ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ceffect LC, 75 mg, intramammary ointment for lactating cows
(Belgium, Bulgaria, Czech Republic, Hungary, Ireland, Italy, Luxembourg, The Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, United Kingdom)

Cefaxxess LC, 75 mg, intramammary ointment for lactating cows
(Austria, Germany, France)

Ceffect Lactación, 75 mg, pomade intramammaria
(Spain)

PuAR correct as of 17/05/2018 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0483/001/DC
Name, strength and pharmaceutical form	Ceffect LC, 75 mg, intramammary ointment for lactating cows
Applicant	Emdoka bvba John Lijsentraat 16 B-2321 Hoogstraten Belgium
Active substance(s)	Cefquinome (as sulphate)
ATC Vetcode	QJ51DE90
Target species	Cattle (lactating cows)
Indication for use	For the treatment of clinical mastitis in the lactating dairy cow caused by the following cefquinome-sensitive organisms: *Streptococcus uberis, Streptococcus dysgalactiae, Staphylococcus aureus* and *Escherichia coli.*

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	26 February 2014
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Czech Republic, France, Germany, Hungary, Ireland, Italy, Luxembourg, The Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain

I. SCIENTIFIC OVERVIEW

Ceffect LC, 75 mg, intramammary suspension for cows has been developed as a generic of Cobactan LC, 75 mg intramammary ointment for cows, which was first authorised in the UK in 1996. Bioequivalence to the reference product has been accepted.

The product is indicated to treat clinical mastitis in lactating dairy cows and should be administered at a dose rate of 1 syringe infused into the teat of the affected quarter every 12 hours following 3 consecutive milkings. The product is contraindicated in cattle known to be hypersensitive to β-lactam antibiotics or any of the excipients. The cleaning towels should not be used if lesions are present on the teat.

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; the slight reactions observed are indicated in the SPC[1].

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.

[1] SPC – Summary of Product Characteristics

II. QUALITY ASPECTS

A. Composition

The product contains cefquinome (sulphate) as the active substance and the excipients white soft paraffin and liquid paraffin. The paper cleaning towels contain 70% isopropanol.

The container/closure system consists of white, low-density polyethylene intramammary syringes with a dual push-fit nozzle cap. Each syringe contains 8g of ointment and is packaged in cartons of 3, 15, 20 or 24 syringes with 3, 15, 20 or 24 cleaning towels respectively. The cleaning towels are packaged in individual laminate sachets with a copolymer inner layer. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and 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.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The product is manufactured by mixing heated liquid paraffin and melted white soft paraffin. Once mixed the solution is heated further to sterilise the mixture. The mixture is cooled and cefquinome sulphate is added under aseptic conditions before the suspension is homogenised. Under aseptic conditions the suspension is filled into sterilised injector bodies with caps and closed with sterilised plungers. Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is cefquinome sulphate, an established active substance not described in a Pharmacopoeia. An Active Substance Master File (ASMF) and an in-house monograph have been provided for the active substance manufacturers. 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 excipients comply with their respective Ph. Eur. monographs and are tested upon receipt.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

E. Control on intermediate products

Not applicable.

F. 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. The tests include those for identification and assay of the active substance, appearance, particle size, deliverable mass, related substances and sterility.

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.

G. 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. A retest period of 12 months is supported for the active substance stored at 2 - 8°C.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions. Data were provided for the finished product stored at 25°C/60%RH for 12 months, 30°C/65%RH for 12 months and 40°C/75%RH for 6 months. Freeze thaw data were also provided for 1 batch of the finished product. A shelf life of 32 months has been established.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

- Shelf life of the finished product as packaged for sale is 32 months.
- Use immediately after first opening the immediate packaging.
- Do not store above 30°C.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of pharmacological studies are not required.

Toxicological Studies

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of toxicological studies are not required.

User Safety

The applicant has not provided a user safety assessment on the basis that the product is essentially similar to the reference product and has the same toxicity, user hazards, exposure risk and is likely to be administered by the same users as the reference product. The same warnings and precautions are included on the SPC and product literature as the reference product and are adequate to ensure safety to users of the product.

- 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.

    1. Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.
    2. Handle this product with great care to avoid exposure, taking all recommended precautions.
    3. 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 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.

Ecotoxicity

The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

The PEC_{soil}[2] values for both intensively reared dairy cattle (indoors) and pasture reared dairy cattle were calculated as 1.7 µg/kg and 1.5 µg/kg respectively. The assessment concluded that the PEC_{soil} values are well below the trigger value of 100 µg/kg and is therefore not expected to pose a risk to the environment. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

This is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended, the test product is essentially similar to the reference product and bioequivalence has been accepted, therefore residue studies were not required.

Withdrawal Periods

Meat and offal: 4 days
Milk: 5 days (120 hours)

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of pharmacological studies are not required.

Tolerance in the Target Species of Animals

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of tolerance studies are not required.

Resistance

Information on resistance has been provided for the target organisms. The MIC values taken from recent studies were submitted and the highest MIC_{90} value was found for *Staphylococcus aureus* of approximately 1 µg/ml. The resistance was also determined and shown to be absent for three of the target organisms and only minimal resistance was seen in *E. coli*. Appropriate information and warnings appear on the product literature.

[2] PEC – Predicted environmental concentration

IV.B Clinical Studies

Laboratory Trials

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of laboratory trials are not 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 for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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.

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

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.

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