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French agency for veterinary medicinal products

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(Reference Member State)

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

MENDOTIZER 100 mg/mL Solution for injection

Date : 27/07/2023

PRODUCT SUMMARY

EU procedure number	FR/V/0458/001/DC
Name, strength and pharmaceutical form	MENDOTIZER, 100 mg/ml, solution for injection.
Applicant	DOPHARMA RESEARCH / ZALMWEG 24 – 4941 VX RAAMSDONKSVEER – PAYS-BAS
Active substance(s)	Menbutone
ATC vetcode	QA05AX90
Target species	Cattle, pigs, horses, sheep and goats.
Indication for use	Stimulation of hepato-digestive activity in case of digestive disorders and hepatic insufficiency.

PRODUCT INFORMATION

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).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Generic application in accordance with Article 18 of Regulation (EC) 2019/6 as amended.
Reference product (RP)	GENABILINE
Marketing authorisation holder	Boehringer Ingelheim Animal Health France
Marketing authorisation number	FR/V/7302331 5/1981
Date of authorisation	11/12/1981
Date of completion of the original decentralised procedure	03/05/2023
Concerned Member States for original procedure	BE, IT, NL, PL

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the observed reactions are indicated in the SPC.

The VMP 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 VMP was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP contains 100 mg/mL of menbutone and the excipients chlorocresol, ethanolamine and water for injections.

The container/closure system is a 100 ml colourless type I glass vial closed with grey rubber stopper and sealed by an aluminium cap with centre hole. Each vial is placed in a cardboard box to protect vials from light.

The choice of the formulation is justified.

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

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

Process validation data on the VMP have been presented in accordance with the relevant European guidelines.

C. Production and control of starting materials

The active substance is menbutone, an established active substance. 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.

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

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 VMP.

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 tests

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 have been provided in accordance with applicable European guidelines, demonstrating the stability of the VMP throughout its shelf life when stored under the approved conditions.

The in-use shelf-life of the broached VMP is supported by the data provided. The recommendations in the product leaflet should be followed.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of safety tests are not required.

A. Safety tests

Pharmacological studies

See part 4.

Toxicological studies

The application is made in accordance with Article 18 of Regulation 2019/6 (generic application), and therefore specific toxicological data on safety relating to the active substance are not required.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

This application is submitted in accordance with article 18 of Regulation 2019/6. No ERA is required as a similar product (Menbutil 100 mg/ml solution) has been authorized after October 2005. According to the Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/6 (EMA/CVMP/ERA/622045/2020), an ERA for the product under application is not requested.

B. Residues documentation

Residue tests

No residue depletion studies were conducted.

Maximum Residue Limits

The active substance, menbutone, is an allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010, as follows :

Marker residue	Animal Species	MRL	Target Tissues	Other Provisions	Regulation
Not applicable	Bovine, ovine, caprine, porcine, *Equidae*	No MRL required	Not applicable	No entry	37/2010 of 22.12.2009

An acceptable daily intake (ADI) of 60 µg/kg, i.e. 3600 µg/person is defined for menbutone.

The MRL status of excipients of the product MENDOTIZER is indicated in the following table.

Excipient	MRL status
Chorocresol	No MRL required without ADI, for all food producing species
Monoethanol amine	No MRL required without ADI, for all food producing species
Water for injection	Out of scope

The composition of the product MENDOTIZER is acceptable according to the European regulation (EC) No 470/2009.

Withdrawal Periods

The applicant proposed the withdrawal periods of the reference product.

As the product can be administered intramuscularly, an ADI was defined for the active substance and as the qualitative composition is different, the “meat and offal” withdrawal period of 1 day is notified following intramuscular route.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

MENDOTIZER is a solution for injection containing menbutone. This product is indicated for stimulation of hepato-digestive activity in case of digestive disorders and hepatic insufficiency in cattle, pigs, horses, sheep and goat for cattle, pigs, horses, sheep and goats. The product is administered via intramuscular or intravenous administration at a recommended dose of 2.5 to 10 mg of menbutone per kg bw according to the species.

MENDOTIZER is submitted in accordance with Article 18 of Regulation (EU) 2019/6.

Pharmaceutical form

The test and the reference products have the same pharmaceutical form: solution for injection.

Active substance qualitative and quantitative composition

The test and reference products have the same qualitative and quantitative composition in active substance: 100 mg of menbutone per ml of product.

Bioequivalence studies

No study was provided.

The bioequivalence was satisfactorily demonstrated according to the section 7.1. of the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4).

The test and the reference products can be considered as bioequivalent.

A. Pre-Clinical Studies

No pre-clinical studies were performed.

Pharmacology

Given the legal basis of this application and the claim of bioequivalence between candidate and reference products, the omission of pharmacodynamic & pharmacokinetic data can be accepted, as this information may be extrapolated from the reference product.

The RMS notes that the information proposed for inclusion in sections 4.2 & 4.3 of the SPC of the test product are in line with the text approved for sections 5.1 & 5.2 of the SPC of the reference product.

Dose determination and confirmation

No dose determination and confirmation studies are required since the bioequivalence of the candidate product to the reference product is considered demonstrated in accordance with the “Guideline on the conduct of bioequivalence studies for veterinary medicinal products” (EMA/CVMP/016/2000-Rev.4).

Tolerance in the target species of animals

No tolerance study has been provided. It is accepted that the target animal safety profile of the test product will be the same as that of the reference product. The text in sections 4.6 and 4.10 of the proposed SPC is in line with the text agreed for the reference product

B. Clinical trials

No clinical trials were performed.

As this is a generic application according to Article 18 of Regulation (EC) 2019/6, clinical trials are not required to demonstrate the efficacy.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP 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 VMP for humans and the environment is acceptable.

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. The current SPC is available in the Union Product Database (UPD).

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 VMP.

None