



**Veterinary
Medicines
Directorate**

**United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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NATIONAL PROCEDURE

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT**

Mastic Lacto 200mg + 50mg + 10mg Intramammary Suspension for Cattle

Date Created: March 2025

MODULE 1

PRODUCT SUMMARY

| | |
|--|--|
| Name, strength and pharmaceutical form | Mastic Lacto 200mg + 50mg + 10mg Intramammary Suspension for Cattle, Intramammary suspension |
| Applicant | Bioveta, a.s., Komenského 212/12, 683 23 Ivanovice na Hané, Czech Republic |
| Active substances | Amoxicillin (as amoxicillin trihydrate) Clavulanic acid (as potassium clavulanate) Prednisolone |
| ATC Vet code | QJ51RV01 |
| Target species | Cattle (lactating cows) |
| Indication for use | For the treatment of clinical mastitis including cases associated with infections with the following pathogens: <ul style="list-style-type: none">• Staphylococci (including b-lactamase producing strains)• Streptococci (including <i>S. agalactiae</i>, <i>S. dysgalactiae</i> and <i>S. uberis</i>)• <i>Escherichia coli</i> (including b-lactamase producing strains) |

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

www.gov.uk/check-animal-medicine-licensed

MODULE 3

PUBLIC ASSESSMENT REPORT

| | |
|-------------------------------------|---|
| Legal basis of original application | Generic hybrid application in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10a) as amended. |
| Date of conclusion of the procedure | 13/03/2025 |

I. SCIENTIFIC OVERVIEW

This is a generic hybrid application in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10a) as amended, for authorisation in Great Britain (GB). The reference product is Synulox Lactating Cow Intramammary Suspension, which has been authorised in the UK since 11/12/1986. The application is determined a generic 'hybrid' as the product is administered and acts locally, and it is not possible to demonstrate bioequivalence through bioavailability studies. The applicant submitted data to show evidence of chemical similarity with the reference product.

Mastic Lacto 200mg + 50mg + 10mg Intramammary Suspension for Cattle contains 200 mg amoxicillin (as trihydrate), 50 mg clavulanic acid (as potassium clavulanate) and 10 mg prednisolone per 3 g syringe. The indication is for the treatment of clinical mastitis, via the intramammary route. The content of one syringe should be infused into each affected quarter via the teat canal, immediately after milking, at 12hour intervals for three consecutive milkings.

The distribution category of the product in GB is POM-V, a veterinary medicinal product subject to prescription.

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, any reactions observed are indicated in the SPC¹. 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 efficacy² 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.

¹ SPC – Summary of product Characteristics.

² Efficacy – The production of a desired or intended result.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains amoxicillin (as amoxicillin trihydrate), clavulanic acid (as potassium clavulanate) and prednisolone and the excipients sodium aluminosilicate, emulsifying cetostearyl alcohol (type B), white soft paraffin and light liquid paraffin.

The container/closure system consists of 4.5 ml low-density polyethylene syringe barrels with low-density polyethylene plungers and end caps. The product is to be marketed with or without disinfectant wipes moistened with 65% v/v isopropyl alcohol solution, to clean the teats. The particulars of the containers and controls performed are provided and conform to the appropriate regulation.

The choice of the formulation and the absence of preservative are justified.

The product is an established pharmaceutical form, and its development is adequately described in accordance with the relevant regulatory guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of sequential addition and mixing steps and terminal sterilisation.

The product is manufactured using conventional manufacturing techniques, standard for the manufacturing company. Process validation for full-scale batches will be performed post-authorisation.

II.C. Control of Starting Materials

The active substances amoxicillin, clavulanic acid and prednisolone, are all established active substances described in the European Pharmacopoeia, and are each sourced from suppliers holding certificates of suitability. The active substances are manufactured in accordance with the principles of good manufacturing practice.

All active substance specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with this specification have been provided.

All excipients are well known pharmaceutical ingredients, and their quality is compliant with Ph. Eur. standards, except for sodium alumina silicate. The applicant's specification for this material is acceptable.

The packaging for both the active substance and the final product are satisfactory with Certificates of Analysis for all materials of the primary packaging supplied.

The syringe components comply with Commission Regulation (EU) No 10/2011 Plastic materials and articles intended to come into contact with food. In addition, the raw material complies with Ph. Eur. 3.1.3 Polyolefines.

II.C.4. Substances of Biological Origin

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.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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. Control tests on the finished product are those appropriate for this pharmacological form.

II.F. Stability

Stability data on the active substances have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on two pilot scale batches of the finished product have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information

The shelf life of the veterinary medicinal product, as packaged for sale, is 18 months. After first opening the immediate packaging, the product should be used immediately. The product should be stored in a dry place, not above 25°C

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACOTOXICOLOGICAL)

Due to the legal nature of the application as a generic hybrid, there are no new toxicological or pharmacological data required.

Warnings and precautions as listed on the product literature are based on those of the reference product with some alterations as needed, and are adequate to ensure safety of the product to users/ the environment/consumers.

III.A Safety Documentation

Pharmacological Studies

Data submitted by the applicant demonstrated sufficient evidence of chemical similarity with the reference product.

Amoxicillin is a broad-spectrum bactericidal b-lactam antibiotic. Clavulanic acid inactivates b-lactamases. This combination is effective against b-lactamase producing organisms, with exception of most extended spectrum Beta-lactamase (ESBL) and AmpC beta-lactamase (AmpC) producing gram-negative bacteria.

In vitro, clavulanic acid and amoxicillin in combination are active against a wide range of clinically important bacteria.

Prednisolone is an anti-inflammatory corticosteroid.

User Safety

A user risk assessment was provided 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. Therefore, the following applicant's user recommendations are appropriate:

- Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-reactions to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.
- People with known hypersensitivity to penicillins and/or cephalosporins should avoid contact with the veterinary medicinal product.
- If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty breathing are serious symptoms and require urgent medical attention.
- This veterinary medicinal product may cause irritation of skin and eyes. Avoid contact with skin and eyes. In case of contact with skin or eyes, flush the affected area with plenty of clean water.
- The cleaning wipes supplied with the veterinary medicinal product contain isopropyl alcohol, which may cause skin or eye irritation in some people.
- Personal protective equipment consisting of gloves should be used when handling the veterinary medicinal product and cleaning wipes.
- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

The Phase I assessment continued through the decision tree to the end, and the predicted environmental concentration in soil (PEC_{soil}) values were calculated for the three active substances. The sum of these was lower than the trigger limit of 100 $\mu\text{g}/\text{kg}$, and therefore, a Phase II ERA was not required

Given the presence of prednisolone on the formulation, an environmental warning has been included in the SPC, about the danger to fish and other aquatic organisms.

III.B.2 Residues documentation

Residue Studies

No new residue depletion studies were conducted, due to the legal nature of the application as a generic hybrid. The applicant has displayed evidence of chemical similarity with the reference product so the same withdrawal periods as those of the reference product are justified.

MRLs

Amoxicillin is listed in Table 1 of Commission Regulation (EU) 37/2010 and MRLs have been established for edible tissues/milk. The marker substance is amoxicillin.

MRLs are listed below:

| | Bovine |
|--------|----------------------------|
| Muscle | 50 $\mu\text{g}/\text{kg}$ |
| Liver | 50 $\mu\text{g}/\text{kg}$ |
| Kidney | 50 $\mu\text{g}/\text{kg}$ |
| Fat | 50 $\mu\text{g}/\text{kg}$ |
| Milk | 4 $\mu\text{g}/\text{kg}$ |

Clavulanic acid is listed in Table 1 of Commission Regulation (EU) 37/2010 and MRLs have been established for edible tissues/milk. The marker substance is clavulanic acid.

MRLs are listed below:

| | Bovine |
|--------|-----------------------------|
| Muscle | 100 $\mu\text{g}/\text{kg}$ |
| Liver | 200 $\mu\text{g}/\text{kg}$ |
| Kidney | 400 $\mu\text{g}/\text{kg}$ |
| Fat | 100 $\mu\text{g}/\text{kg}$ |

| | |
|------|----------------|
| Milk | 200 µg/kg milk |
|------|----------------|

Prednisolone is listed in Table 1 of Commission Regulation (EU) 37/2010 and MRLs have been established for edible tissues/milk. The marker substance is prednisolone.

MRLs are listed below:

| | Bovine |
|--------|----------|
| Muscle | 4 µg/kg |
| Liver | 10 µg/kg |
| Kidney | 10 µg/kg |
| Fat | 4 µg/kg |
| Milk | 6 µg/kg |

Withdrawal Periods

Based on the data provided, a withdrawal period of 7 days for meat and offal in cows, and 84 hours for milk are justified.

IV. CLINICAL DOCUMENTATION

As this is a generic hybrid application, and chemical similarity with the reference product has been established, no new pharmacodynamic, pharmacokinetic, tolerance or clinical data is required. The efficacy claims, dosing regimens, and pharmacology for this product are equivalent to those of the reference product.

Resistance

The applicant submitted information describing general mechanisms of resistance, including prevalence of resistance development in the last 5 years. The applicant presented antimicrobial resistance/ susceptibility trends based on antibiotic resistance monitoring results from several European regions available from the national assessment reports. The available recent data show good efficacy and low MIC values for *Streptococcus* spp. and coagulase-negative staphylococci. Resistance monitoring reports in various regions of the EU, show a decreasing or slightly increasing trend in the prevalence of resistance to amoxicillin-clavulanate for *E. coli* isolates. Adequate warnings and precautions appear on the product literature.

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 of the product is favourable.

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 Product Information Database of the Veterinary Medicines Directorate website.

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The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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