[Version 8, 10/2012]

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, BG, CZ, DE, EL, ES, HU, IE, IT, LT, NL, PL, PT, RO, SK, UK: Penethaone 236.3 mg/ml powder and solvent for suspension for injection for cattle
DK, IS, SE: Penethaone vet 236.3 mg/ml powder and solvent for suspension for injection for cattle
NO: Vetmast 236.3 mg/ml powder and solvent for suspension for injection for cattle
FR: Penethaone 182.5 mg/ml powder and solvent for suspension for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of the reconstituted suspension contains:
Active substance
Penethamate hydriodide 236.3 mg (equivalent to 182.5 mg penethamate)
Equivalent to 250,000 IU of penethamate hydriodide

5,000,000 IU presentation
Powder vial contains 4.75 g of powder
Active substance
Penethamate hydriodide 4726 mg (equivalent to 3649 mg of penethamate)
Equivalent to 5,000,000 IU of penethamate hydriodide
Excipients, q.s.f.

Solvent vial contains 18 ml
Excipients, q.s.f.

Total amount of reconstituted suspension 20 ml

10,000,000 IU presentation
Powder vial contains 9.50 g of powder
Active substance
Penethamate hydriodide 9452 mg (equivalent to 7299 mg of penethamate)
Equivalent to 10,000,000 IU of penethamate hydriodide
Excipients, q.s.f.

Solvent vial contains36 ml
Excipients, q.s.f.

Total amount of reconstituted suspension 40 ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection
Powder vial: white-cream fine powder
Solvent vial: clear colourless solution
Reconstituted suspension: white-cream suspension

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (lactating cows)

4.2 Indications for use, specifying the target species

Treatment of mastitis in lactating cows caused by *Streptococcus uberis*, *Streptococcus dysgalactiae*, *Streptococcus agalactiae* and *Staphylococcus aureus* (beta-lactamase non-producing), sensitive to penicillin.

4.3 Contraindications

Do not use in animals known to be hypersensitive to penicillins, cephalosporins, and/or any of the excipients.
Do not administer intravenously.
Do not use in lagomorphs and rodents such as guinea pigs, hamsters or gerbils.
Do not administer to animals with renal disease including anuria or oliguria.

4.4 Special warnings for each target species

Treatment should be carried out during lactation.

4.5 Special precautions for use

This veterinary medicinal product does not contain any antimicrobial preservative.

Special precautions for use in animals

Using penethamate hydriodide for the treatment of mastitis must be accompanied by hygienic measures to prevent reinfection.
Where local (regional, farm-level), epidemiological information indicate possible reduced susceptibility of the relevant strains of the bacterial species involved in mastitis, use of the product should be based on susceptibility testing on bacteria isolated from diseased animals.

The veterinary medicinal product is not effective against beta-lactamase producing organisms.

Official national and regional antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to benzylpenicillin and may decrease the effectiveness of treatment with other beta-lactam antimicrobials due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

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 substances 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.

Handle this product with great care to avoid exposure.

Wear gloves when handling the veterinary medicinal product to avoid contact sensitization.

In case of accidental self-injection or if you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the package leaflet or the label to the doctor

Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

The symptoms of adverse reactions range from mild skin reactions such as urticaria and dermatitis to severe reactions such as anaphylactic shock with tremors, vomiting, salivation, gastrointestinal disorders and laryngeal oedema.

In some situations the treatment may lead to secondary infections due to overgrowth of non-target organisms.

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

The product should not be administered with antibiotics that have a bacteriostatic mode of action.

4.9 Amounts to be administered and administration route

Administer by deep intramuscular injection.
Directions for use: Reconstitute the suspension using the entire contents of the solvent vial.

To provide the correct dose:

Use the powder vial, which contains penethamate hydriodide 5,000,000 IU with the solvent vial, which contains 18 ml of a sterile solvent.
Or alternatively, use the powder vial, which contains penethamate hydriodide 10,000,000 IU with the solvent vial, which contains 36 ml of a sterile solvent.

Shake well after reconstitution. A minimum of 10 inversions of vials can be necessary.
Each ml of suspension contains 250,000 IU (236.3 mg) of penethamate hydriodide.

Dose: 15,000 IU (14.2 mg) of penethamate hydriodide per kg of body weight / day (equivalent to 6 ml of reconstituted medicinal product / 100 kg body weight) for three to four consecutive days. Shake well before use.

Administer the recommended daily dose every 24 hours, for three to four consecutive administrations.

To ensure administration of a correct dose, body weight should be determined as accurately as possible.

The recommended maximum volume to be administered at a single injection site is 20 ml.

The stopper should not be punctured more than 10 times.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In cases of overdose, adverse reactions such as those described in Section 4.6 may occur.

4.11 Withdrawal period(s)

Meat and offal: 4 days
Milk: 60 hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, beta- lactam antibacterials, penicillins.
ATCvet code: QJ01CE90

5.1 Pharmacodynamic properties

The active substance, penethamate hydriodide, is a prodrug which releases benzylpenicillin. Chemically, it is a diethylaminoethanol ester of penicillin.

Mode of action:
Benzylpenicillin works by blocking the biosynthesis of the bacterial cell wall. Benzylpenicillin covalently attaches to and subsequently inactivates penicillin-binding proteins (PBPs), which are located on the inner surface of the bacterial membrane. The PBPs (transpeptidase, carbopeptidasas, endopeptidases) are enzymes involved in the terminal stages of bacterial cell-wall synthesis. Penicillins are only active against bacteria in the multiplication phase.

The antimicrobial spectrum of the active substance corresponds to that of benzylpenicillin which is effective against beta-lactamase negative *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis* and *Staphylococcus aureus*.

Mechanisms of resistance:
The most frequent mechanism is producing beta-lactamases (more specifically penicillinase **especially in *S. aureus***), which break the beta-lactam ring of penicillins making them inactive.

5.2 Pharmacokinetic particulars

Following intramuscular administration to dairy cows, C_{max} is rapidly achieved in blood and milk (3 and 7 hours respectively). Ninety percent of the antibiotic is hydrolysed in blood and 98% in milk. As a result of hydrolysis, diethylaminoethanol and benzylpenicillin are produced, with the latter being the therapeutically active molecule. The distribution is rapid within the organism, with particular affinity for lung and mammary gland tissues. It crosses the placenta and enters the foetal circulation slowly.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder vial:
Silica colloidal anhydrous

Solvent vial:
Potassium dihydrogen phosphate (for pH adjustment)
Sodium citrate (for pH adjustment)
Povidone
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product should not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 5 years.
Shelf life after reconstitution according to directions: 24 hours.

6.4. Special precautions for storage

Before reconstitution, the powder and solvent vials do not require any special storage conditions.
The reconstituted suspension should be stored in the refrigerator (2-8°C).

6.5 Nature and composition of immediate packaging

Carton box containing either:

5 MIU presentation
Powder vial: 25 ml type I colourless glass vial closed with a bromobutyl stopper and sealed with an aluminium flip-top seal
Solvent vial: 20 ml type II colourless glass vial closed with a bromobutyl stopper and sealed with an aluminium flip-top seal

or

10 MIU presentation
Powder vial: 50 ml type II colourless glass vial closed with a bromobutyl stopper and sealed with an aluminium flip-top seal.
Solvent vial: 50 ml type II colourless glass vial closed with a bromobutyl stopper and sealed with an aluminium flip-top seal

Pack sizes:
5,000,000 IU powder vial and 18 ml solvent vial
5,000,000 IU powder vial and 18 ml solvent vial x 5
5,000,000 IU powder vial and 18 ml solvent vial x 10
10,000,000 IU powder vial and 36 ml solvent vial
10,000,000 IU powder vial and 36 ml solvent vial x 5
10,000,000 IU powder vial and 36 ml solvent vial x 10

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Cyton Biosciences Ltd.
68 Macrae Road
Eden Office Park
Ham Green
Bristol BS20 0DD
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: <{DD/MM/YYYY}><{DD month YYYY}.>

10 DATE OF REVISION OF THE TEXT

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

PROHIBITION OF SALE, SUPPLY AND/OR USE

Veterinary medicinal product subject to veterinary prescription.

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, BG, CZ, DE, EL, ES, HU, IE, IT, LT, NL, PL, PT, RO, SK, UK: Penethaone 236.3 mg/ml powder and solvent for suspension for injection for cattle
DK, IS, SE: Penethaone vet 236.3 mg/ml powder and solvent for suspension for injection for cattle
NO: Vetmast 236.3 mg/ml powder and solvent for suspension for injection for cattle
FR: Penethaone 182.5 mg/ml powder and solvent for suspension for injection for cattle
penethamate hydriodide

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Powder vial: 5,000,000 IU (4726 mg) penethamate hydriodide
Solvent vial: 18 ml

Powder vial: 10,000,000 IU (9452 mg) penethamate hydriodide
Solvent vial: 36 ml

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

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection.

4. PACKAGE SIZE

5,000,000 IU powder vial and 18 ml solvent vial
5,000,000 IU powder vial and 18 ml solvent vial x 5
5,000,000 IU powder vial and 18 ml solvent vial x 10
10,000,000 IU powder vial and 36 ml solvent vial
10,000,000 IU powder vial and 36 ml solvent vial x 5
10,000,000 IU powder vial and 36 ml solvent vial x 10

5. TARGET SPECIES

Cattle (lactating cows)

6. INDICATION

7. METHOD AND ROUTE(S) OF ADMINISTRATION

IM
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 4 days
Milk: 60 hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once reconstituted, use within 24h.

11. SPECIAL STORAGE CONDITIONS

Before reconstitution, the powder and solvent vials do not require any special storage conditions.
The reconstituted suspension can be stored in a refrigerator (2-8°C) for 24h.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Cyton Biosciences Ltd.
68 Macrae Road
Ham Green
Bristol BS20 0DD
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

<Lot> {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

GLASS VIAL LABEL (POWDER)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, BG, CZ, DE, EL, ES, HU, IE, IT, LT, NL, PL, PT, RO, SK, UK: Penethaone 236.3 mg/ml powder for suspension for injection for cattle
DK, IS, SE: Penethaone vet 236.3 mg/ml powder for suspension for injection for cattle
NO: Vetmast 236.3 mg/ml powder for suspension for injection for cattle
FR: Penethaone 182.5 mg/ml powder and solvent for suspension for injection for cattle
penethamate hydriodide

2. QUANTITY OF THE ACTIVE SUBSTANCE

Each vial contains 5,000,000 IU (4726 mg) of penethamate hydriodide
Each vial contains 10,000,000 IU (9452 mg) of penethamate hydriodide

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

5,000.000 IU (4726 mg)
10,000,000 IU (9452 mg)

4. ROUTE(S) OF ADMINISTRATION

IM
Read package leaflet before use.

5. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 4 days
Milk: 60 hours

6. BATCH NUMBER

<Batch><Lot> {number}

7. EXPIRY DATE

EXP {month/year}
Once reconstituted, use within 24h.

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING (LABEL) OF THE DILUENT

GLASS VIAL LABEL (SOLVENT)

1. NAME OF THE DILUENT

AT, BE, BG, CZ, DE, EL, ES, HU, IE, IT, LT, NL, PL, PT, RO, SK, UK: Solvent for penethaone 236.3 mg/ml
DK, IS, SE: Solvent for penethaone vet 236.3 mg/ml
NO: Solvent for Vetmast 236.3 mg/ml
FR: Solvent for penethaone 182.5 mg/ml

2. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

18 ml
36 ml

3. ROUTE(S) OF ADMINISTRATION

4. STORAGE CONDITIONS

5. BATCH NUMBER

<Lot> {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
AT, BE, BG, CZ, DE, EL, ES, HU, IE, IT, LT, NL, PL, PT, RO, SK, UK: Penethaone 236.3 mg/ml powder and solvent for suspension for injection for cattle
DK, IS, SE: Penethaone vet 236.3 mg/ml powder and solvent for suspension for injection for cattle
NO: Vetmast 236.3 mg/ml powder and solvent for suspension for injection for cattle
FR: Penethaone 182.5 mg/ml powder and solvent for suspension for injection for cattle

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Cyton Biosciences Ltd.
68 Macrae Road
Eden Office Park
Ham Green
Bristol BS20 0DD
United Kingdom

Manufacturer responsible for batch release:
Divasa-Farmavic S.A.
Ctra. Sant Hipòlit, km 71
08503 Gurb – Vic, Barcelona
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, BG, CZ, DE, EL, ES, HU, IE, IT, LT, NL, PL, PT, RO, SK, UK: Penethaone 236.3 mg/ml powder and solvent for suspension for injection for cattle
DK, IS, SE: Penethaone vet 236.3 mg/ml powder and solvent for suspension for injection for cattle
NO: Vetmast 236.3 mg/ml powder and solvent for suspension for injection for cattle
FR: Penethaone 182.5 mg/ml powder and solvent for suspension for injection for cattle
penethamate hydriodide

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Powder and solvent for suspension for injection.
Powder vial: white-cream fine powder
Solvent vial: clear colourless solution
Reconstituted suspension: white-cream suspension

1 ml of the reconstituted suspension contains
Active substance
Penethamate hydriodide 236.3 mg (equivalent to 182.5 mg penethamate)
Equivalent to 250,000 IU of penethamate hydriodide

5,000,000 IU presentation
Powder vial contains 4.75 g of powder
Active substance
Penethamate hydriodide 4726 mg (equivalent to 3649 mg of penethamate)
Equivalent to 5,000,000 IU of penethamate hydriodide)
Excipients, q.s.f.

Solvent vial contains 18 ml
Excipients, q.s.f.

Total amount of reconstituted suspension 20 ml

10,000,000 IU presentation
Powder vial contains 9.50 g of powder
Active substance
Penethamate hydriodide 9452 mg (equivalent to 7299 mg of penethamate)
Equivalent to 10,000,000 IU of penethamate hydriodide
Excipients, q.s.f.

Solvent vial contains 36 ml
Excipients, q.s.f.

Total amount of reconstituted suspension 40 ml

4. INDICATION

Treatment of mastitis in lactating cows caused by *Streptococcus uberis*, *Streptococcus dysgalactiae*, *Streptococcus agalactiae* and *Staphylococcus aureus* (beta-lactamase non-producing) , sensitive to penicillin.

5. CONTRAINDICATIONS

Do not use in animals known to be hypersensitive to penicillins, cephalosporins, and/or any of the excipients.
Do not administer intravenously.
Do not use in lagomorphs and rodents such as guinea pigs, hamsters or gerbils..
Do not administer to animals with renal disease including anuria or oliguria.

6. ADVERSE REACTIONS

The symptoms of adverse reactions range from mild skin reactions such as urticaria and dermatitis to severe reactions such as anaphylactic shock with tremors, vomiting, salivation, gastrointestinal disorders and laryngeal oedema.

In some situations the treatment may lead to secondary infections due to overgrowth of non-target organisms.

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle (lactating cows)

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Administer by deep intramuscular injection.

Directions for use: Reconstitute the suspension using the entire contents of the solvent vial.

To provide the correct dose:

Use the powder vial, which contains penethamate hydriodide 5,000,000 IU with the solvent vial, which contains 18 ml of a sterile solvent.
Or alternatively, use the powder vial, which contains penethamate hydriodide 10,000,000 IU with the solvent vial, which contains 36 ml of a sterile solvent.

Shake well after reconstitution. A minimum of 10 inversions of vials can be necessary. Each ml of suspension contains 250,000 IU (236.3 mg) of penethamate hydriodide.

Dose: 15,000 IU (14.2 mg) of penethamate hydriodide per kg of body weight / day (equivalent to 6 ml of reconstituted medicinal product / 100 kg body weight) for three to four consecutive days. Shake well before use.
Administer the recommended daily dose every 24 hours, for three to four consecutive administrations.

The recommended maximum volume to be administered at a single injection site is 20 ml.

9. ADVICE ON CORRECT ADMINISTRATION

To ensure administration of a correct dose, body weight should be determined as accurately as possible.

The stopper should not be punctured more than 10 times.

10. WITHDRAWAL PERIOD

Meat and offal: 4 days
Milk: 60 hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not use this veterinary medicinal product after the expiry date which is stated on the label/carton. The expiry date refers to the last day of the month.
Before reconstitution, the powder and solvent vials do not require any special storage conditions.
Shelf life after reconstitution according to directions: 24 hours.
The reconstituted suspension should be stored in the refrigerator (2-8°C).

12. SPECIAL WARNING(S)

This veterinary medicinal product does not contain any antimicrobial preservative.

Special precautions for use in animals:

Using penethamate hydriodide for the treatment of mastitis must be accompanied by hygienic measures to prevent reinfection.

Where local (regional, farm-level), epidemiological information indicate possible reduced susceptibility of the relevant strains of the bacterial species involved in mastitis, use of the product should be based on susceptibility testing on bacteria isolated from diseased animals.

The veterinary medicinal product is not effective against beta-lactamase producing organisms.

Official national and regional antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to benzylpenicillin and may decrease the effectiveness of treatment with other beta-lactam antimicrobials due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

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 substances 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.

Handle this product with great care to avoid exposure.

Wear gloves when handling the veterinary medicinal product to avoid contact sensitization.

In case of accidental self-injection or if you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the package leaflet or the label to the doctor

Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

Wash hands after use.

Pregnancy and lactation:

Can be used during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:

The product should not be administered with antibiotics that have a bacteriostatic mode of action.

Overdose (symptoms, emergency procedures, antidotes):

In cases of overdose, adverse reactions such as those described in Section 6 may occur.

Incompatibilities:

In the absence of compatibility studies, this veterinary medicinal product should not be mixed with other veterinary medicinal products.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack sizes:
5,000,000 IU powder vial and 18 ml solvent vial
5,000,000 IU powder vial and 18 ml solvent vial x 5
5,000,000 IU powder vial and 18 ml solvent vial x 10
10,000,000 IU powder vial and 36 ml solvent vial
10,000,000 IU powder vial and 36 ml solvent vial x 5
10,000,000 IU powder vial and 36 ml solvent vial x 10

Not all pack sizes may be marketed.