Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Cefshot DC 250 mg Intramammary Suspension for Cattle

Date Created: November 2015

PuAR correct as of 19/09/2018 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0414/001/DC
Name, strength and pharmaceutical form	Cefshot DC 250 mg Intramammary Suspension for Cattle
Applicant	Zoetis UK Limited 5th Floor, 6 St. Andrew Street London EC4A 3AE
Active substance(s)	Cefalonium (as cefalonium dehydrate)
ATC Vetcode	QJ51DB90
Target species	Cattle (dry cow)
Indication for use	For the treatment of subclinical mastitis at drying-off and the prevention of new bacterial infections of the udder during the non-lactating period of cows caused by *Staphylococcus aureus, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus uberis, Trueperella pyogenes, Escherichia coli* and *Klebsiella* spp.

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 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	17 June 2015
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, Slovakia, Slovenia, Spain

I. SCIENTIFIC OVERVIEW

Cefshot DC 250 mg Intramammary Suspension for Cattle has been developed as a generic hybrid of Cepravin Dry Cow 250 mg Intramammary Suspension. The reference product has been authorised in the UK since 1993. A waiver has been granted to Cefshot DC from the study requirements as therapeutic equivalence to the reference product was accepted on the basis that the products are identical.

The product is for use in dry cows and is indicated for treatment of subclinical mastitis and the prevention of new bacterial infections during the dry period. Cefshot is contraindicated in animals with a known hypersensitivity to cephalosporins, β-lactam antibiotics or any of the excipients.

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 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.

[1] SPC – Summary of product Characteristics.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains cefalonium as the active substance and the excipients are aluminium distearate and liquid paraffin.

The container/closure system consists of a single dose white polyethylene intramammary syringe with a polyethylene cap containing 3g of product. The syringes are packaged in either a cardboard carton or plastic bucket with cleaning towels. 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 mixing the excipients before adding the cefalonium. Once fully mixed the product is filled to the target weight in plastic syringes and sterilised. Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is cefalonium, an established active substance described in the British Veterinary Pharmacopoeia. Data on the active substance were provided in an Active Substance Master File (ASMF). 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.

Data were provided for the excipients, which are provided in accordance with the respective European Pharmacopeia (Ph. Eur.) Monograph or in-house specification. Certificates of analysis have been provided.

II.C.4. Substances of Biological Origin

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

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

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. Control tests on the finished products include those for identification and assay cefalonium, water content, deliverable mass and sterility.

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.

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. A retest period of 12 months is supported.

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 batches of the product stored at 25°C/60% RH for 36 months and at 40°C/75% RH for 6 months. A shelf life of 3 years has been established.

G. Other Information

Shelf life of the finished product as packaged for sale is 3 years.
Do not freeze.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

As this is a generic hybrid application according to Article 13 (3), and therapeutic equivalence with a reference product has been accepted, the results of pharmacological studies are not required.

Toxicological Studies

As this is a generic hybrid application according to Article 13 (3), and therapeutic equivalence with a reference product has been accepted, the results of toxicological studies are not required.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the routes of exposure are the same as the reference product and will pose the same risk to the user. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

- Wash hands after use.
- Penicillin and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-sensitivity 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 breathing are more serious symptoms and require urgent medical attention.

Environmental Safety

An environmental risk assessment (ERA) was provided. The ERA was conducted in accordance with VICH and CVMP guidelines.

Phase I:
The product is an intramammary containing 250 mg/ syringe cefalonium and is indicated for routine dry cow therapy. The contents of the syringe are infused into each quarter via the teat following the last milking. The product has the potential to be released into the environment via the spreading of manure and direct excretion by animals reared on pasture.

The initial predicted environmental concentration (PEC) in soil was calculated for intensively reared cattle and for pasture reared cattle. It was determined based on all four quarters of the udder being infused with the product and assuming 100% of the herd had been treated. The PEC_{soil} for both intensively reared and

pasture reared animals is less than 100 µg/ kg. A Phase II assessment was not required.

III.B.2 Residues documentation

Residue Studies

As this is a generic hybrid application according to Article 13 (3), and therapeutic equivalence with a reference product has been accepted, the results of residue depletion studies are not required.

MRLs

MRLs have been established for cefalonium in milk. No MRL is required for tissues following intramammary use of cefalonium.

MRLs are listed below:

	Bovine
Muscle	No MRL required
Liver	No MRL required
Kidney	No MRL required
Fat / skin	No MRL required
Milk	20 µg/kg

Withdrawal Periods

As the test product is essentially similar to the reference product the same withdrawal periods have been applied.

Meat and offal:
21 days

Milk:
96 hours after calving if the dry period is higher than 54 days.
58 days following treatment if the dry period is below or equal to 54 days.

IV CLINICAL DOCUMENTATION

This is a generic hybrid application submitted according to Article 13 (3) of Directive 2001/82/EC as amended. A waiver was granted from the study requirements as therapeutic equivalence to the reference product was demonstrated on the basis that the products are identical. 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

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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.

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