College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
3531 AH Utrecht
The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ceftiosan 50 mg/ml, injectable suspension for pigs and cattle

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0148/001/DC
Name, strength and pharmaceutical form	Ceftiosan 50 mg/ml, injectable suspension for pigs and cattle
Applicant	Alfasan Nederland B.V., Kuipersweg 9, 3449 JA Woerden, The Netherlands
Active substance(s)	Ceftiofur (as hydrochlorid)
ATC Vetcode	QJ01DD90
Target species	Pigs and cattle
Indication for use	In pigs: -Treatment of bacterial respiratory disease associated with Pasteurella multocida, Actinobacillus pleuropneumoniae and Streptococcus suis. This product is not to be used in pigs with a bodyweight more than 125 kg. In cattle: -Treatment of bacterial respiratory disease associated with *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni (*previously *Haemophilus somnus)*. -Treatment of acute interdigital necrobacillosis (panaritium, foul in the foot), associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus* (*Porphyromonas asaccharolytica*). -Treatment of the bacterial component of acute post-partum (puerperal) metritis within 10 days after calving associated with *Escherichia coli*, *Arcanobacterium pyogenes* and *Fusobacterium necrophorum*, sensitive to ceftiofur. The indication is restricted to cases where treatment with another antimicrobial has failed.

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MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

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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	23 February 2011
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Germany, Czech Republic, Denmark, Estonia, Greece, Spain, France, Hungary, Ireland, Italy, Lithuania, Latvia, Poland, Portugal, Romania, Slovenia, United Kingdom

I. SCIENTIFIC OVERVIEW

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.
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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains Ceftiofur (as hydrochloride) 50.0 mg ceftiofur (quantitative) and the excipients (qualitative) Hydrogenated soya lecithin, Sorbitan mono-oleate, Cotton seed oil, Water for injections

The container/closure system contains:

Carton box with 1 glass vial type II 50 ml with a rubber stopper and aluminium cap.
Polystyrene box with 12 vials glass type II 50 ml with rubber stopper and aluminium cap.
Carton box with 1 glass vial type II 100 ml with a rubber stopper and aluminium cap.
Polystyrene box with 12 vials glass type II 100 ml with rubber stopper and aluminium cap.
Carton box with 1 glass vial type II 250 ml with a rubber stopper and aluminium cap.
Polystyrene box with 6 vials glass type II 250 ml with rubber stopper and aluminium cap.
The choice of the formulation are justified.

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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 at a licensed manufacturing site.
The product is manufactured in accordance with the Pharmacopoeia of USP and relevant European guidelines.

C. Control of Starting Materials

The active substance is Ceftiofur (as hydrochloride) 50.0 mg ceftiofur, an established active substance described in the Pharmacopoeia of USP 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.

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

D. Control on intermediate products)

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

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.

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.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 36 months.
Shelf-life after first broaching of the container: 28 days.

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III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological tests are not required.

The pharmacological and toxicological aspects of this product is/are identical to the reference product.

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 and the environment

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological tests are not required.

Toxicological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological and toxicological tests are not required.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that:
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 substance 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.

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.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

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Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because The initial predicted environmental concentration in soil is less than 100 µg/kg.

III.B Residues documentation

Withdrawal Periods

Based on the data provided above, a withdrawal period of 8 days for meat and offal in pigs are justified. Based on the data provided a withdrawal period of 8 days for meat and offal in cattle and 0 days for milk are justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are 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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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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 Heads of Veterinary Medicines 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.

Summary of change	**Section updated**	**Approval date**
Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet intended to implement the outcome of a Union referral procedure. (NL/V/0148/001/IA/001)	NA	29th March 2012
Change in the fill volume of the finished product and changes to the labelling or package leaflet, which are not connected with the summary of product characteristics. (NL/V/0148/II/002/G)	Module 3 II.A	31st August 2012
Change in the QPPV and the contact details of the QPPV (NL/V/xxxx/IA/005/G)	NA	5th October 2012
Introduction of a new manufacturer of the active substance and addition of a site where manufacturing operations take place, excluding batch release, batch control and secondary packaging (NL/V/0148/II/004/G)	NA	16th January 2014
Renewal – NL as CMS (NL/V/0148/001/R/001)	NA	15th February 2016
Extension of shelf life as packaged for sale (supported by real time data) (NL/V/0148/001/IB/005)	Module 3 II.G	14th September 2016
Substantial change to the manufacturing process of the active substance and change in the ASMF. (NL/V/0148/II/006/G)	NA	5th December 2016

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Specification of the water content and extension of the shelf life of the finished product as packaged for sale (supported by real time data) (NL/V/0148/IB/007/G)	Module 3 II.G	23rd February 2017

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