ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

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

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Pathozone 250 mg Intramammary Suspension for Cattle

Updated: December 2017

PuAR correct as of 03/10/2018 when RMS was transferred to BG.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0421/001/DC
Name, strength and pharmaceutical form	Pathozone 250 mg Intramammary Suspension for Cattle
Applicant	Zoetis UK Limited 5th Floor, 6 St Andrew Street, London, UK, EC4A 3AE
Active substance	Cefoperazone
ATC Vetcode	QJ51DD12
Target species	Cattle
Indication for use	The product is indicated for the treatment of clinical mastitis in lactating cows. Clinical mastitis caused by a wide range of organisms including the following pathogens have been shown to respond to treatment with cefoperazone. - *Streptococcus dysgalactiae* - *Streptococcus uberis* - *Streptococcus agalactiae* - *Staphylococcus aureus* (including penicillinase producing strains) - *Escherichia coli* - *Trueperella pyogenes* - *Pseudomonas aeruginosa* - *Micrococcus spp.* - *Klebsiella spp*.

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	16th November 2012
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Germany Concerned member states for Repeat Use procedure: Bulgaria, Estonia, Germany, Latvia, Lithuania

I. SCIENTIFIC OVERVIEW

This was a generic application for Pathozone 250 mg Intramammary Suspension for Cattle, for which the reference product was Pathocef 250 mg Intramammary Suspension, first authorised in the United Kingdom in 1985. This application for Pathozone 250 mg Intramammary Suspension for Cattle was submitted in accordance with Article 13 (1), in accordance with of Directive 2001/82/EC, as amended by 2004/28/EC. The proposed product is identical to the reference product, and is marketed by the same Marketing Authorisation Holder that markets the reference product.

The product is intended to treat clinical mastitis in lactating cattle, and has efficacy against a wide range of organisms; *Streptococcus dysgalactiae, Streptococcus uberis, Streptococcus agalactiae, Staphylococcus aureus* (including penicillinase producing strains), *Escherichia coli, Trueperella pyogenes, Pseudomonas aeruginosa, Micrococcus spp. and Klebsiella spp*. The product is for intramammary use and is given via a single administration. The contents of a 10 ml syringe are injected into the infected quarter of the udder immediately after milking. The teat should be thoroughly cleansed and disinfected prior to treatment.

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

[1] SPC – Summary of Product Characteristics.

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

A. Composition

The product contains cefoperazone and excipients all-rac-α-Tocopherol (E307), glycerol monostearate, sorbitan stearate and arachis oil, refined.

The container/closure system consists of a 10 ml white, opaque, low density polyethylene syringe, closed with a protective cap of red low density polyethylene. There are four or ten syringes in a carton. 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.

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. Three sets of batch analysis data were provided. Process validation data on the product were not presented, the process having been well established for the reference product.

C. Control of Starting Materials

The active substance is cefoperazone, an established active substance described in the European Pharmacopoeia (Ph. Eur.). 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. All tests for cefoperazone are specified in the Ph. Eur. All excipients are monographed in the Ph. Eur, and packaging materials were also adequately specified.

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

Lactose and milk powder are produced according to the guidelines on Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products. No other excipients needed to be considered under the guidelines.

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. 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 include those for appearance, identification of active substance and impurities, water content, extractable mass, particle size, specific gravity and sterility.

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. Six commercial batches were analysed for the finished product, and when taken into account against the established stability of the reference product, these data were acceptable.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

The shelf-life of the product as packaged for sale is eighteen months.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and the product is identical to the reference product being produced by the same Marketing Authorisation Holder, the results of bioequivalence, pharmacological and toxicological tests were not required. A user risk assessment (URA) and an environmental risk assessment (ERA) were provided.

Warnings and precautions as listed on the product literature, updated to include a warning with regard to the prudent use of cephalosporins with regard to resistance are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing

User Safety

The applicant provided a user safety assessment in compliance with the relevant guideline which reflected that already approved for the reference product. Warnings and precautions as listed on the product literature 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-reactions to cephalosporins and vice-versa. Allergic reaction 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, such as a skin rash, you should seek medical advice and show the doctor this warning or the package leaflet. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and may require urgent medical attention.
- Wash hands after use.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. The assessment concluded that the $PEC^{2}_{soil\ initial}$ for both intensively reared (2.0 µg/kg) and pasture-raised cattle (1.2 µg/kg), were within acceptable limits. 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

As the proposed product was identical to the reference product, there was no requirement for data in this section. The withdrawal periods for meat and milk remain the same as those of the reference product.

Withdrawal Periods

Based on the data provided, withdrawal periods were established as follows:-

Meat and offal:	2 days
Milk:	72 hours

[2] PEC – Predicted Environmental Concentration.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, 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, which is produced by the same Marketing Authorisation Holder.

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)