Veterinary Medicines Directorate

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Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Bimacure 500mg Intrauterine Suspension for Cattle

Date Created: September 2022

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Bimacure 500mg Intrauterine Suspension for Cattle
Applicant	Oy Medfiles Ltd Volttikatu 5 Kuopio FI – 70700 Finland
Active substance	Cefapirin (as cefairin benzathine)
ATC Vetcode	QG51AA05
Target species	Cattle
Indication for use	For the treatment of subacute and chronic endometritis in cows (at least 14 days after parturition) caused by bacteria susceptible to cefapirin.

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	Hybrid generic application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	15/6/2022

I. SCIENTIFIC OVERVIEW

The application is for generic product submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended (for a 'hybrid' generic). The reference product is Metricure 500 mg Intrauterine Suspension, authorised 14 October 2003.

This was determined a generic 'hybrid' application because bioequivalence could not be demonstrated or inferred through bioavailability studies/waivers from bioequivalence study requirements.

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, 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.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains cefapirin benzathine and the excipients hydrogenated castor oil, macrogol cetostearyl ether 12 and ether 20 and medium chain triglycerides.

The container/closure system consists of a syringe formed from a linear low density polyethethylene (LDPE) body, a LDPE plunger and a LDPE cap. The

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

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.

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 homogenisation of the excipients, sterilisation, addition of the active substance and mixing.

The product is manufactured using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

II.C. Control of Starting Materials

The active substance is cefapirin benzathine, an established active substance described in the United States Pharmacopoeia. 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.

The specification is based upon that from the ASMF.

The excipients and packaging materials both comply with Ph. Eur.

II.C.4. Substances of Biological Origin

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. 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. Control tests on the finished product are those for appearance, particle size, viscosity, water, identification, related substances, assay, deliverable mass, uniformity of dosage units, sterility.

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.

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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
This veterinary medicinal product does not require any special storage conditions.
Syringes are for single use only.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

As this is an application for a generic 'hybrid' product, the applicant is not required to submit pharmacological or toxicological data on the active substance.

Toxicological Studies

As this is an application for a generic 'hybrid' product, the applicant is not required to submit pharmacological or toxicological data on the active substance.

User Safety

This application is made in accordance with Article 13(3) of Council Directive 2002/28/EC, as amended, identical user safety precautions are advised for this product.

A user risk assessment was provided in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore, the following applicant’s user recommendations are appropriate:

- Penicillin and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillin may lead to cross reactions to cephalosporins and *vice versa*.
- Allergic reactions to these substances are occasionally 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 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.

- Gloves should be worn in order to avoid skin contact during preparation and administration of the product.
- Accidental spillage on the skin should be washed off immediately with soap and water.
- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The product will be used to treat a small number of animals in a flock or herd and as such environmental exposure will be low. A Phase II ERA was not required.

III.B.2 Residues documentation

Residue Studies

Residues data were not submitted on the basis that the generic product is bioequivalent to the reference product.

MRLs

Cefaparin benzathine is listed in Table 1/ of Regulation 37/2010. All excipients are listed with No MRL Required.

MRLs are listed below:

MRLs (µg/kg)	Bovine
Muscle	50
Kidney	100
Fat / skin	50

Milk	60

Withdrawal Periods

Based on the data provided, a withdrawal period of 1 day for meat in cattle and 0 hours for milk are justified.

IV. CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

The product is exempt from bioequivalence testing as the applicant demonstrated that both the formulations of the test and reference product are identical.

Resistance

The applicant has concluded that the published studies indicate that resistance to cefapirin can be present in the main pathogens isolated from bovine metritis cases, but globally the overall prevalence of resistance across different geographical regions and farming practices is not known.

Adequate warnings and precautions appear on the product literature.

IV.II. Clinical Documentation

No data have been submitted.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that the benefit/risk profile of the product is favourable.

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.

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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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