Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

FINAL PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

PENETHAONE 236.3 mg/ml

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0226/001/DC
Name, strength and pharmaceutical form	Penethaone 236.3 mg/ml
Applicant	Cyton Biosciences Ltd
Active substance(s)	Penethamate hydriodide
ATC Vet code	QJ01CE90
Target species	Cattle (lactating cows)
Indication for use	Treatment of mastitis in lactating cows caused by *Streptococcus uberis*, *Streptococcus dysgalactiae*, *Streptococcus agalactiae* and *Staphylococcus aureus* (beta-lactamase non-producing), sensitive to penicillin.

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MODULE 2

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

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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	22/04/2015
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	AT, BE, BG, CZ, DE, DK, EL, FR, HU, IE, IS, IT, LT, NL, NO, PL, PT, RO, SE, SK, UK

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

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 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

Powder vial contains penethamate hydriodide (4726 mg (5 MIU) or 9452 mg (10 MIU)) as active substance and silica colloidal anhydrous as excipient.

Solvent vial contains potassium dihydrogen phosphate, sodium citrate, povidone and water for injections.

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The reconstituted suspension contains 236.3 mg (250,000 IU) /ml of penethamate hydriodide.

The container/closure system consists at a powder vial of type I colourless glass vial (25 ml for
5MIU presentation) or powder vial of type II colourless glass vial (50 ml for 10MIU presentation) both closed with a bromobutyl stopper and sealed with an aluminium flip-top seal. And the solvent vial consists at type II colourless glass vial closed with a bromobutyl stopper and sealed with an aluminium flip-top seal (20 ml for 5MIU presentation and 50 ml for 10MIU presentation). 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. 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 substance, penethamate hydriodide, is not described in any Pharmacopoeia. It 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.

Details of the active substance manufacture are provided in the form of an ASMF in CTD format.

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.

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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.

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.

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 (5 years), when stored under the approved conditions.

The claim of a 24 hours stability after reconstitution is based on the demonstration of stability for a batch broached and stored 2 days at room temperature.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

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As this was a generic application according to Article 13 of Directive 2001/82/EC, amended by Directive 2004/28/EC, and pharmaceutical equivalence of test and reference product has been shown, results of safety and residue tests are not required.

The safety aspects of this product 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, the environment and consumers.

III.A Safety Testing

Pharmacological Studies

Since this is an application under Article 13(1) and pharmaceutical equivalence of test and reference product has been shown, pharmacological data have not provided.

Toxicological Studies

Since this is an application under Article 13(1) and pharmaceutical equivalence of test and reference product has been shown, toxicological data have not provided.

User Safety

The applicant has not provided a user safety assessment since this is an application under Article 13. Risks from use of the product will be identical to those for 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. The assessment concluded that the product has an acceptable risk for the environment.

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

Residue Studies

No residue depletion studies were conducted since this is a generic application and pharmaceutical equivalence of test and reference product has been shown.

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MRLs

Penethamate is listed in Table 1 of the Annex of Commission Regulation (EU) No. 37/2010 in accordance with the following table:

Pharmacologically active substance	Marker residue	Animal species	MRL	Target tissues
Penethamate	Benzylpenicillin	All mammalian food producing species	50 µg/kg 50 µg/kg 50 µg/kg 50 µg/kg 4 µg/kg	Muscle Fat Liver Kidney Milk

Withdrawal Periods

Based on the data provided above, a withdrawal period of 4 days for meat and offal and 60 hours for milk in cattle are justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this was a generic application according to Article 13 of Directive 2001/82/EC, amended by Directive 2004/28/EC, and pharmaceutical equivalence of test and reference product has been shown, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

As this was a generic application according to Article 13 of Directive 2001/82/EC, amended by Directive 2004/28/EC, and pharmaceutical equivalence of test and reference product has been shown, pre-clinical studies are not required.

IV.B Clinical Studies

As this was a generic application according to Article 13 of Directive 2001/82/EC, amended by Directive 2004/28/EC, and pharmaceutical equivalence of test and reference product has been shown, clinical studies are not required.

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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 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>

or

Complete this section for extensions to the same VPA range or defined, significant variations, using the table shown below.

Some examples of significant changes in safety or efficacy data are:

- Changes to pharmacokinetic data leading to a change in the SPC
- Changes to toxicological data leading to a change in the SPC
- Changes to user safety warnings
- Changes to ecotoxicological information as given in the SPC or changes to disposal warnings
- New residue studies in new target species or tissues
- Reassessment of residue data or new studies resulting from changes to MRL
- Changes to withdrawal period
- Changes to target species
- Changes to target species tolerance data leading to change in warnings/precautions for target species New or changed indications

Significant changes in administrative or quality data include any Type II change, which affects the initial report. The following Type IA or IB changes may also apply:

- Name of product [Type IA: 2]
- Name of active substance [Type IA: 3}
- MAH [Type IA: 1]
- Composition of the medicinal product [Type IB: 18, Type IA/B: 25, 34, 35, 39]
- Container/closure system [Type 1/B: 26, 28, 29, 36, 41, 43]
- Method of preparation [Type 1B: 33]
- Active substance specification [Type IB: 25]
- CEP [Type IA/B: 15]

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- Re-test period or storage conditions of active substance [Type IB: 17]
- Excipient specifications [Type 1A/B: 25]
- Packaging materials[Type 1A/B: 28, 29, 36, 41, 43]
- TSE [Type 1A: 16, 22]
- Shelf-life or storage conditions of the finished product [Type 1B: 42]

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
<Example: Change to active substance specification> (MS/V/XXX/X/IB/XX)	N/A	

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated in Module 3**	**Approval date**
<Example: Addition of target species - pigs> (MS/V/XXX/X/II/XX)	<IIIA> <IIIB> <IV>	

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