DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

DRAFT PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

PERMAWAY 600 mg intramammary suspension for cattle

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0384/001/DC
Name, strength and pharmaceutical form	PERMAWAY 600 mg intramammary suspension for cattle
Applicant	LABORATORIOS KARIZOO, S.A. Pol. Ind. La Borda, Mas Pujades 11-12 08140 Caldes de Montbui Spain VETOQUINOL S.A. Magny-Vernois 70200 LURE France
Active substance(s)	Cloxacillin (as benzathine)
ATC vet code	QJ51CF02
Target species	Dairy cattle (dry cows).
Indication for use	For the treatment of subclinical mastitis at dry-off and prevention of new intramammary infections occurring during the dry period, caused by Trueperella pyogenes, Staphylococcus spp., Streptococcus agalatiae, Streptococcus dysgalactiae and Streptococcus uberis, susceptible to cloxacillin.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (http://www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13(3) Hybrid application of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	Day 210: 21/10/2020
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	AT, BE, CY, CZ, DE, EE, EL, FR, HU, IE, IT, LT, LU, LV,MT, NL, PL, PT, RO, SI, SE, SK, UK

I. SCIENTIFIC OVERVIEW

This was an hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended. PERMAWAY 600 mg is the generic veterinary medicinal product and contains Cloxacillin (as benzathine) as active substance for intramammary use. The product is indicated for the treatment of subclinical mastitis at dry-off and prevention of new intramammary infections occurring during the dry period. The reference product is Orbenin 600 mg authorised in Spain since 1989.

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 cloxacillin benzathine 600 mg/3.6 g and aluminium stearate, stearic acid and liquid paraffin as excipients.

The container/closure system is a 7 ml LDPE white intramammary syringe containing 3.6 g of product.

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 from 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 is cloxacillin benzathine an established active substance described in the British Veterinary 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.

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.

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.

G. Other Information

None

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

For generics, insert in the relevant sections as appropriate:

As this is a hybrid application according to Article 13 (3), and bioequivalence with a reference product has been demonstrated, results of safety and residues tests are not required.

The safety aspects of this product are identical to the reference product.

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 users, the environment and the consumers.

III.A Safety Testing

Pharmacological Studies

As this is a hybrid application according to Article 13(3), and bioequivalence with a reference product has been demonstrated, results of pharmacological studies are not required.

Toxicological Studies

As this is a hybrid application according to Article 13(3), and bioequivalence with a reference product has been demonstrated, results of toxicological studies are not required.

The safety aspects of this product are identical to the reference product.

User Safety

The applicant has not provided a user safety assessment. As bioequivalence with the reference product has been demonstrated, and the composition of both the VMP and the reference product is similar for excipients and active substance, the product is not expected to pose a higher risk on the user.

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 predicted environmental concentration of the VMP in soil (PECsoil) is below 100 µg/kg.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used in accordance with the SPC.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted on the basis that bioequivalence with the reference product has been demonstrated.

MRLs

The active substance, Cloxacillin, is and allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010.

MRLs are listed below:

Compound	**Edible tissues (µg/kg)**	**Milk (µg/kg)**
Cloxacillin	300	30

The excipients are classified as follows:

Excipient	***Status***
Stearic acid	*Included in table 1 of Commission Regulation (EU) No 37/2010 – No MRL required. Food additive E-570*
Aluminium stearate	*Included in table 1 of Commission Regulation (EU) No 37/2010 – No MRL required.*
Liquid paraffin	*Included in table 1 of Commission Regulation (EU) No 37/2010 – No MRL required*

Withdrawal Periods

The same withdrawal periods than the reference product are proposed for the VMP as follows:

Meat and offal: 28 days
Milk: Interval between treatment and calving is 42 days or longer: 4 days after calving.
Interval between treatment and calving is less than 42 days: 46 days after treatment.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence 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.

The applicant has justified the omission of bioequivalence studies by referring to the guideline on the conduct of efficacy studies for intramammary products for use in cattle (EMEA/CVMP/EWP/141272/2011), section 8 ‘Generic products.

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 veterinary Heads of 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