Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

DIACEF 50 mg/ml suspension for injection for pigs and cattle

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0187/001/DC
Name, strength and pharmaceutical form	DIACEF 50 mg/ml suspension for injection for pigs and cattle
Applicant	SUPER'S DIANA, S.L. Ctra. C-17, km 17 08150 Parets del Vallès (Barcelona) Spain
Active substance(s)	Ceftiofur (hydrochloride)
ATC Vet code	QJ01DD90
Target species	Pigs and cattle
Indication for use	Infections associated with bacteria susceptible to ceftiofur: In pigs: For the treatment of bacterial respiratory disease associated with *Pasteurella multocida*, *Actinobacillus pleuropneumoniae* and *Streptococcus suis*. In cattle: For the treatment of bacterial respiratory disease associated with *Mannheimia haemolytica* (previously *Pasteurella haemolytica*), *Pasteurella multocida* and *Histophilus somni* (previously *Haemophilus somnus*). For the treatment of acute interdigital necrobacillosis (panaritium, foot rot), associated with *Fusobacterium necrophorum* and *Porphyromonas asaccharolytica* (previously *Bacteroides melaninogenicus*) . For the treatment of the bacterial component of acute post-partum (puerperal) metritis within 10 days after calving associated with *Escherichia coli*, *Trueperella pyogenes* (previously *Arcanobacterium pyogenes*) and *Fusobacterium necrophorum*, susceptible to ceftiofur, where treatment with another antimicrobial has failed.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13.1 of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	18/02/2013
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	CZ, HU, PL, RO

I. SCIENTIFIC OVERVIEW

The veterinary medicinal 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 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 of the constituents

The product contains ceftiofur (hydrochloride) 50 mg/ml and excipients (aluminium stearate, hydrogenated castor oil and medium-chain triglycerides).

The container/closure system are type I colourless glass vials of 100 and 250 ml with bromobutyl rubber stopper and aluminium cap. 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.

B. Description of the manufacturing method

The product is manufactured and sterilised fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

The manufacturing process is a non-standard one. Process validation on full-scale batches was performed.

C. Control of starting materials

The active substance is ceftiofur hydrochloride, an established active substance. The manufacturing authorisation holder certifies that 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.

A copy of the ASMF of the API manufacturer has been included.

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

D. Control tests carried out at intermediate stages of the manufacturing process

The tests performed during production are described and correspond to those carried out after primary packaging before terminal sterilization.

E. 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 test

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.

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.

The claim of 28 days stability after broaching is based on the demonstration of stability for two batches broached and stored 28 days at 25±2ºC/60±5% RH.

G. Other information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT

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

User Safety

The user safety aspects of this product are identical to the reference product. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product

Ecotoxicity

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

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed

Residue Studies

Residue depletion studies in injection sites using the final formulation have also been conducted in pigs and cattle. Samples of muscle at injection site were taken from animals at several time points. The analytical method was fully validated.

MRLs

Ceftiofur is included in the Regulation 470/2009 as a pharmacological active substance with the following MRLs:

Active substance	Marker residue	Animal specie	MRL (µg/kg)	Target tissue
Ceftiofur	Sum of all residue retaining the betalactam structure expressed as Desfuroylceftiofur	All mammalian food producing species	1000 2000 2000 6000 100	Muscle Fat Liver Kidney Milk

Withdrawal Periods

Based on the data provided above, the following withdrawal periods are justified:

Pigs: meat and offal 5 days
Cattle: meat and offal: 6 days; milk: zero days.

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.

The applicant conducted an *in vivo* bioequivalence study in each of the target species to address a comparable bioavailability between the test and the reference product. The results obtained confirmed bioequivalence.

In order to assess the local tolerance, the applicant provided an injection site tolerance study in both target species in compliance with GLP and the relevant guideline VICH GL 43. The same local reaction lesions were found similar to those described for the reference product. The observed local adverse reactions are properly addressed on section 4.6 of SPC.

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.

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 veterinary Heads of Agencies website (www.hma.eu).

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated in Module 3**	**Approval date**
Addition of target species - cattle (ES/V/0187/001/DX/002)	IIIA IIIB IV	15/09/2017

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