# Summary of Product Characteristics

## 1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Marfloxin 100 mg/ml solution for injection for cattle and pigs

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml 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 *E.coli* mastitis.

In pigs:
- treatment of Metritis Mastitis Agalactia (MMA) syndrome caused by susceptible strains of organisms.

### 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 fluoroquinolones, 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.

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

People with known hypersensitivity to fluoroquinolones should avoid contact with the product.
In case of contact with skin or eyes, rinse with plenty of water.
Accidental self-injection can induce a slight irritation.
In case of accidental self-injection or ingestion, seek medical advice immediately and show package leaflet or the label to the physician.

## 4.6 Adverse reactions (frequency and seriousness)

Administration by the intramuscular route in cattle may cause transient local reactions such as pain and swelling at the injection site and inflammatory lesions which may persist for at least 12 days after injection.
Occasionally, the subcutaneous use of the product in cattle may be associated with pain and localized inflammatory reaction without clinical impact.
Fluoroquinolones are known to induce arthropathies. Nevertheless, this effect has never been observed with marbofloxacin in cattle.

## 4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals (rats, rabbits) did not show any evidence of a teratogenic, embryotoxic or maternotoxic effect associated with the use of marbofloxacin.
Marbofloxacin may be used in pregnant and lactating cows and sows when administered at 2 mg/kg.
Safety of the product at 8 mg/kg has not been determined in pregnant cows or in suckling calves when used in cows.
Use therefore according to the benefit/risk assessment carried out 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:
- treatment of acute *E. coli* mastitis: 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular, subcutaneous or intravenous routes. Treatment duration is 3 to 5 days.

- treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida, Mannheimia haemolytica* and *Histophilus somni*:

either 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular, subcutaneous or intravenous routes. Treatment duration is 3 to 5 days.

or 8 mg/kg i.e. 2 ml/25 kg body weight in a single intramuscular injection on a single occasion.

If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

Pigs:
- treatment of Metritis Mastitis Agalactia (MMA) syndrome caused by sensitive strains of organisms: 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular route. Treatment duration is 3 days.

In cattle and pigs, the preferred injection site is the neck area.

To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing.

The cap may be safely punctured up to 25 times. It is recommended that a draw-off needle be used to reduce the number of times the septum is punctured.

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

No sign of overdosage has been observed after administration of 3 times the recommended dose and no severe side-effects are to be expected at doses up to 3 to 5 times the recommended dose in cattle and pigs.
Overdosage may cause signs such as acute neurological disorders which should be treated symptomatically.

## 4.11 Withdrawal Period(s)

Cattle

2 mg/kg for 3 to 5 days (IV/IM/SC)
Meat and offal: 4 days.
Milk: 24 hours.

8 mg/kg on a single occasion (IM)
Meat and offal: 3 days.
Milk: 72 hours.

Pigs

Meat and offal: 2 days.

## 5 PHARMACOLOGICAL or IMMUNOLOGICAL 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 is effective against a wide range of Gram positive bacteria (in particular Staphylococci, Streptococci) and Gram negative bacteria (*Citrobacter* spp., *Enterobacter* spp., *Escherichia coli, Histophilus somni., Klebsiella* spp., *Mannheimia haemolytica, Pasteurella multocida*). It should be noted that some strains of Streptococci and Pseudomonas may not be sensitive to marbofloxacin.

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 $\leq$ 1 µg/ml are sensitive to marbofloxacin whereas strains with MIC $\geq$ 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 properties

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).
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).

After a single intramuscular administration in cattle at the recommended dose of 8 mg/kg, the maximum plasma concentration of marbofloxacin (Cmax) is 7.3 µg/ml reached in = 0.78 h (Tmax). Binding to plasma proteins is about 30 %. Marbofloxacin is eliminated slowly (T1/2 = 15.60 h), 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 any 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

50 ml or 100 ml or 250 ml amber glass vial (Ph. Eur. type II) sealed with a bromobutyl rubber stopper and aluminium closure packaged in an outer carton.

Not all pack sizes may be marketed.

## 6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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(S)

VPA 10774/014/002

## 9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th August 2011
Renewal of the last authorisation: 25th August 2016

## 10 DATE OF REVISION OF THE TEXT

October 2016