Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Noroclav Intramammary Suspension for Lactating Cows (DE)

Paraclav Intramammary Suspension for Lactating Cows (UK)

Date: 01 March 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0328/001/DC
Name, strength and pharmaceutical form	Noroclav Intramammary Suspension for Lactating Cows
Applicant	Norbrook Laboratories (Ireland) Ltd. Rossmore Industrial Estate Monaghan IRELAND
Active substance(s)	Amoxicillin (as amoxicillin trihydrate) Clavulanic acid (as potassium clavulanate) Prednisolone
ATC Vetcode	QJ51RV01
Target species	Cattle (lactating cows)
Indication for use	For the treatment of clinical mastitis caused by the following bacteria susceptible to the combination of amoxicillin and clavulanic acid: - Staphylococci (including β-lactamase producing strains) - Streptococci (including *S. agalactiae, S. dysgalactiae and S. uberis*) - *Escherichia coli* (including β-lactamase producing strains)

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised procedure	01 August 2018
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	UK (former RMS)

I. SCIENTIFIC OVERVIEW

This product was submitted as generic 'hybrid' applications in accordance with Article 13 (3) of Directive 2001/82/EC, as amended.

It was determined generic 'hybrid' application because bioequivalence could not be demonstrated or inferred through bioavailability studies. Approval was granted in light of the principles behind the bioequivalence waivers set out in section 7 of the current Guideline (EMA/CVMP/016.00-Rev.2)

The composition and pharmaceutical form of the active substances are the same as those of the reference product. The excipients are essentially similar to those of the reference product. The reference product was Synulox Lactating Cow Intramammary Suspension, marketed in the UK since December 1996.

The product is indicated for lactating cattle, for the treatment of clinical mastitis caused by the following bacteria susceptible to the combination of amoxicillin and clavulanic acid:

- Staphylococci (including β-lactamase producing strains)
- Streptococci (including *S. agalactiae, S. dysgalactiae and S. uberis*)
- *Escherichia coli* (including β-lactamase producing strains)

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC.[1] The product is safe for the user, the consumer of foodstuffs

[1] SPC – Summary of product Characteristics.

from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [2] 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

II.A. Composition

The product contains in each syringe of 3 g: amoxicillin (as amoxicillin trihydrate) 200 mg, clavulanic acid (as potassium clavulanate) 50 mg, and prednisolone 10 mg. The product also contains the excipients aluminium sodium silicate, cetostearyl alcohol (Type B) emulsifying, paraffin white soft and paraffin light liquid.

The container/closure system consists of single dose, 3g, white LDPE syringes with a white LDPE dual push-fit cap. Packed into cartons of 3, 12, and 24 syringes, or into buckets of 120 syringes, including 3, 12, 24, or 120 individually wrapped teat cleaning towels containing isopropyl alcohol.

The particulars of the containers and controls performed are provided and conform to the regulation.

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.

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 a heating and mixing process, followed by the loading aseptically of the product into syringes.

II.C. Control of Starting Materials

The active substances are amoxicillin trihydrate, potassium clavulanate and prednisolone, established active substances described in the European Pharmacopoeia (Ph. Eur). 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 materials. Batch analytical data demonstrating compliance with this specification have been provided. Certificates of Suitability were received from each manufacturing site.

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

All excipients complied with monographs as cited in the Ph. Eur, except for sodium alumina silicate, which was supported by a Certificate of Analysis. Suitable data were provided with regard to packaging.

II.C.4. Substances of Biological Origin

A TSE (transmissible spongiform encephalopathy) declaration and completed EMA Tables A, B and C: 'Materials of animal origin covered by the Note for Guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via medicinal products' were provided.

None of the ingredients include material of animal origin, except for amoxicillin trihydrate from one manufacturer, made using calf rennet. Suitable documentation was provided.

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 sites have been provided demonstrating compliance with the specification. Control tests on the finished product are those for: appearance, identification of active substances, related substances and impurities, water content, particle size, viscosity, uniformity of dosage units, package integrity, deliverable mass and sterility.

II.F. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. Suitable data were provided on the finished products. The SPC and product literature carry appropriate information.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 18 months

Special precautions for storage:

Do not store above 25°C.

Store in a dry place.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

Due to the nature of the application, pharmacological and toxicological data, other than a user risk assessment (URA) and environmental risk assessment (ERA) were not required.

III.A Safety Documentation

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:

- This product may cause skin and eye irritation. Avoid contact with the skin and eyes. In the event of skin or eye contact rinse with plenty of clean water.
- The cleaning towels supplied with the product contain isopropyl alcohol, which many cause skin or eye irritation in some people.
- The wearing of gloves is recommended during administration of the product and when handling the cleaning towels.
- 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.
- Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.
- Handle this product with great care to avoid exposure, taking all recommended precautions.
- If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning.
- Swelling of the face, lips or eyes or difficulty with breathing, are more serious symptoms and require urgent medical attention.
- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines. The assessment ended at the Phase I decision tree. Data provided on the SPC and product literature are sufficient to preclude risk to the environment when the products are used as recommended.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were required because the product was considered essentially similar to the reference product.

Withdrawal Periods

Meat and offal: 7 days

Milk: 84 hours.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.I. Pre-Clinical Studies

Due to the nature of the application, no data were required.

Resistance

A literature review was provided.
Adequate warnings and precautions appear on the SPC and product literature.

IV.II. Clinical Documentation

Due to the nature of the application, no data were required.

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 products 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 Heads of Veterinary Medicinal 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.

•	28 March 2019	Change in manufacturer responsible for batch release in the EU from UK to Ireland.
•	01 March 2019	Change in RMS from UK to DE.