1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Kanacef M.C. 200 mg/10g + 10000 IU/10g intramammary suspension for lactating cows

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 g syringe contains:

Active substance:

Cefalexin (as cefalexin monohydrate)	200 mg
Kanamycin monosulphate	100,000 I.U.

Excipients:

Qualitative composition of excipients and other constituents
Yellow soft paraffin
Liquid paraffin

An off-white oily paste.

3. CLINICAL INFORMATION

3.1 Target species

Lactating cows.

3.2 Indications for use for each target species

Treatment of clinical mastitis in lactating dairy cows caused by bacteria susceptible to the combination of cefalexin and kanamycin such as *Staphylococcus aureus* (see section 4.2), *Streptococcus dysgalactiae, Streptococcus uberis* and *Escherichia coli.*

3.3 Contraindications

Do not use in non-lactating cows.
Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Recommendations for responsible use:
The veterinary medicinal product should be used for treatment of clinical mastitis only.

Use of the veterinary medicinal 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 veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to cefalexin and kanamycin and may decrease the effectiveness of treatment with other cephalosporins or aminoglycosides due to the potential for cross- resistance.

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

People with known hypersensitivity of cefalexin or kanamycin monosulfate should avoid contact with the veterinary medicinal product.

Cephalosporin may cause sensitisation (allergy) following injection, inhalation, ingestion or skin contact. Sensitivity to penicillin may lead to cross sensitivity to cephalosporin and vice versa. Allergic reactions to these substances may occasionally be serious.

1. Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.

2. Handle this product with great care to avoid exposure, taking all recommended precautions.

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

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 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
Laboratory studies in laboratory animals (including mice and rats) have not produced any evidence of teratogenic effects. The product is not for use in dry cows.

3.8 Interaction with other medicinal products and other forms of interaction

In case of resistance to cefalexin, cross-resistance with other cephalosporins is likely to occur.
In case of resistance to kanamycin, cross-resistance occurs between kanamycin, neomycin and Paromomycin. A one way resistance with streptomycin is known.

3.9 Administration routes and dosage

Intramammary use.
One syringe per infected quarter after milking.

Repeat at the next milking.
Before infusion, the teat should be thoroughly cleaned and disinfected and care should be taken to avoid contamination of the injector nozzle. Following infusion, it is advisable to use a teat dip or spray.

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

Meat and offal: 7 days.
Milk: 4.5 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATC vet code: QJ51RD01

4.2 Pharmacodynamics

This veterinary medicinal product is a combination consisting of cefalexin and kanamycin at ratio 1.5: 1. Cefalexin represents a first generation cephalosporin and belongs to the class of beta-lactam antibiotics. It provides a mainly time-dependent antibacterial activity against gram-positive pathogens by inhibiting the synthesis of the bacterial peptidoglycan cell wall.

Kanamycin belongs to the class of aminoglycosides and provides bactericidal activity against gram-negative pathogens and against *Staphylococcus aureus.* Kanamycin provides mainly a concentration-dependent antibacterial activity through inhibition of bacterial protein synthesis and reduction of translation fidelity at ribosomal level.

The combination of cefalexin and kanamycin showed a bactericidal mode of action against *Staphylococcus aureus, Streptococcus dysgalactiae, Streptococcus uberis* and *Escherichia coli.* The effect of cefalexin and kanamycin in combination is mainly time-dependent.

Minimum inhibitory concentration, checkerboard analysis, kill kinetic and post antibiotic effect data demonstrate an advantage of the combination by broadening the activity spectrum and by showing synergistic antibacterial activity: the effect of cefalexin is enhanced by kanamycin and vice versa.

Further, the combination produces a larger suppression of bacterial growth (post antibiotic effect) against all target mastitis pathogens compared with the individual compounds.

Staphylococcus aureus has the potential to evade the immune system and establish deep-seated infection in the mammary gland. Thus, as is the case for other intramammary products, bacteriological cure rates in the field are expected to be low. *In vitro* studies have demonstrated that isolates (2002-2004) of *S.aureus* are susceptible to the combination of active substances.

In vitro studies demonstrate that isolates (collected in 2004) of S. *agalactiae* and coagulase-negative staphylococci are susceptible to the combination of active substances.

Three mechanisms of resistance to cephalosporin are known: reduced permeability of the cell wall, enzymatic inactivation and absence of specific penicillin binding sites.
Exogenous beta-lactamase production is the main method for *Staphylococcus aureus* and other gram-positive bacteria to inactivate cephalosporins. Genes for beta-lactamases are found in both, chromosome and plasmids, and may be removed by transposons. Gram-negative bacteria express low levels of species specific beta-lactamases within the periplasmic space, which contributes to resistance by hydrolysis of susceptible cephalosporins.
Resistance to kanamycin can be either chromosomal or plasmid-mediated. The clinical resistance to aminoglycosides is mainly caused by plasmid-specified enzymes, which are found in the periplasmic space of the bacteria. The enzyme binds to the aminoglycoside and prevents it binding to the ribosome and thus aminoglycoside can no longer inhibit protein synthesis.

The occurrence of co-resistance, induced by specific enzyme systems that are encoded for resistance, is particularly family specific for the beta-lactams and aminoglycosides. There are incidences of multiple resistances and this is mainly due to the way in which a resistance gene is transferred either by transposons or intergrons to plasmids, which then encode for resistance to both the beta-lactams and aminoglycosides.

4.3 Pharmacokinetics

After intramammary infusion on two consecutive days at 24 hour intervals the absorption and distribution of both active ingredients in the blood stream were fast but limited.
The available metabolism data indicate that both parent substances, cefalexin and kanamycin, are the major compounds with antimicrobial activity.
Following intramammary administration of the veterinary medicinal product, cefalexin and kanamycin were mainly excreted via milk during milking.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: use immediately.

5.3 Special precautions for storage

Do not store above 25 °C.
Do not freeze.

5.4 Nature and composition of immediate packaging

A white 10 g LPDE intramammary syringe (12 ml) comprising of barrel, plunger and a blue sealed sterile tip (cap).
Carton box with 10 or 20 syringes.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Interchem (Ireland) Ltd.

7. MARKETING AUTHORISATION NUMBER(S)

VPA10555/001/001

8. DATE OF FIRST AUTHORISATION

18/04/2008

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

14/03/2024

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).
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