

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Penethaone 236.3 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 contains 36 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), susceptible to penicillin.

4.3 Contraindications

Do not use in cases of hypersensitivity 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.

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria. "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.
- People with known hypersensitivity to penicillins, cephalosporins or any of the excipients should avoid contact with the veterinary medicinal product..
- 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)

In very rare cases 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.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Pregnancy:

Can be used during pregnancy.

Lactation:

Can be used during 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.

Anti-inflammatories such as salicylates, produce an increase in the elimination half-life of penetamate (iohydrate). In case of joint administration, adjust the dose of the antibacterial

4.9 Amounts to be administered and administration route

For deep intramuscular use.

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: 2.5 days (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, carboxypeptidases, endopeptidases) are enzymes involved in the terminal stages of bacterial cell-wall synthesis. Penicillins are only active against bacteria in the multiplication phase, so its activity is primarily bactericidal and time-dependent.

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, Maximum serum concentrations 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 Major 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

Divasa-Farmavic, S.A.
Ctr. Sant Hipòlit, km 71
08503 Gurb-Vic (Barcelona)
Spain

8. MARKETING AUTHORISATION NUMBER

Vm 33229/4004

9. DATE OF FIRST AUTHORISATION

04 August 2015

10. DATE OF REVISION OF THE TEXT

May 2020

PROHIBITION OF SALE, SUPPLY AND/OR USE

Veterinary medicinal product subject to veterinary prescription.
To be administered by a veterinary surgeon or under their direct responsibility.

Approved 14 May 2020

