Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Kanacef M.C. Intramammary Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 g syringe contains:

Active Substances

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

For a full list of excipients, see Section 6.1

3 PHARMACEUTICAL FORM

Intramammary suspension.
An off white smooth oily paste.

4 CLINICAL PARTICULARS

4.1 Target Species

Lactating cows.

4.2 Indications for use, specifying the 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 5.1), *Streptococcus dysgalactiae, Streptococcus uberis* and *Escherichia coli*.

4.3 Contraindications

Do not use in non-lactating cows.
Do not use in cows with a known hypersensitivity to Kanamycin Monosulfate and/or Cefalexin.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Recommendations for prudent use:
The product should be used for treatment of clinical mastitis only.
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 and farm level) epidemiological information about susceptibility of the target bacteria as well as by taking into account official national antimicrobial policies.
Inappropriate use of the 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 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 medial 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.

4.6 Adverse reactions (frequency and seriousness)

None.

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals have not produced any evidence of teratogenic effects. The product is not for use in dry cows.

4.8 Interaction with other medicinal products and other forms of interactions

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.

4.9 Amounts to be administered and administration route

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.

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

Not applicable.

4.11 Withdrawal period(s)

Meat and offal: 7 days
Milk: 4.5 days (108 hours)

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for intramammary use
ATC vet code: QJ51RD01

5.1 Pharmacodynamic properties

This 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.

5.2 Pharmacokinetic particulars

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 product, cefalexin and kanamycin were mainly excreted via milk during milking.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Yellow soft paraffin
Liquid paraffin

6.2 Major incompatibilities

None known.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
In-use shelf-life: Each syringe is for single use only.

6.4 Special precautions for storage

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

6.5 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).
10 or 20 tubes per carton.

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

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

7 MARKETING AUTHORISATION HOLDER

Interchem Ireland Ltd
29 Cookstown Industrial Estate
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA10555/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 05 June 2001
Date of last renewal: 05 June 2006

10 DATE OF REVISION OF THE TEXT

August 2021