Irish Medicines Board

Company:
Cyton Biosciences Ltd

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ubrostar Dry Cow Intramammary Suspension for Cattle

MODULE 1

PRODUCT SUMMARY

EU Procedure number	IE/V/0271/001/DC
Name, strength and pharmaceutical form	Ubrostar Dry Cow Intramammary Suspension for Cattle
Applicant	Cyton Biosciences Ltd 2 St. Pauls Road, Clifton, Bristol BS8 1LT, United Kingdom.
Active substance	Penethamate Hydriodide Benethamine Penicillin Framycetin Sulphate
ATCvet code	QJ51RC25
Target species	Cattle (at dry off)
Indication for use	For the treatment of subclinical mastitis at drying off, and the prevention of new bacterial infections of the udder during the dry period in dairy cows, caused by bacteria susceptible to penicillin and framycetin.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Article 13(1) of Directive 2001/82/EC, as amended (a generic application)
Date of completion of the original decentralised procedure	28/09/2011
Concerned Member States for procedure	BE, BG, CZ, FR, HU, NL, PL, RO, SI, SK, UK

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. Composition

The product contains Penethamate Hydriodide 100 mg (equivalent to 77.2 mg penethamate), Benethamine Penicillin 280 mg (equivalent to 171.6 mg penicillin), Framycetin Sulphate 100 mg (equivalent to 71.0 mg framycetin) and the excipients aluminimum monostearate, hydrogenated castor oil and liquid paraffin.

The product is packaged in a cardboard box or plastic container containing 20 or 60 single use intramammary syringes and 20 or 60 teat wipes (containing isopropanol 70%). Each 7 ml syringe (cylinder with piston and cap, all made of low density polyethylene) contains 4.5 g intramammary suspension.

The particulars of the containers and controls performed are provided and conform to the regulation.

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.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substances Penethamate Hydriodide, Benethamine Penicillin and Framycetin Sulphate are all established active substances. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with the specifications have been provided.

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

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

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 has been provided demonstrating compliance with the specification.

G. Stability

Stability data on the active substances has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances 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.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

The application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended (a generic application).

Exemption from bioequivalence studies with Benestermycin Dry Cow Intramammary Suspension (in accordance with paragraph 4(c) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016/00-corr-FINAL)) is accepted on the basis that:

"The formulations are identical (identical active and inactive substances as well as physicochemical properties e.g. identical concentration, dissolution profile, crystalline form, dosage form, and similar particle size distribution with identical manufacturing process) and bioavailability of the reference formulation has been adequately demonstrated in the target species."

Toxicological Studies

As this is a generic application according to Article 13, results of toxicological tests are not required.

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 / the environment / consumers.

User Safety

The applicant has provided a user safety assessment which shows that when used in accordance with label recommendations, the product will not pose any greater risk to the user than the risks associated with use of the reference product, Benestermycin Dry Cow Intramammary Suspension.

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. The assessment concluded that the use of the product as recommended does not constitute a risk for the environment.

No warnings regarding the environment are therefore required.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted using the final formulation. Given that Ubrostar Dry Cow is identical to the reference product in all respects, the depletion of residues from the mammary gland will be identical for both products.

As a consequence the withdrawal periods approved for the reference product can be applied to the test product.

MRLs

Benzylpenicillin is included in Table 1 of the Annex of Commission Regulation (EU) No. 37/2010 (O.J. 20.1.2010, L 15/11). The marker substance is benzylpenicillin.

MRLs are listed below:

	Cattle
Muscle	50 µg/kg
Liver	50 µg/kg
Kidney	50 µg/kg
Fat	50 µg/kg
Milk	4 µg/kg

Framycetin is included in Table 1 of the Annex of Commission Regulation (EU) No. 37/2010 (O.J. 20.1.2010, L 15/48). The marker substance is neomycin B.

MRLs are listed below:

	Cattle
Muscle	500 µg/kg
Liver	500 µg/kg
Kidney	5000 µg/kg
Fat	500 µg/kg
Milk	1500 µg/kg

Withdrawal Periods

Based on the data provided above, a withdrawal period of 10 days for meat in cattle is justified. For milk, the following periods were justified:
If treated at least 35 days before calving, milk must not be used for 36 hours after calving. If treated less than 35 days before calving, milk must not be used for 37 days after treatment.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

A target animal safety study specific to the test product has not been presented with the application. Given that:

- The test and reference product are qualitatively and quantitatively identical in terms of active substance and excipient content,
- The toxicological profile of the active substances are well known,
- The proposed indications and posology for the test product are identical to the authorised indications and posology of the reference product,

the absence of tolerance studies specific to the test product can be accepted.

The information relating to adverse reactions and overdose included on the SPC for the test product is the same as that included on the SPC of the reference product, Benestermycin Dry Cow Intramammary Suspension.

Resistance

As this is a generic application according to Article 13, and bioequivalence with a reference product has been accepted, it can be said that the risk of development of resistance to the active ingredients in the product is no different to that of the reference product, Benestermycin Dry Cow Intramammary Suspension.

IV.B Clinical Studies

The application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended (a generic application).

Exemption from bioequivalence studies is claimed in accordance with paragraph 4(c) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016/00-corr-FINAL).

As the test product is considered to be bioequivalent to Benestermycin Dry Cow Intramammary Suspension, it is accepted that the efficacy profile will be equivalent to that 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.

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).

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.

None.