# Summary of Product Characteristics

## 1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Ubropen 600 mg intramammary suspension for lactating cows

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 g intramammary syringe contains:

**Active substance:**

| | | |
|---|---|---|
| Benzylpenicillin procaine monohydrate | 600 | mg |
| (equivalent to benzylpenicillin | 340.8 | mg) |

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Intramammary suspension.

White to yellowish, oily suspension.

## 4 CLINICAL PARTICULARS

### 4.1 Target Species

Cattle (lactating cow).

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

Treatment of clinical mastitis caused by penicillin sensitive streptococci or staphylococci occurring during the lactation phase.

### 4.3 Contraindications

Do not use in animals with known hypersensitivity to penicillins, other substances of the β-lactam group, procaine or to any of the excipients.
Do not use in the case of infections with β-lactamase-forming pathogens.

### 4.4 Special warnings for each target species

If the product is used in treatment of mastitis caused by invasive *Staphylococcus aureus*, an appropriate parenteral antimicrobial will also be required.

## 4.5 Special precautions for use

Special precautions for use in animals

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. . 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. In some geographical areas or in some individual herds resistance to penicillin in *S. aureus* is widespread.

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 taking all recommended precautions.
- If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of theface, 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)

Hypersensitive reactions to penicillin or procaine may include symptoms like oedema, dermatological changes such as urticaria, angio-oedema or erythema and anaphylactic shock.
In case adverse reactions occur the current treatment should be withdrawn and symptomatic treatment should be initiated.

## 4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy, but not during the dry period.

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

Do not combine with bacteriostatic agents. Tetracyclines, macrolides, sulphonamides, lincomycin or tiamulin may inhibit the antibacterial effect of penicillins because of the rapid onset of bacteriostatic action.

## 4.9 Amounts to be administered and administration route

Intramammary use.
Infuse the contents of one syringe (equivalent to 600 mg benzylpenicillin procaine monohydrate) per affected udder quarter once daily after milking. The treatment is continued for 3-5 days.
Parenteral therapy may also be required depending upon the clinical presentation.

Clean the end of the teat carefully before applying the product. Remove the cover of the tip and infuse the product into the teat. The syringe has a double tip. In a normal case it is recommended to remove only the outer cover, revealing a tip about 5 mm long. Using the shorter tip reduces the mechanical irritation of the teat canal when the drug is applied. If the inner cover is removed as well, a tip of about 20 mm is revealed. This can be used to facilitate infusion, for instance to a teat with pronounced oedema. After infusion, the quarter is massaged so that the drug is evenly distributed.

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

Not applicable.

## 4.11 Withdrawal Period(s)

Milk: 6 days.
Meat and offal: 3 days.

## 5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

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

## 5.1 Pharmacodynamic properties

Benzylpenicillin is a bactericidal antibiotic belonging to the betalactam group of antibiotics. It inhibits the peptidoglycan synthesis of Gram-positive bacteria. Benzylpenicillin has no effect on vegetative bacteria or on most of the Gram-negative bacteria.
Mastitis-causing streptococci are commonly sensitive to penicillin. Both Staphylococcus aureus and coagulase-negative staphylococci may synthesise betalactamase enzyme. These strains are resistant to penicillin. Penicillin is active against betalactamase-negative bacteria. The MIC values of penicillin to sensitive pathogens are ordinarily smaller than 0.15 μg/ml.
Most resistance results from production of a beta-lactamase enzyme, although modifications of PBPs with reduced drug affinity or reduced bacterial permeability are additional and sometimes concurrent mechanisms of intrinsic and acquired resistance to penicillins.
State of resistance of the target pathogens across Europe:
According to European surveillance reports and literature published in 2009-2013 proportion of the strains sensitive to penicillin from the isolates tested varied from 67 to 98 % for *S. aureus*, from 63 to 71 % for coagulase negative staphylococci and from 97 to 100 % for streptococci.
The resistance situation remained stable throughout 2002-2013.
Clinical MIC Breakpoints according to CLSI Standards have been set for the evaluation of the resistance development.

Clinical breakpoints for Benzylpenicillin procaine on penicillin-sensitive mastitis pathogens

| Pathogen | Source: CLSI Standard M31 /A3 | | |
|---|---|---|---|
| | Breakpoint (μg/mL) | | |
| | S[1] | I[3] | R[2] |
| *Staphylococcus aureus* | ≤ 0.12 | - | ≥0.25 |
| *Coagulase negative Staphylococci* | ≤ 0.12 | - | ≥0.25 |
| *Streptococcus agalactiae* | ≤ 0.12 | - | - |
| *Streptococcus dysgalactiae* | ≤ 0.12 | - | - |
| *Streptococcus uberis* | ≤ 0.12 | - | - |

[1]Sensitive, [2]Resistant, [3]Intermediate

## 5.2 Pharmacokinetic properties

Penicillin is minimally absorbed from the udder. Mammary oedema and exudate may inhibit the tissue distribution of the penicillin contained in the product. Thus sufficient drug concentrations might not be achieved. In healthy cows, after one dose of the product administered intramammarily the penicillin concentration in milk remained above 0,15 µg/ml for at least 24 h, even when the quarter is emptied at 2 h intervals for a period of 10 h after the administration.

Most of the penicillin in the product is excreted in milk unchanged. About 40% of the drug is eliminated in the milk at the first evacuation, and about 10% at the second evacuation. Therefore, about half of the penicillin dose has been eliminated after two milkings. Penicillin absorbed systemically is excreted via the kidneys unchanged.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Wool wax alcohol ointment
Liquid paraffin
Lecithin (E322)

## 6.2 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: 2 years.

## 6.4 Special precautions for storage

Store below 25 °C.

## 6.5 Nature and composition of immediate packaging

White syringe (LDPE) with a double tip (LDPE) packed in a cardboard container.
Pack sizes: 3 x 10 g with 3 cleaning towels, 5 x 10 g with 5 cleaning towels, 20 x 10 g with 20 cleaning towels, 40 x 10 g with 40 cleaning towels and 100 x 10 g with 100 cleaning towels.

Not all pack sizes may be marketed.

## 6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

Vetcare Oy
P.O. Box 99
24101 Salo
Finland

## 8 MARKETING AUTHORISATION NUMBER(S)

VPA 10832/002/001

## 9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd April 2016

## 10 DATE OF REVISION OF THE TEXT

May 2017