SUMMARY OF PRODUCT CHARACTERSITICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Quiflor Multi 100 mg/ml solution for injection for cattle and pigs (sows)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution for injection contains:

Active substance:
Marbofloxacin 100 mg

Excipients:
Disodium edetate 0.10 mg
Monothioglycerol 1 mg
Metacresol 2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, greenish yellow to brownish yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pigs (sows).

4.2 Indications for use, specifying the target species

Cattle
Treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica, Mycoplasma bovis* and *Histophilus somni*.
Treatment of acute mastitis caused by *Escherichia coli* strains sensitive to marbofloxacin during the lactation period.

Sows
Treatment of Metritis Mastitis Agalactia Syndrome (postpartum dysgalactiae syndrome, PDS) caused by bacterial strains sensitive to marbofloxacin.

4.3 Contraindications

Do not use in animals with known hypersensitivity to the active substance or to any of the excipients.
Do not use in cases where the pathogen involved is resistant to other fluoroquinolones (cross resistance).

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Official and local antimicrobial policies should be taken into account when the product is used. Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials. Whenever possible, fluoroquinolones should only be used based on susceptibility testing. Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.

The efficacy data showed that the product has insufficient efficacy for the treatment of acute forms of mastitis induced by Gram-positive bacteria.

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

People with known hypersensitivity to (fluoro)quinolones should avoid contact with the veterinary medicinal product.
Avoid contact of the skin and eyes with the product. In case of accidental spillage onto skin or eyes, rinse the affected area with large amounts of water.
Avoid accidental self-injection, since this can cause local irritation. In case of self-injection or ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Administration by the intramuscular route may cause transient local reactions such as pain and swelling at the injection site and inflammatory lesions which persist at least 12 days after injection. However, in cattle, subcutaneous route was shown to be better tolerated locally than intramuscular route. Therefore, the subcutaneous route is recommended in heavy cattle.

No other undesirable effects have been observed in pigs.

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals (rats, rabbits) have not produced any evidence of a teratogenic, embryotoxic or maternotoxic effect associated with the use of marbofloxacin.
The safety of marbofloxacin has been demonstrated following treatment of animals with a daily dose of 2 mg/kg in pregnant cattle. Its safety has also been demonstrated in piglets and suckling calves when used in sows and cows.
Safety of the product at 8 mg/kg has not been determined in pregnant cows or in suckling calves when used in cows. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Cattle:
Respiratory infections:

This product may be administered as a single dose given on one day only or as a multiple dose injection given over 3 – 5 days.

Single dose - Intramuscular use:
The recommended dosage is 8 mg/kg bodyweight i.e. 2 ml/25 kg bodyweight in a single injection with the exception of the situations listed below.If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

Multiple dose - Intramuscular, intravenous or subcutaneous use:
The recommended dosage is 2mg/kg bodyweight i.e. 1 ml/50 kg in a single daily injection for 3-5 days. This dosing regimen should be used for treatment of specific cases (such as those which require intravenous treatment, for instance in case of *Mycoplasma*).

Acute mastitis:
- *Intramuscular, intravenous or subcutaneous use:*
The recommended dosage is 2 mg/kg i.e. 1 ml/50 kg bodyweight in a single daily injection, for 3-5 days.

Pigs (sows):
- *Intramuscular use:*
The recommended dosage is 2 mg/kg i.e.1 ml/50kg bodyweight in a single daily injection, for 3 days.
To ensure administration of a correct dose, body weight should be determined as accurately as possible, to avoid underdosing.
The cap may be safely punctured up to 25 times. The user should choose the most appropriate vial size according to the target species to treat.

In both cattle and pigs, injections should preferably be given in the neck.

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

No sign of overdose has been observed after administration of 3 times the recommended dose.
Overdoses exceeding this may cause signs in the form of acute neurological disorders which would have to be treated symptomatically.

4.11 Withdrawal period(s)

Cattle:
8 mg/kg single dose
Meat and offal: 3 days
Milk : 72 hours

2 mg/kg single daily injection, for 3 to 5 days:
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, Fluoroquinolones, ATCvet code: QJ01MA93

5.1 Pharmacodynamic properties

Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the fluoroquinolone group which acts by inhibition of DNA gyrase. It has a broad-spectrum activity in vitro against Gram-negative (*Pasteurella multocida, Mannheimia haemolytica, Histophilus somni, E. coli*) and against Gram-positive bacteria and Mycoplasma. Resistance in *Streptococcus* may occur.

The marbofloxacin in vitro activity against pathogens isolated in 2004 from bovine respiratory diseases during a clinical field trial in France, Germany, Spain and Belgium, is good: MIC values are comprised between 0.015 and 0.25 µg/ml for *M. haemolytica* (MIC_{90} = 0.124 µg/ml; MIC_{50} = 0.025 µg/ml), between 0.004 and 0.12 µg/ml for *P. multocida* (MIC_{90} = 0.022 µg/ml; MIC_{50} = 0.009 µg/ml) and between 0.015 and 2 µg/ml for *Histophilus somni*. Strains with MIC ≤ 1 µg/ml are sensitive to marbofloxacin whereas strains with MIC ≥ 4 µg/ml are resistant to marbofloxacin.

Resistance to fluoroquinolones occurs by chromosomal mutation with three mechanisms: decrease of the bacterial wall permeability, expression of efflux pump or mutation of enzymes responsible for molecule binding.

5.2 Pharmacokinetic particulars

After subcutaneous or intramuscular administration in cattle and intramuscular administration in pigs at the recommended dose of 2 mg/kg bw, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.5 µg/ml within less than 1 hour and its bioavailability is close to 100%.
It is weakly bound to plasma proteins (less than 10% in pigs and 30% in cattle), extensively distributed and in most tissues (liver, kidney, skin, lung, bladder, uterus, digestive tract) it achieves higher concentrations than in plasma.

In cattle, marbofloxacin is eliminated slowly in pre-ruminating calves ($t_{1/2}$ β = 5-9 h) predominantly in the active form in urine (3/4) and faeces (1/4).

In pigs, marbofloxacin is eliminated slowly ($t_{1/2}$ β = 8-10 h) predominantly in the active form in urine (2/3) and faeces (1/3).

After a single intramuscular administration in cattle at the recommended dose of 8 mg/kg bw, the maximum plasma concentration of marbofloxacin (Cmax) is 7.3 µg/ml reached in 0.78 hours (Tmax). Marbofloxacin is eliminated slowly (T1/2 terminal = 15.60 hours), predominantly in the active form in urine and faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gluconolactone
Disodium edetate
Metacresol
Monothioglycerol
Water for injections

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: 3 years.
Shelf-life after first opening the immediate packaging: 28 days.

6.4. Special precautions for storage

Store in the original package in order to protect from light.
Do not freeze.

6.5 Nature and composition of immediate packaging

Bottle (amber glass type II), bromobutyl rubber stopper, aluminium closure: 50 ml solution for injection, in a box.

Bottle (amber glass type II), bromobutyl rubber stopper, aluminium closure: 100 ml solution for injection, in a box.
Bottle (amber glass type II), bromobutyl rubber stopper, aluminium closure: 250 ml solution for injection, in a box.
Not all pack sizes may be marketed.

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

Any unused veterinary medical product or waste materials derived from such veterinary medical product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

KRKA, d.d., Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

8. MARKETING AUTHORISATION NUMBER

Vm 01656/4055

9. DATE OF FIRST AUTHORISATION

12 October 2011

10. DATE OF REVISION OF THE TEXT

December 2018

11. PROHIBITION OF SALE, SUPPLY AND/OR USE

Veterinary prescription.

Approved: 20 December 2018