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 340.8 mg benzylpenicillin)

Excipients:

Qualitative composition of excipients and other constituents
Wool wax alcohol ointment
Paraffin, liquid
Lecithin (E322)

White to yellowish, oily suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (lactating cow).

3.2 Indications for use for each target species

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

3.3 Contraindications

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

3.4 Special warnings

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

3.5 Special precautions for use

Special precautions for safe use in the target species:
Use of the product should be based on identification and 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.
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 antimicrobials to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select for antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

The cleaning towel should not be used in presence of teat injuries.

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.

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 in case of hypersensitivity 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 taking all recommended precautions.
- Persons handling or administering the veterinary medicinal product should wear appropriate disposable gloves. Avoid contact with the eyes. Wash exposed skin after use. In case of eye contact, wash the eyes thoroughly with copious amounts of clean running water.
- If you develop symptoms following exposure such as a skin rash, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty with breathing, are more serious symptoms and require urgent medical attention.

The cleaning towels provided contain isopropyl alcohol, which may be irritating to skin and eyes. It is recommended that disposable gloves are also worn when using the cleaning towels.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitive reaction, anaphylactic shock, allergic oedema, urticaria, angioedema, erythema.

In case adverse reactions occur, the current treatment should be withdrawn, and symptomatic treatment should be initiated.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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

3.8 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.

3.9 Administration routes and dosage

Intramammary use.

Infuse the contents of one intramammary 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 and disinfect the end of the teat and teat orifice thoroughly before applying the product. Remove the cover of the tip and infuse the product gently into the teat. The intramammary syringe has a double tip. 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 veterinary medicinal product is applied (partial insertion). If the inner cover is removed as well, a tip of about 20 mm is revealed. This can be used only exceptionally to facilitate infusion, for instance to a teat with pronounced oedema (full insertion). The partial insertion technique is preferred, whenever achievable. After infusion, the quarter is massaged so that the drug is evenly distributed.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Not applicable.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

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

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ51CE09

4.2 Pharmacodynamics

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 dormant/non-growing bacteria or on most of the Gram-negative bacteria.
Mastitis-causing streptococci are commonly susceptible to penicillin. Both Staphylococcus aureus and coagulase-negative staphylococci may synthesise betalactamase. These strains are resistant to penicillin. Penicillin is active against betalactamase-negative bacteria. The MIC values of penicillin to susceptible pathogens are ordinarily smaller than 0.15 mcg/ml.
Most resistance results from production of a beta-lactamase, 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 2009-2018 proportion of the strains susceptible/non-resistant to penicillin from the isolates tested varied from 64 to 98 % for *S. aureus*, from 63 to 73 % for coagulase negative staphylococci and from 97 to 100 % for streptococci. However, although resistance in streptococci is rare, decrease in susceptibility of *Streptococcus uberis* has been reported.
The resistance situation remained stable throughout 2002-2018.
Clinical MIC Breakpoints according to CLSI Standards have been set for the evaluation of the resistance development.

Clinical breakpoints for Benzylpenicillin procaine on penicillin-susceptible mastitis pathogens (human derived data)

Pathogen	Source: CLSI Standard VET01S Breakpoint (mcg/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	0.25 – 2	≥4-

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

4.3 Pharmacokinetics

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 mcg/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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

5.3 Special precautions for storage

Store below 25 °C.

5.4 Nature and composition of immediate packaging

Cardboard container containing 10 g white low-density polyethylene syringes with a low-density polyethylene double tip, sealed with a low-density polyethylene cap.
Each syringe is supplied with a cleaning towel.
Pack sizes: 3, 5, 20, 40 or 100 syringes.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Vetcare Oy

7. MARKETING AUTHORISATION NUMBER(S)

VPA10832/002/001

8. DATE OF FIRST AUTHORISATION

22/04/2016

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

02/07/2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).