IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Huvebiotic 330 mg/100 mg Intramammary solution

PRODUCT SUMMARY

EU Procedure number	IE/V/0651/001/DC
Name, strength and pharmaceutical form	Huvebiotic 330 mg/100 mg Intramammary solution
Active substance(s)	Lincomycin (as Lincomycin hydrochloride), Neomycin (as Neomycin sulfate)
Applicant	Huvepharma N.V Uitbreidingstraat 80, Berchem, Antwerpen 2600 Belgium
Legal basis of application	Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of procedure	22/09/21
Target species	Lactating cattle
Indication for use	For the treatment of mastitis in cattle during the lactation period caused by: • Staphylococcus species (both penicillinase and non-penicillinase producers) including *Staphylococcus aureus* susceptible to lincomycin and/or neomycin, • Streptococcus species including *Streptococcus agalactiae*, *Streptococcus dysgalactiae* and *Streptococcus uberis* susceptible to lincomycin and/or neomycin, • Coliform bacteria including *Escherichia coli* susceptible to neomycin.
ATC vet code	QJ51RF03
Concerned Member States	BG, IT, RO

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.
The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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

II. QUALITY ASPECTS

A. Qualitative and Quantitative Particulars
The product contains 330 mg lincomycin (as hydrochloride), 100 mg neomycin (as sulfate) as active substances. The excipients are disodium edetate, hydrochloric acid, sodium hydroxide and water for injections.
The container/closure system consists of a 10 ml polyethylene intramammary syringe supplied in an outer cardboard box, with 24 syringes per cardboard box.
The choice of the formulation is 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 fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.
Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials
The active substances are lincomycin hydrochloride, and neomycin sulfate, both established substances described in the European Pharmacopoeia. The active substances are 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 has been provided.
Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies
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.

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 has been provided.
Batch analytical data from the proposed production site has 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 has 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
Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This application was submitted in accordance with paragraph 3 of Article 13 of Directive 2001/82/EC (a "hybrid" veterinary medicinal product). The reference veterinary medicinal product is Albiotic 330 mg/100 mg Intramammary Solution (VPA 10782/028/001) containing lincomycin (as Lincomycin Hydrochloride) and neomycin (as neomycin sulphate) as active substances.

The product is an intramammary suspension and it is used in the same species, for the same indications, in the same doses and using the same administration method.
The Applicant is also the MAH of the reference product and has declared that they therefore have full access to the manufacture processes and to the qualitative and quantitative composition of the reference product formulation, and that the manufacture processes and the qualitative and quantitative composition of the candidate formulation are identical. Based on

this, an exemption from the requirement to conduct an *in vivo* bioequivalence study was justified in accordance with current guidance, section 7.1(d) of the CVMP Guideline (EMA/CVMP/016/00-Rev.3). This approach is in line with the advice published in the July-September 2016 CMDv Report for Release on 'Biowaiver for hybrids'.

III.A Safety Testing

Pharmacological Studies
As this is a hybrid application under Article 13(3) and as bioequivalence with a reference product is accepted, results of pharmacokinetics and pharmacodynamics are not required. The pharmacological aspects of this product reflect those of the reference product.

Toxicological Studies
As this is a hybrid application under Article 13(3) and as bioequivalence with a reference product is accepted, results of toxicological tests are not required. The safety aspects of this product are expected to be identical to those of the reference product. Warnings and precautions as listed on the product literature are broadly in line with those of the reference product.

User Safety
The Applicant has provided a user safety assessment in compliance with the relevant guideline which shows that when used in accordance with label recommendations, the product will not pose any greater risk to the user than the risks associated with use of the reference product.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment
The Applicant provided an environmental risk assessment in compliance with the relevant guideline. The environmental risk assessment can stop at Phase I and no Phase II assessment is required because the sum of the predicted environmental concentration for both active substances in soil will not exceed the trigger of 100 µg/kg.
Precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues Documentation

Residue Studies
As this is a hybrid application under Article 13(3) and as bioequivalence with a reference product is accepted, studies investigating the depletion of residues are not required.

MRLs
The active substances lincomycin and neomycin are listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 as follows:

	Lincomycin (all food-producing species)	**Neomycin (all food-producing species)**
Muscle	100 µg/kg	500 µg/kg
Liver	500 µg/kg	500 µg/kg
Kidney	1,500 µg/kg	5,000 µg/kg
Fat / skin	50 µg/kg	500 µg/kg
Milk	150 µg/kg	1,500 µg/kg

Withdrawal Periods
The proposed withdrawal periods are identical to those approved for the reference product in the RMS and are considered adequate to ensure consumer safety.

IV. CLINICAL ASSESSMENT

IV. CLINICAL ASSESSMENT (EFFICACY)
As this is a hybrid application according to Article 13(3) 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.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance
Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies
As this is a hybrid application according to Article 13(3) and bioequivalence with a reference product has been accepted, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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 benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.