1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cetrimilk 250 mg intramammary suspension for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each intramammary syringe (8 g) contains:

Active substances:

Cefacetrile	234.8 mg
equivalent to cefacetrile sodium	250 mg

Excipients:

Qualitative composition of excipients and other constituents
Stearic acid
Microcrystalline wax
Liquid paraffin

Homogeneous white to yellowish suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (lactating cows).

3.2 Indications for use for each target species

Treatment of acute, chronic and subclinical mastitis in lactating cows caused by *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, *Staphylococcus aureus* (both penicillin-sensitive and resistant strains), *Escherichia coli, Klebsiella*.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance, to beta-lactam antibiotics or to any of the excipients.

3.4 Special warnings

Cross-resistance has been shown between 1st generation cephalosporins, such as cefacetrile, and other beta-lactam antimicrobials. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to penicillins or cephalosporins because its effectiveness may be reduced.

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 target pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.
Use of the product should be in accordance with official, national and regional antimicrobial policies.
The prevalence of resistance to cefacetrile for target pathogens (such as *Staphylococcus aureus*) may vary and an increase in resistance has been observed in certain geographical areas; therefore, local information on susceptibility should be considered.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cefacetrile and may decrease the effectiveness of treatment with other penicillins and cephalosporins due to the potential for cross-resistance.

After intramammary administration, cefacetrile is poorly absorbed from the mammary gland into the systemic circulation. This limited systemic passage could results in sub-therapeutic concentrations in plasma and non-target tissues, which could pose a risk of selecting for resistant bacteria and the potential development of cross-resistance to other beta-lactams.

Not for use for prophylaxis and metaphylaxis.

The feeding of waste milk containing residues of cefacetrile 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.

The efficacy of the veterinary medicinal product is only established against the pathogens mentioned in Section 3.2 “Indications for use for each target species”. Consequently, serious acute mastitis (potentially fatal) due to other pathogen species, particularly *Pseudomonas aeruginosa*, can occur. Good hygienic practices should be thoroughly respected in order to reduce this risk.

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 reaction to these substances may occasionally be serious.

People with known hypersensitivity to penicillins or cephalosporins, or who have been advised not to work with penicillin or cephalosporin preparations, should avoid contact with the veterinary medicinal product.

Handle this veterinary medicinal product with great care to avoid exposure. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product and wash hands after use.

In case of accidental contact with skin or eyes, wash immediately with clean 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.

Those developing a reaction after contact with the veterinary medicinal product should avoid handling the product (and other cephalosporin and penicillin containing products) in future.

If provided, the cleaning towels supplied with the veterinary medicinal product contain isopropyl alcohol, which may cause skin or eye irritation in some people. The wearing of gloves is recommended during the administration of the veterinary medicinal product and when handling the cleaning towels.

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

3.6 Adverse events

None known.

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

Pregnancy and lactation:
Can be used during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

Cephalosporins should not be administered concurrently with bacteriostatic antimicrobials.
Concomitant use of cephalosporins and nephrotoxic drugs may increase renal toxicity.

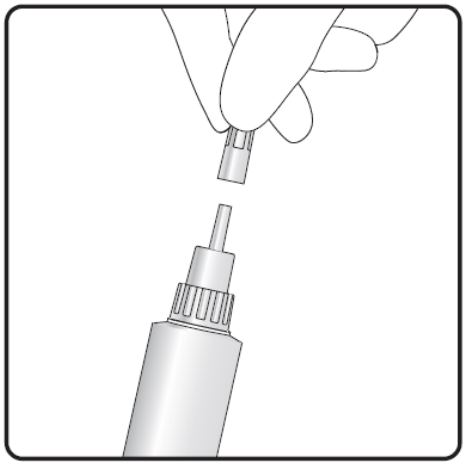
3.9 Administration routes and dosage

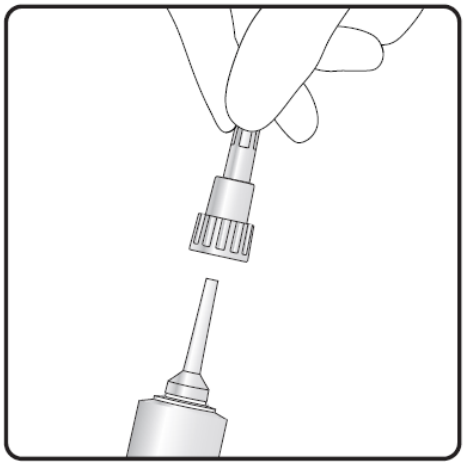
For intramammary use.
The contents of 1 syringe (8 g) should be administered once to each affected udder quarter.
The veterinary medicinal product should be injected into the udder after a thorough milking and disinfection of the teat opening area with suitable preparation or wipes.
Care must be taken not to introduce pathogens into the teat.
A single administration of the contents of 1 syringe is usually sufficient. In severe or chronic cases, the procedure should be repeated after 24 - 48 hours.
It is advisable to regularly empty the affected udder, which does not cause a significant reduction in the concentration of the antibiotic in the mammary gland environment.

Directions for correct administration
This veterinary medicinal product has a twin cap system: the cap of the syringe can be partially or fully removed.
The twin cap system permits both partial and complete insertion of the syringe cannula of the intramammary syringe into the teat canal, according to operating requirements. The long tip option may be used for treatment convenience for example to prevent the tip from flipping out due to a moving or nervous cow.

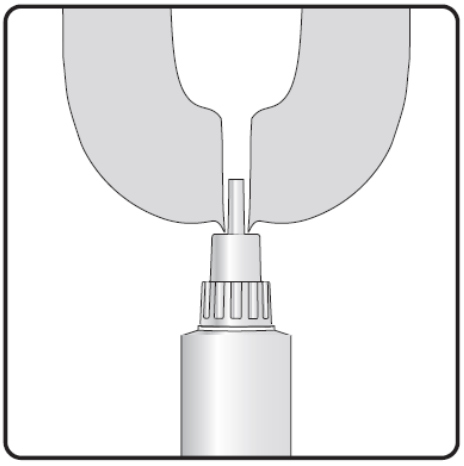
Insert the cannula into the teat duct and inject the entire contents of the syringe tube. Remove the cannula, pinch the base of the teat with the fingers of one hand and with the thumb and forefinger of the other hand gently push the veterinary medicinal product contained in the teat duct upwards.
Massage the quarter gently with both hands, always pushing upwards to spread the veterinary medicinal product uniformly throughout the cistern.

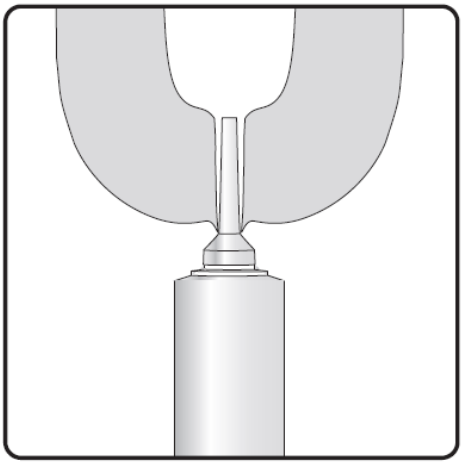
Step 1: Removal of the breakable cap.





Step 2: Short or long tip insertion





Use the syringe only once.

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

No data available

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

Meat and offal: 7 days
Milk: 84 hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ51DB10

4.2 Pharmacodynamics

Cefacetrile belongs to the first generation of cephalosporin antibiotics. These are beta-lactam semisynthetic antibiotics with a broad-spectrum of action. Antibiotics from this group have a bactericidal activity, and their mechanism of action is based on inhibiting the synthesis of the bacterial cell wall. It is also characterized by low toxicity, because the target site of its action is the cell wall, which mammalian cells do not have. Cefacetrile is active against *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, *Staphylococcus aureus* (both penicillin-sensitive and resistant strains), *Escherichia coli* and *Klebsiella* in cattle.

The main mechanisms of resistance against beta-lactams are the production of enzymes (beta-lactamases) that inactivate the drug, the alteration of penicillin-binding proteins and the alteration of the permeability of the bacterial outer membrane. Cefacetrile is relatively resistant to beta - lactamase. There is cross resistance (involving the same resistance mechanism) between antibiotics of the beta-lactam group due to structural similarities. Co-resistance (involving different resistance mechanisms) has been described in *E. coli* due to the fact that a plasmid carries various genes encoding resistance.

4.3 Pharmacokinetics

The bioavailability of cefacetrile after intramammary administration is low.
After administration to cows at a dose of 250 mg/quarter, the C_{max} is 170µg eq/l, the T_{max} - approx. 4h and plasma concentration decreases very rapidly - after 23.5 h it is less than 10µg eq/l.
After intramammary administration of cefacetrile (C^{14}) at a dose of 210 - 216 mg/quarter, 54.6% is excreted in milk, 21% in urine and faeces within 5 days (only 2.5% remains in tissues during this time).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

5.3 Special precautions for storage

Store below 25 °C.

5.4 Nature and composition of immediate packaging

Single dose low-density polyethylene (LDPE) intramammary syringe (barrel and plunger) closed with a LDPE cap, in a cardboard box. The box may also include cleaning wipes.

Package sizes:
Cardboard box with 8 syringes
Cardboard box with 24 syringes
Cardboard box with 60 syringes
Cardboard box with 8 syringes and 8 cleaning wipes
Cardboard box with 24 syringes and 24 cleaning wipes
Cardboard box with 60 syringes and 60 cleaning wipes

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

FATRO S.p.A.

7. MARKETING AUTHORISATION NUMBER(S)

VPA10836/013/001

8. DATE OF FIRST AUTHORISATION

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

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).