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Czech Republic
(Reference Member State)

SUBSEQUENT RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

INTRAMAR SEAL 2.6 g intramammary suspension for cattle

MODULE 1

PRODUCT SUMMARY

EU Procedure number	CZ/V/0182/001/E/001
Name, strength and pharmaceutical form	INTRAMAR SEAL 2.6 g intramammary suspension for cattle (CZ, AT, BE, BG, DE, EE, EL, HU, IT, LV, LT, PL, RO, SK) INTRAMAR SEAL intramammary suspension for cattle (FR) Dryseal vet (DK, SE) Rumiseal 2.6 g intramammary suspension for cattle (ES, PT) MASTIC SEAL 2.6 g intramammary suspension for cattle (IE, UK(NI))
Applicant	Bioveta, a.s. Komenského 212 683 23 Ivanovice na Hané Czech Republic
Active substance(s)	Bismuth subnitrate, heavy
ATCvet code	QG52X
Target species	Cattle (dairy cows at drying-off).
Indication for use	For the prevention of new intramammary infections throughout the dry period. In cows considered likely to be free of subclinical mastitis, the veterinary medicinal product can be used on its own in dry cow management and mastitis control.

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	Art. 19 – Hybrid application
Date of completion of the original mutual recognition/subsequent recognition procedure	31/05/2023 28/02/2024
Date product first authorised in the Reference Member State	31/03/2022
Concerned Member States	Old CMSs: BG, EE, LT, LV, PL, RO, SK New CMSs (SRP-1th wave): AT, BE, DE, DK, EL, ES, FR, HU, IE, IT, PT, SE, UK(NI)

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.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains 2.6 g of the active substance bismuth subnitrate, heavy in each intramammary syringe and the excipients aluminium stearate, silica colloidal anhydrous and liquid paraffin.

The container/closure system consist of LDPE intramammary syringes (LDPE cover, LDPE cuff, LDPE plunger) closed with a LDPE cap containing 4 g of suspension and packed in a cardboard box or in a plastic container with a lid. The authorised package sizes are a paper box containing 24 intramammary syringes or a plastic container with a lid containing 160 intramammary syringes. Each package includes 24 or 160 disinfectant wipes moistened with 65% v/v isopropyl alcohol solution (2.4 ml/wipe) to clean teats.

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 substance bismuth subnitrate, heavy is an established active 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 considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

Scientific data and a certificate of suitability issued by the EDQM has been provided.

The excipients are described in the Ph. Eur. monographs and are controlled accordingly.

The quality control of the packaging material and its components is adequately described.

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 site have been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substance has been provided in accordance with applicable European guidelines demonstrating the stability of the active substance when stored under the approved conditions or are covered by the relevant certificate of suitability issued by the EDQM.
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.

III. SAFETY AND RESIDUES ASSESSMENT

As this is a hybrid application according to Article 19, results of pharmacological and toxicological tests are not required.

The amended warnings and precautions as listed on the product literature 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. 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 initial predicted environmental concentration in soil for dairy cows (dry cows) both intensively (PECsoil, initial = 78.58 µg/kg) and pasture reared (PECsoil, initial = 48.52 µg/kg) is less than 100 µg/kg.

III.B Residues documentation

Residue Studies

The application was submitted in accordance with Article 19 of Regulation 2019/6, i.e. as a hybrid application.

Based on the information provided by the applicant on the physico-chemical properties (qualitative and quantitative composition, particle size, viscosity and density) of the reference and candidate formulation, the similarity of both products has been demonstrated.

MRLs

The active substance is 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
Bismuth subnitrate	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	For oral use only.
		Bovine	No MRL required	NOT APPLICABLE	For intramammary use only

The excipients (aluminium di/tri stearate, liquid paraffin, silica colloidal anhydrous) are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 with the entry "No MRL required".

Withdrawal Periods

On the basis of the above data, the withdrawal periods of zero days for cattle meat and offal and zero hours for milk have been established.

The withdrawal periods are as follows:
Meat and offal: Zero days.
Milk: Zero hours.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a hybrid application according to Article 19, and a waiver from bioequivalence studies was accepted according to the relevant guideline (EMA/CVMP/344/1999-Rev.2 "Guideline on the conduct of efficacy studies for intramammary products for use in cattle"), efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

Tolerance studies were not required due to the legal base of the application.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies

Based on the information on the physico-chemical properties (qualitative and quantitative composition, particle size, viscosity and density) of reference Orbeseal 2.6 g intramammary suspension and candidate formulation provided by the applicant, similarity of both products has been demonstrated. The requirements on quality according to the guideline EMA/CVMP/344/1999-Rev.2 "Guideline on the conduct of efficacy studies for intramammary products for use in cattle" were provided and therefore no further data are 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 in the Union Product Database (UPD).