# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Procapen Injector 3g intramammary suspension for cattle (CZ, DE, EE, EL, HR, HU, IE, IT, LT, LV, NL, PL, PT, RO, SK, UK)
Procapen 3 g intramammary suspension for cattle (ES)
Procapen vet 3 g intramammary suspension for cattle (FI, IS, SE)
Procapen Injector intramammary suspension for cattle (FR)
Procain-Penicillin Injector aniMedica 3 g intramammary suspension for cattle (SI)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml intramammary syringe contains:

**Active substance:**
Benzylpenicillin, procaine monohydrate 3.0 g
(equivalent to 1.7 g benzylpenicillin)

**Excipients:**
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Intramammary suspension
White to yellowish suspension.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Cattle (lactating cows)

### 4.2 Indications for use, specifying the target species

For treatment of udder infection in lactating cows caused by benzylpenicillin-susceptible staphylococci and streptococci.

### 4.3 Contraindications

Do not use in the cases of
- infections with β-lactamase-producing pathogens
- hypersensitivity to penicillins, other substances of the β-lactam group or to any of the excipients.

### 4.4 Special warnings for each target species

None.

### 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 beta lactam antimicrobials (penicillins and cephalosporins) due to the potential for cross-resistance.
The feeding of waste milk containing residues of penicillin to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

Care must be taken when applying the product in case of severe udder quarter swelling, milk duct swelling and/or congestion of detritus in the milk duct. Treatment should only be discontinued early after consultation with the veterinarian as this could lead to the development of resistant bacterial strains.

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 penicillin 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 to penicillins or cephalosporins or if you have been advised not to work with such preparations.
- Handle this product with great care to avoid exposure by accidental contact with the skin or eyes. Persons developing a reaction after contact with the product should avoid handling the product (and other penicillin and cephalosporin containing products) in future.
- It is recommended to wear gloves when handling or administering the product. Wash exposed skin after use. In case of any eye contact, wash the eyes thoroughly with copious amounts of clean running water.
- If you develop symptoms following exposure such as skin rash, you should seek medical advice and show the doctor this warning. 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)**

Allergic reactions (anaphylactic shock, allergic skin reactions) are to be expected in animals which are sensitive to penicillin and/or to procaine.
As the product contains polyvidone, rare cases of anaphylactic reaction may occur in cattle.
The animal should be treated symptomatically if an adverse reaction occurs.

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**

Use only accordingly to the benefit-risk assessment by the responsible veterinarian.

**4.8 Interaction with other medicinal products and other forms of interaction**

There is the possibility of antagonism towards antibiotics and chemotherapeutics with quick-onset bacteriostatic effect. The effect of aminoglycosides may be strengthened by penicillins.
Combinations with other medicines for intramammary use should be avoided because of possible incompatibilities.

**4.9 Amounts to be administered and administration route**

For intramammary use:
3.0 g benzylpenicillin, procaine monohydrate per diseased udder quarter, corresponding to: one syringe per diseased quarter every 24 h for 3 consecutive days.
All udder quarters are to be carefully milked immediately prior to each administration. After the teats and the teat tips have been cleaned and disinfected, one syringe is administered per infected udder quarter.

If there is no clear improvement in the condition after 2 days of treatment, the diagnosis should be checked and the treatment changed, if appropriate.

A parenteral antibiotic is also to be administered in cases of mastitis with systemic symptoms.

This product should be thoroughly shaken before use.

**4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary**
Not applicable.

**4.11 Withdrawal period(s)**
Meat and offal: 5 days
Milk: 6 days

## 5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins, for intramammary use
ATCvet code: QJ51CE09

### 5.1 Pharmacodynamic properties
Mode of action:
Benzylpenicillin, procaine is a depot penicillin which is not easily dissolved in water and which releases benzylpenicillin and procaine in the organism by means of dissociation. The free benzylpenicillin is primarily effective against gram-positive pathogens including *Staphylococcus* spp. and *Streptococcus* spp.. Penicillins have a bactericidal effect on proliferating pathogens by inhibiting cell wall synthesis. Benzylpenicillin is acid-labile and is inactivated by bacterial ß-lactamases.
The penicillin-breakpoint proposed in 2015 by CLSI (Clinical and Laboratory Standards Institute) can be summarised as follows:

| | **Clinical Breakpoints** | | |
|---|---|---|---|
| | **Susceptible** | **Intermediate** | **Resistant** |
| *Staphylococcus* spp. (e. g. *S. aureus; coagulase-negative staphylococci*) | ≤ 0.12 µg/ml | - | ≥ 0.25 µg/ml |
| Streptococci viridans group (e.g. *S. uberis*) | ≤ 0.12 µg/ml | 0.25 – 2 µg/ml | ≥ 4 µg/ml |
| Streptococci beta-haemolytic group (e.g. *S. dysgalactiae* and *S. agalactiae)* | ≤ 0.12 µg/ml | - | - |

Data from various European surveillance programs confirm a very favourable sensibility profile for *S. uberis*, *S. dysgalactiae* and *S. agalactiae* towards penicillin. Some level of resistance is consistently reported for staphylococci, of which beta-lactamase positive strains occur naturally. According to data published in 2018 from a large survey conducted in Belgium, Czech Republic, Denmark, France, Germany, Italy, The Netherlands, Spain and United Kingdom proportion of the strains sensitive to penicillin from the isolates tested was 75 % for *S. aureus* and 71 % for coagulase negative staphylococci, while no resistance was reported for streptococci.

Mechanisms of resistance:
The most frequent mechanism of resistance is production of beta-lactamases (more specifically penicillinase especially in S. aureus), which cleave the beta-lactam ring of penicillins making them inactive. Modification of penicillin-binding proteins is another mechanism of acquired resistance.

### 5.2 Pharmacokinetic particulars
Benzylpenicillin is partially resorbed from the udder following intramammary use. Only the non-dissociated penicillin ions enter the serum as a result of passive diffusion. As benzylpenicillin is strongly

dissociated, only very low serum levels occur. One part (25%) of the intracisternally applied benzylpenicillin becomes irreversibly bound to milk and tissue protein.
Following intramammary use, benzylpenicillin is largely secreted in unchanged form via milk from the treated udder quarter, to a small extent via milk from the untreated quarters and also via the urine.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients
Sodium citrate
Propylene glycol
Povidone K 25
Lecithin
Potassium dihydrogen phosphate
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
Syringes are for single use only.

### 6.4. Special precautions for storage
Store in a refrigerator (2°C – 8°C).
Protect from light

### 6.5 Nature and composition of immediate packaging
Cardboard box containing 24 white linear low-density polyethylene intramammary syringes of 10 ml each.

### 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 products should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER
aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell
Germany

## 8. MARKETING AUTHORISATION NUMBER(S)
*[Number allocated by the Member State. To be completed in accordance with national requirements after conclusion of the DC/MR phase.]*

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Date of first authorisation:<{DD/MM/YYYY}>
Date of last renewal: <{DD/MM/YYYY}>

*[To be completed in accordance with national requirements after conclusion of the DC/MR phase.]*

## 10. DATE OF REVISION OF THE TEXT

*[To be completed in accordance with national requirements after conclusion of the DC/MR phase.]*

## PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

*[To be completed in accordance with national requirements after conclusion of the DC/MR phase.]*