

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Procipen 300mg/ml suspension for injection for cattle sheep and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance

Benzylpenicillin procaine 300 mg
(corresponding to 175.8 mg of benzylpenicillin)

Excipients

Methyl Parahydroxybenzoate E218 2.0 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suspension for injection.
An off-white suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, sheep and pigs.

4.2 Indications for use, specifying the target species

For the treatment of acute systemic infections caused by bacteria susceptible to benzylpenicillin.

4.3 Contraindications

Do not inject intravenously.

Do not use in known cases of hypersensitivity to penicillin, cephalosporins, procaine or to any of the excipients.

Do not use in case of severe renal dysfunction with anuria and oliguria.

Do not use in very small herbivores such as guinea pigs, gerbils and hamsters.

Do not use in the presence of β -lactamase producing pathogens.

4.4 Special warnings for each target species

Complete cross-resistance has been shown between benzylpenicillin procaine and other penicillins.

After absorption, benzylpenicillin poorly penetrates biological membranes (e.g., blood-brain barrier) since it is ionised and poorly lipid soluble. Use of the product for treatment of meningitis or CNS infections due to e.g., *Streptococcus suis* or *Listeria monocytogenes* may not be efficacious. Furthermore, benzylpenicillin penetrates mammalian cells poorly and hence this product may have little effect in treating intracellular pathogens e.g., *Listeria monocytogenes*.

Elevated MIC values or bi-modal distribution profiles suggesting acquired resistance have been reported for the following bacteria:

- *Glaesserella parasuis*, *Staphylococcus* spp. causing MMA/PPDS, *Streptococcus* spp. and *S. suis* in pigs;

- *Fusobacterium necrophorum* causing metritis and *Mannheimia haemolytica* (only in some member states), as well as *Bacteroides* spp., *Staphylococcus chromogenes*, *Actinobacillus lignieresii* and *Trueperella pyogenes* in cattle;

Use of the veterinary medicinal product may result in a lack of clinical efficacy when treating infections caused by these bacteria.

4.5 Special precautions for use

Special precautions for use in animals

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.

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 penicillins and cephalosporins due to the potential for cross-resistance.

The feeding of waste milk containing residues of antibiotics to calves should be avoided up to the end of the milk withdrawal period (except during the colostrum phase), because it could select antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

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

Penicillins and cephalosporins may cause sensitisation 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.

This product also contains a paraben preservative which may cause a contact hypersensitivity reaction in previously sensitised individuals.

Do not handle this product if you know that you are sensitized, or if you have been advised not to work with such preparations. People developing a reaction after contact with the product should avoid handling the product and other penicillin and cephalosporin containing products in the future.

It is recommended to wear gloves when handling and administering the product.

Handle this product with care to avoid exposure.

In case of accidental contact with eyes, rinse immediately with copious amounts of water.

Accidental spillage on the skin should be washed immediately with soap and water.

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

If you develop symptoms such as a skin rash following exposure, seek medical advice and show this warning to the doctor. Swelling of the face, lips, eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

In suckling and fattening pigs, administration of the product may cause a transient pyrexia, vomiting, shivering, listlessness and incoordination uncommonly.

Systemic toxic effects have been observed in young piglets, which are transient but can be potentially lethal, especially at higher doses.

Anaphylactic reactions may occur in rare cases in cattle, due to the povidone content. Allergies to penicillin have been observed but these are very rare. Reactions may occasionally be serious and include anaphylactic shock.

In pregnant sows and gilts a vulval discharge which could be associated with abortion has been reported.

In case of side effects, the animal should be treated symptomatically.

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

There is no evidence that this product presents any particular hazard to the dam or foetus. However, in pregnant sows and gilts a vulval discharge which could be associated with abortion has been reported.

Use during pregnancy and lactation only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

The effect of aminoglycosides can be enhanced by penicillins.

The excretion of benzylpenicillin is prolonged by acetylsalicylic acid. Cholinesterase inhibitors delay the degradation of procaine.

Benzylpenicillin is bactericidal. Avoid concurrent use of bactericidal and bacteriostatic antibiotics as they can antagonise the bactericidal effect of penicillins.

4.9 Amounts to be administered and administration route

For intramuscular use only.

Dosage: 12 mg procaine benzylpenicillin (corresponding to 7 mg benzylpenicillin) per kg bodyweight (equivalent to 2 ml of the product per 50 kg bw) per day.

The treatment duration is 3 to 7 days.

The appropriate treatment duration should be chosen based on the clinical needs and individual recovery of the treated animal. Consideration should be given to the accessibility of the target tissue and characteristics of the target pathogen.

The maximum volumes to be injected at any one site are 20 ml (Cattle), 3 ml (Pigs) and 2 ml (Sheep).

The vials can only be broached a maximum of 30 times.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

Before use, shake the vial gently for a minimum of 10 seconds until all sediment is readily dispersed.

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

Tolerance studies have been conducted at twice the recommended dosage rate in all three target species without any ill-effects being observed.

In the case of overdose, central nervous symptoms and/or convulsions may occur.

4.11 Withdrawal period(s)

Cattle

Meat and offal: 10 days for treatment duration 3 days.
12 days for treatment duration 4-7 days.

Milk: 108 hours (4.5 days)

Pigs

Meat and offal: 7 days for treatment duration 3 days.
9 days for treatment duration 4-7 days.

Sheep

Meat and offal: 4 days for treatment duration 3 days.
6 days for treatment duration 4-7 days.

Not authorised for use in sheep producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, Beta-lactamase sensitive penicillins

ATCvet Code: QJ01CE09

5.1 Pharmacodynamic properties

Procaine benzylpenicillin is a complex, sparingly soluble organic salt of benzylpenicillin. Benzylpenicillin exerts its effect on multiplying bacteria by blocking the biosynthesis of the bacterial wall.

Penicillin is a β -lactam antibiotic which has bactericidal activity against mainly Gram-positive bacteria and some Gram-negative organisms susceptible to penicillin.

Enterobacteriales, *Bacteroides fragilis*, most *Campylobacter* spp., *Nocardia* spp. and *Pseudomonas* spp. as well as beta-lactamase-producing *Staphylococcus* spp. are resistant.

Resistance to benzylpenicillin is recognised to occur in some isolates of pathogens for which this product is indicated. The most common resistance mechanism is the production of β -lactamase enzyme. Resistance may also result from alterations to penicillin binding proteins (PBP).

There is cross-resistance between penicillins and other beta-lactam antibiotics. Where a pathogen has acquired penicillin resistance by the transfer of mobile genetic elements, co-resistance to other antimicrobial classes may also be present.

5.2 Pharmacokinetic particulars

Following intramuscular injection of the product, peak concentrations of penicillin in plasma are reached within 1 to 2 hours.

Use of the procaine salt is intended to delay absorption of the drug from the injection site and to give rise to a longer duration of action.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone K30

Methyl Parahydroxybenzoate E218

Sodium Citrate

Disodium Edetate

Lecithin

Potassium dihydrogen phosphate

Potassium chloride

Water for Injections

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years
Shelf Life after first opening the immediate packaging: 28 days.

6.4. Special precautions for storage

Store in a refrigerator (2°C - 8°C).

6.5 Nature and composition of immediate packaging

The product is packaged in clear 100 ml Type I and 250 ml clear Type III glass vials sealed with red or grey, siliconised bromobutyl rubber stoppers and aluminium overseal, containing a sterile aqueous suspension.

Carton box with 1 vial of 100 ml

Carton box with 1 vial of 250 ml

12 shrink-wrapped boxes containing 1 vial of 100 ml

12 shrink-wrapped boxes containing 1 vial of 250 ml

Carton box with 48 boxes containing 1 vial of 100 ml

Carton box with 48 boxes containing 1 vial of 250 ml

The vials are colourless. 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 the veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bimeda Animal Health Limited

8. MARKETING AUTHORISATION NUMBER(S)

VPA 22033/075/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/06/2021

10. DATE OF REVISION OF THE TEXT

07/08/2024

