocobalaminum (vitamin B12) and the excipients benzyl alcohol, sodium hydroxide, diluted hydrochloride acid and water for injections.

The product is filled in amber type II glass vials of either 100 or 250 ml that are closed with a bromobutyl rubber stopper and an aluminium cap.

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 for the smallest batch size and process validation on two batches produced at the largest batch size scale will be performed post-authorisation.

C. Control of Starting Materials

The active substance cyanocobalamin is an established active substance described in the European Pharmacopoeia. 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.
The active substance butafosfan is an established active substance which is not described in the pharmacopoeia. The control of butafosfan is in line with specification given in ASMF.

The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substances specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with this specification have been provided.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

The active substances specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with these specifications have been provided.

The excipients are in conformity with Ph. Eur. requirements. No excipients are within the scope of the TSE Guideline present or used in the manufacture of this product.

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

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 butafosfan and cyanocobalamin from respective manufacturers have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance butafosfan over 60 months and cyanocobalamin over 60 months when stored under the approved conditions.
The active substance cyanocobalamin from the other manufacturer 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 (protected from light). Shelf life of the veterinary medicinal product as packaged for sale is 2 years.

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

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a hybrid application according to Article 13, results of pharmacological and toxicological tests are not required.

Warnings and precautions as listed on the product literature of the reference product were updated and are adequate to ensure safety of the product to users.

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 the environment / consumers.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline and 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 assessment can stop at question no. 3 for dogs and cats and for cattle and horses at question no. 5 of the decision tree.

Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to the environment.

III.B Residues documentation

Residue Studies

The application has been submitted in accordance with article 13.3. of Directive 2001/82/EC as amended, so called hybrid application.
The product is quantitatively and qualitatively the same as the reference product as regards the active substances, and contains comparable excipients in similar quantities. Biowaiver according to the section 7.1 a) and b) of the CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4) has been accepted.
No residue depletion studies have been performed.

MRLs

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

Pharmacologically active substance	**Marker residue**	**Animal species**	**MRLs**	**Target tissues**	**Other provisions**
Butafosfan	Not applicable	All mammalian food producing species	No MRL required	Not applicable	No entry
Vitamin B12	Not applicable	All food producing species	No MRL required	Not applicable	No entry

The excipients (benzyl alcohol, hydrochloric acid, sodium hydroxide, water for injections) are included in Table 1 in Annex of Commission Regulation (EU) No 37/2010 of December 22 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin or are considered as not falling within the scope of Council Regulation 470/2009.

Withdrawal Periods
On the basis of the data mentioned above, the withdrawal periods of zero days for cattle´s meat and offal and zero hours for milk have been established. The withdrawal periods of zero days for meat and offal and zero hours for milk have been extrapolated from cattle to horses (for intravenous route of administration) based on the principles, which are mentioned in the Guideline (EMA/CVMP/SWP/66781/2005–Rev.1 - point 7.2.1.1. Identical products).

The withdrawal periods of the product are the following:
Cattle, horses:
Meat and offal: zero days
Milk: zero hours

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a hybrid application according to Article 13(3) of Directive 2001/82/EC, as amended, and an exemption from bioequivalence studies according to the section 7.1a) and b) of the CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4) was accepted, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

Due to the nature of the application, which was for a hybrid product, no data were required for this section.

Tolerance in the Target Species of Animals

Due to the nature of the application, which was for a hybrid product, no data were required for this section.

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

None.