SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbiflox 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.

4.2 Indications for use, specifying the target species

In cattle:
- treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni.*
- treatment of acute forms of mastitis induced by marbofloxacin-sensitive *Escherichia coli* strains, during lactation.

In pigs:
- treatment of the Metritis Mastitis Agalactia syndrome caused by marbofloxacin-sensitive bacterial strains.

4.3 Contraindications

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

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i) 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.

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

Wash hands after use.
People with known hypersensitivity to (fluoro)quinolones should avoid contact with the product.
In case of contact with skin or eyes, rinse with plenty of water.
Care should be taken to avoid accidental self injection.
In case of accidental self injection, seek medical advice and show the label to the doctor.
Accidental self-injection can induce a slight irritation.

iii) Other precautions

None.

4.6 Adverse reactions (frequency and seriousness)

Administration by the intramuscular route may cause transient local reactions such as pain or an oedema at the injection site and inflammatory reactions which may persist for at least 12 days after injection.
Fluoroquinolones are known to induce arthropathies. Nevertheless, this effect has never been observed with marbofloxacin in cattle.
In cattle and pigs, the prefered injection site is the neck area.

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 at treatment of animal with daily dose 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 responsibleveterinarian.

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:
- *Intramuscular use:*
The recommended dosage is 8 mg/kg bodyweight i.e. 2 ml/25 kg bodyweight in a single injection.
If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.
Acute mastitis:
- *Intramuscular or subcutaneous use:*
The recommended dosage is 2 mg/kg i.e. 1 ml/50 kg bodyweight in a single daily injection, for 3 days.
The first injection may also be given by the intravenous route too.

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.

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.

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

No sign of overdosage has been observed with the product after administration of 3 times the recommended dose.
Overdosage symptoms of marbofloxacin are acute neurological disorders that should 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 days:

Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Intramuscular use:
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 (in particular *Staphylococcus*). Resistance to *Streptococcus* may occur.

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, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.5 µg/ml within less than 1 hour. 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 a higher concentration than in plasma.

In cattle, marbofloxacin is eliminated slowly in pre-ruminating calves ($t_{½\beta}$ = 5-9 h) but faster in ruminant cattle ($t_{½\beta}$ = 4-7 h) predominantly in the active form in urine (3/4 in pre-ruminating calves, ½ in ruminants) and faeces (1/4 in pre-ruminating calves, ½ in ruminants).

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).

In pigs, marbofloxacin is eliminated slowly ($t_{½\beta}$ = 8-10 h) predominantly in the active form in urine (2/3) and faeces (1/3).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gluconolactone
Disodium edetate
Metacresol
Monothioglycerol
Water for injections

6.2 Incompatibilities

Do not mix with other 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), bromobutlyl rubber stopper, aluminium closure: 50 ml solution for injection, in a box.
Bottle (amber glass type II), bromobutlyl rubber stopper, aluminium closure: 100 ml solution for injection, in a box.
Bottle (amber glass type II), bromobutlyl 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 medicinal product or waste materials derived from such veterinary medicinal 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

01656/4023

9. DATE OF FIRST AUTHORISATION

15 June 2011

10. DATE OF REVISION OF THE TEXT

February 2016

PROHIBITION OF SALE, SUPPLY AND/OR USE

Veterinary prescription.

Approved: 16 February 2016