IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Cefquinome Norbrook LC, 75 mg Intramammary Ointment for Lactating Cows

PRODUCT SUMMARY

EU Procedure number	IE/V/0553/001 (formerly UK/V/0499/001)
Name, strength and pharmaceutical form	Cefquinome Norbrook LC, 75 mg Intramammary Ointment for Lactating Cows
Active substances(s)	Cefquinome (as cefquinome sulfate)
Applicant	Norbrook Laboratories (Ireland) Limited Rossmore Industrial Estate Monaghan Ireland
Legal basis of application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target species	Cattle
Indication for use	For the treatment of clinical mastitis in the lactating cow caused by bacteria susceptible to cefquinome, namely *Staphylococcus aureus, Streptococcus uberis, Streptococcus dysgalactiae, Escherichia coli*.
ATCvet code	QJ51DE90
Date of completion of the original decentralised procedure	23 July 2014 (UK) 12 September 2014 (IE)
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States	Austria, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland (now RMS), Italy, The Netherlands, Portugal, Slovakia, Slovenia, Sweden. UK added via RMS change

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the 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

This was a generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended. The reference product was Cobactan MC, Intramammary Suspension 75 mg Milking Cow, marketed in the UK since 1997.
The product is intended for the treatment of mastitis in the lactating dairy cow, caused by bacteria sensitive to cefquinome. 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 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

II.A. Composition

The product contains cefquinome 75 mg as cefquinome sulphate, and the excipients white soft paraffin and liquid paraffin. The container/closure system consists of a pre-filled 8 g intramammary syringe consisting of a white opaque low density polyethylene (LDPE) barrel, with a white opaque LDPE plunger and white opaque LDPE end-cap.
Cartons comprise of 12, 24 and 36 syringes including 12, 24 and 36 individually wrapped teat cleaning towels.
The particulars of the containers and controls performed are provided and conform to the 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 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. Process validation data on the product have been presented in accordance with the relevant European guidelines. The manufacturing process consists of a mixing of the soft and liquid paraffin, followed by heating and cooling steps and subsequent addition of the active substance. Syringes are then filled with the product.

II.C. Control of Starting Materials

The active substance is cefquinome, an established active substance for which appropriate data in line with an acceptable specification were obtained. The active substance is 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 have been provided.

Both white soft paraffin and liquid paraffin are controlled to meet the specifications of the monograph cited in the European Pharmacopoeia.

II.C.4. Substances of Biological Origin

A TSE declaration provided stated that the product complies with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products.

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. Tests on the finished product include those for appearance, identity of the active and related substances, water content, particle shape and size, viscosity, packaging seal and sterility.

II.F. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. For the active substance, a re-test period of 2 years was agreed, when stored in a refrigerator at 2-8^{o}C, in an airtight container, protected from light.
For the finished product, several studies of commercial scale batches at real time and accelerated conditions were submitted. In light of finished studies, a shelf-life as now stipulated on the SPC was acceptable.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Do not store above 30°C.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this was a generic application according to Article 13 (1), and bioequivalence with a reference product was established, results of pharmacological and toxicological data were not required.
Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

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. The warnings are the same as those for the reference product:

- When infusing the product, protective gloves should always be worn in order to avoid skin contact.
- Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross sensitivity to cephalosporin 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 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 skin rash, you should seek medical advice and show the Doctor this warning. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
- Wash hands after using the cleaning towels and wear protective gloves if skin irritation due to Isopropyl alcohol is known or suspected.

Environmental Safety

A risk assessment was submitted in accordance with VICH and CVMP guidelines. The product will be used primarily by farmers and veterinarians on farms. There is a potential for cefquinome to be released from the environment via the spread of manure on agricultural land from treated animals, and also directly excreted from cattle.

Phase I:
The product will be used to treat a small number of animals in a flock or herd and as such environmental exposure will be low. The initial predicted environmental concentration (PEC) in soil is less than 100 microgram/kg, therefore a Phase II environmental risk assessment was not required.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because the proposed product was established as being identical to the reference product.

Withdrawal Periods

The same withdrawal periods as those established for the reference product were proposed and accepted:
Meat and offal: 4 days
Milk: 5 days (120 hours)

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13. (1), and bioequivalence with a reference product has been established, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.I. Pre-Clinical Studies

As this was a generic application according to Article 13. (1), and bioequivalence with a reference product was established, pre-clinical studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.II. Clinical Documentation

As this was a generic application according to Article 13. (1), and bioequivalence with a reference product was established, clinical studies were 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 of the product(s) is favourable.

VI. POST-AUTHORISATION ASSESSMENTS