Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Huvebiotic 330 mg/100 mg Intramammary solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances
Each 10 ml syringe contains:
Lincomycin (as hydrochloride) 330 mg
Neomycin (as sulphate) 100 mg

Excipients
Disodium edetate 5 mg

For the full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Intramammary solution.
Clear colourless to slightly yellow liquid.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle (lactating cows).

4.2 Indications for use, specifying the target species

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.

4.3 Contraindications

None.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i. Special precautions for use in animals
Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Official, national and regional antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to lincomycin and neomycin and may decrease the effectiveness of treatment with other liconsamides, macrolides, streptogramin

B and aminoglycosides, due to the potential for cross-resistance. The feeding to calves of milk containing residues of cefalonium that could select for antimicrobial-resistant bacteria (e.g. ESBL) should be avoided up to the end of the milk withdrawal period, except during the colostral phase.

The efficacy of the product is only established against the pathogens mentioned in Section 4.2 Indications for use. Consequently, serious acute mastitis (potentially fatal) due to other pathogen species, particularly *Pseudomonas aeruginosa*, can occur after drying off. Good hygienic practices should be thoroughly respected in order to reduce this risk.

ii. Special precautions to be taken by the person administering the veterinary medicinal product to animals
Some ingredients present in the formulation may act as a potential sensitiser.
People with known hypersensitivity to aminoglycosides (in particular neomycin) and/or lincosamides (in particular lincomycin) should avoid any direct contact with the product.
Avoid contact of the solution with skin and eyes.
Wear gloves.
Wash hands and any exposed skin immediately.
Accidental spillage on the skin should be flushed with plenty of water and then wash the area immediately with soap and water.
In case of accidental contact with eyes, immediately flush with copious amounts of water.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

No restrictions.

4.8 Interaction with other medicinal products and other forms of interactions

This product should not be used concomitantly with macrolides e.g. erythromycin, because lincomycin and the macrolides antagonise each other at the site of action, the 50S ribosomal sub-unit.

4.9 Amounts to be administered and administration route

For intramammary use only. Take aseptic precautions. The syringe must only be used once.

Dosage: infuse one syringe (10 ml. product) into each affected quarter. Repeat this treatment immediately after each of the next two 12 hourly milkings, to give a total of three infusions per infected quarter.

Where necessary, wash teats or whole udder thoroughly with warm water containing a suitable dairy disinfectant and dry them thoroughly. Milk out the udder completely. Disinfect teat end with a pad of alcohol or other suitable disinfectant. Use a separate pad for each teat.

Directions for insertion are as follows:
a. Full insertion: remove the white end cap by pulling straight up. Gently insert full cannula into the teat canal; carefully infuse the product.
b. Partial insertion: remove the white end cap by pulling straight up. Gently insert cannula 1/8" into the teat canal; carefully infuse the product.
Push plunger to dispense entire contents and massage the quarter to distribute the product into the milk cistern. Following infusion, it is advisable to dip all teats in an approved teat dip.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

The product is well tolerated. In the event of accidental overdose, it is unlikely that any local or systemic adverse effects will occur in the animal, however, any signs of adverse effect should be immediately reported to the veterinarian concerned.

4.11 Withdrawal period(s)

Meat and offal: 2 days.
Milk: 60 hours.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Phamacotherapeutic group: Antibacterial for intramammary use, lincomycin, with other antibacterials.
ATCvet code: QJ51RF03

The product contains the active ingredients lincomycin hydrochloride and neomycin sulphate in a sterile aqueous vehicle.

5.1 Pharmacodynamic properties

Lincomycin is a lincosamide antibiotic derived from *Streptomyces lincolnensis*. It possesses specific activity against Gram-positive bacteria, particularly Staphylococcus species and Streptococcus species and has little or no activity against Gram-negative bacteria such as *E.coli* (except anaerobes). Lincomycin has good activity against mycoplasma. Lincomycin binds to the 50S sub-unit of the bacterial ribosome, thereby inhibiting protein synthesis of the cell. It is generally regarded as a bacteriostatic compound.

Neomycin is an aminoglycoside antibiotic derived from *Streptomyces fradiae*. It has a broad spectrum of activity against both Gram-positive bacteria, including Staphylococcus species and Streptococcus species, and Gram-negative bacteria, including *Escherichia coli*. It is more active against Staphylococcus species than against Streptococcus species. Neomycin binds to the 30S sub-unit of the bacterial ribosome resulting in a malconformation of binding ribosomal protein due to errors in reading the amino acid coding of the mRNA. Neomycin thus compromises translation and hence bacterial protein synthesis.
At high concentrations, the aminoglycosides have also been shown to damage the cellular membrane of bacteria and hence are generally regarded as possessing both bacteriostatic and bactericidal properties.
In vitro studies have demonstrated that lincomycin and neomycin in combination have bactericidal activity against *Staphylococcus aureus* and *Escherichia coli* and bacteriostatic activity against streptococci. The combination has also demonstrated synergy against *Staphylococcus aureus*.

Lincomycin, neomycin and the combination have been shown to be active against both penicillinase and non-penicillinase producing staphylococci.

5.2 Pharmacokinetic particulars

After recommended infusion of the product, the following mean concentrations of lincomycin and neomycin were measured in individual treated quarters:

Antibiotic	Concentrations (µg/ml) / Time after first infusion			
	12 hours[1]	24 hours[2]	36 hours	48 hours
Lincomycin	52.7	53.5	56.9	4.6
Neomycin	22.2	29.7	28.0	4.9

[1] immediately before second infusion
[2] immediately before third (last) infusion

Antibiotic levels in milk above the MIC-values for target pathogens are sustained for the full dosage period and for at least 12 hours thereafter.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium Edetate
Hydrochloric Acid (for pH-adjustment)

Sodium Hydroxide (for pH-adjustment)
Water for injections

6.2 Major incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Do not freeze.

6.5 Nature and composition of immediate packaging

10 ml polyethylene intramammary syringe supplied in an outer cardboard box. 24 syringes per cardboard box.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium

8 MARKETING AUTHORISATION NUMBER(S)

VPA10782/037/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 October 2021

10 DATE OF REVISION OF THE TEXT

January 2022