Institute for State Control of Veterinary Biologicals and Medicines
Hudcova 56a
621 00 Brno
Czech Republic
(RMS)

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Intramar Lacto 200 mg + 50 mg + 10 mg intramammary suspension for cattle

PRODUCT SUMMARY

EU procedure number	CZ/V/0188/001/DC
Name, strength and pharmaceutical form	Intramar Lacto 200 mg + 50 mg + 10 mg intramammary suspension for cattle
Applicant	Bioveta, a.s. Komenského 212/12 Ivanovice na Hané 68323 The Czech Republic
Active substance(s)	Each intramammary syringe (3 g) contains: Amoxicillin (as amoxicillin trihydrate) 200.0 mg Clavulanic acid (as potassium clavulanate) 50.0 mg Prednisolone 10.0 mg
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: Staphylococci (including β-lactamase producing strains) Streptococci (including *S. agalactiae, S. dysgalactiae* and *S. uberis*) *Escherichia coli* (including β-lactamase producing strains)

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Bioveta, a.s.	DCP
Publicly available assessment report	

PRODUCT INFORMATION

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).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Hybrid application in accordance with Article 19 of Regulation (EU) 2019/6, as amended.
Reference product (RP)	Synulox LC 260 mg intramammary suspension for cattle
Marketing authorisation holder	Zoetis Czech Republic s.r.o.
Marketing authorisation number EU procedure number	96/037/94-C
Date of authorisation	17/01/1994
Date of completion of the original decentralised procedure	18/12/2024
Concerned Member States for original procedure	AT, BE, CY, DE, EL, ES, FR, HR, HU, IE, IT, LT, LU, LV, PL, PT, RO, SI, SK, UK (NI)
Concerned Member States for subsequent recognition procedure	N.A.
Withdrawn CMS during original <mutual recognition> <decentralised><subsequent recognition> procedure	N.A.

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; <the reactions observed are indicated in the SPC.

The VMP 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 VMP was demonstrated according to the claims made in the SPC.

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

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP contains 200 mg of amoxicillin (as amoxicillin trihydrate), 50 mg of clavulanic acid (as potassium clavulanate) and 10 mg of prednisolone as active substances and the excipients sodium aluminosilicate, cetostearyl alcohol (type B) emulsifying, paraffin white soft and paraffin light liquid.

The container/closure system consist of a LDPE intramammary syringe equipped with a LDPE cap, a LDPE cuff and a LDPE plunger. The authorised package sizes are a carton box containing 24 intramammary syringes or a carton box containing 24 syringes and 24 disinfectant wipes moistened with 65% v/v isopropyl alcohol solution (2.4 ml/wipe) to clean teats.

The choice of the formulation is justified.

The VMP is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at licensed manufacturing sites.

Process validation for full-scale batches will be performed post-authorisation.

C. Production and control of starting materials

The active substances amoxicillin trihydrate, prednisolone and potassium clavulanate are established active substances described in the European Pharmacopeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substances specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with the specification have been provided for each active substance.

Certificates of suitability issued by the EDQM have been provided for each active substance and 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.

The excipients cetostearyl alcohol (type B) emulsifying, paraffin white soft and paraffin light liquid are described in the Ph. Eur. monographs and are controlled accordingly. The excipient

sodium aluminosilicate is not described in the Ph. Eur. and is controlled according to an in-house specification.

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 VMP.

D. Control tests carried out on isolated intermediates during the manufacturing process

The tests performed during production are described and the results conforming to the specifications are provided.

In-process control tests have been carried out on intermediate stages of manufacture in order to verify the consistency of the manufacturing process and the final VMP.

A specification was set for an intermediate and the analytical methods are described and validated, if applicable.

A retest period and storage conditions for the intermediate are defined based on data resulting from stability studies.

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 VMP.

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 tests

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances when stored under the approved conditions or are covered by the relevant certificates 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 VMP throughout its shelf life when stored under the approved conditions.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6, results of toxicological tests are not required. Warnings and precautions as listed on the product literature are adequate to ensure safety of the product.

A. Safety tests

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows the risk of hypersensitivity reactions and irritation of skin and eyes. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

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 is less than 100 µg/kg. In addition, a similar product was authorised after October 2005. In line with similar product on the market, the potential of prednisolone to disrupt the endocrine system has been addressed in the product literature and risk mitigation measures have been implemented.

B. Residues documentation

The application for the product has been made in accordance with Article 19 of Regulation (EU) 2019/6 as amended. The reference and hybrid products have the same pharmaceutical forms, the same qualitative and quantitative composition in term of active substances and a similar qualitative and quantitative composition in terms of excipients. On this basis, the requirement to conduct in vivo studies is waived.

Residue tests

No own residue depletion studies have been submitted.

Maximum Residue Limits

The active substances amoxicillin, clavulanic acid and prednisolone are allowed substances as described in Table 1 of the Annex to Commission Regulation (EU) No 37/2010:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
Amoxicillin	Amoxicillin	All food producing species	50 µg/kg 50 µg/kg 50 µg/kg 50 µg/kg 4 µg/kg	Muscle Fat Liver Kidney Milk	For porcine and poultry species the fat MRL relates to ‘skin and fat in natural proportions.’ Not for use in animals from which eggs are produced for human consumption. For fin fish the muscle MRL relates to ‘muscle and skin in natural proportions’. MRLs for fat, liver and kidney do not apply to fin fish.

Clavulanic acid	Clavulanic acid	Bovine, porcine	100 µg/kg 100 µg/kg 200 µg/kg 400 µg/kg	Muscle Fat Liver Kidney	For porcine species the fat MRL relates to 'skin and fat in natural proportions'.
		Bovine	200 µg/kg	Milk	
Prednisolone	Prednisolone	Bovine	4 µg/kg 4 µg/kg 10 µg/kg 10 µg/kg 6 µg/kg	Muscle Fat Liver Kidney Milk	NO ENTRY
		Equidae	4 µg/kg 8 µg/kg 6 µg/kg 15 µg/kg	Muscle Fat Liver Kidney	

Excipients (paraffin white soft, cetostearyl alcohol, light liquid paraffin, sodium aluminosilicate) are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 with the entry "No MRL required". The excipient sodium calcium aluminosilicate in the reference product has been replaced by sodium aluminosilicate in the hybrid product. The comparison of the similarity of both products (reference/hybrid) have been provided.

The disinfectant wipe complies with the requirements of Regulation (EC) No 1935/2004 of the European Parliament and the Council and isopropanol is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 with the entry "No MRL required".

Withdrawal Periods

Based on the reference product, the following withdrawal periods have been established for cattle (lactating cows) for the hybrid product:
Meat and offal: 7 days.
Milk: 84 hours.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and essential similarity to a reference VMP has been demonstrated, efficacy studies are not required.

The efficacy claims for this VMP are equivalent to those of the reference VMP.

A. Pre-Clinical Studies

No pre-clinical studies were performed.

Pharmacology

The applicant has provided bibliographical data containing information on pharmacodynamic with relevance for antimicrobials (e.g. MIC datasets, mechanism of action and resistance) as appropriate for the products containing antimicrobials.

Development of resistance and related risk in animals

The bibliography / information provided suggests in appropriate manner regarding the time frame, the target species (cattle), the indication (bovine mastitis) and isolates originated from various EU regions that there is no evidence of a real increase/shift in resistance to the β-lactam antibiotics tested (amoxicillin and clavulanic acid in combination or sole substrates tested: penicillin/amoxicillin/ampicillin/cephalosporins) among the mastitis pathogens. Submitted datasets indicate that over the 5 years covered by the data from the EU countries there was no evidence of significant and consistent increases in MIC (minimum inhibitory concentration) levels of the concerned β-lactam antibiotics.

Adequate warnings and precautions appear on the product literature. As the wording proposed in the product texts is in line with the reference product and additionally contains wording according to the Guideline on the summary of product characteristics (SPC) for veterinary medicinal products containing antimicrobial substances (EMA/CVMP/383441/2005-Rev.1-Cor.1).

Dose determination and confirmation

No dose determination and confirmation studies were performed.

Tolerance in the target species of animals

No tolerance studies were provided.

The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

No clinical trials were performed.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP 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 VMP for humans and the environment is acceptable.

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. The current SPC is available in the Union Product Database (UPD).

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 VMP.

None.