Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Marfloxin 20 mg/ml solution for injection for calves, pigs, dogs and cats

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Marbofloxacin 20 mg

Excipients:
Metacresol 2 mg
Disodium edetate 0.10 mg
Monothioglycerol 0.50 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

Calves (pre-ruminant and ruminant), pigs, dogs and cats.

4.2 Indications for use, specifying the target species

Treatment of infections due to marbofloxacin susceptible strains of bacteria.

In Calves
Treatment of respiratory infections caused by *Histophilus somni*, *Mannheimia haemolytica* and *Pasteurella multocida.*

In Pigs
Treatment of respiratory infections.
Treatment of Metritis Mastitis Agalactia (MMA) syndrome.

In Dogs
Treatment of infected wounds and abscesses.
Treatment of lower urinary tract infections due to *Escherichia coli* and *Proteus mirabilis.*
Prevention of surgical infections due to *Staphylococcus intermedius, Escherichia coli* and *Pseudomonas aeruginosa*.

In Cats
Treatment of infected wounds and abscesses.
Prevention of surgical infections due to *Staphylococcus intermedius, Escherichia coli* and *Pseudomonas aeruginosa*.

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 of the product.
In growing pups of large or very large sized breeds, articular impairments (erosion of the articular cartilage) may appear during prolonged treatments with fluoroquinolones. In medium-sized growing dogs marbofloxacin is well tolerated up to doses of 4 mg/kg/day administrated during 13 weeks. However, it is not advised to administer the veterinary medicinal product to pups of large or very large breeds up to the age of 12 and 18 months respectively.

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. Fluoroquinoles should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other class 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 fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.
Some fluroquinolones at high doses may have an epileptogenic potential and a depressor effect on cardiovascular function. Before pre-surgical administration to cats and dogs with a history of seizures or cardiovascular disorders, presurgical examination and anaesthetic protocol should be carefully considered. Experimentally, marbofloxacin has not led to such epileptic reactions in dogs, including in case of over-dosages.
When given IV, the product should be injected slowly.

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

People with known hypersensitivity to fluoroquinolones should avoid any contact with the product.
In case of contact with the skin or eyes, rinse with plenty of water.
In case of accidental ingestion, rinse mouth with clear 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)

Occasionally, the subcutaneous and intramuscular use of the product in calves may be associated with pain and localised inflammatory reaction without clinical impact.
In cats and dogs, neurological signs (seizures, ataxia, mydriasis, muscle tremor), digestive signs (hypersalivation, emesis) and reactions at the injection site have been recorded after treatment on very rare occasions. In case of severe reactions, symptomatic treatment must be initiated.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Studies on laboratory animals (rats, rabbits) did not reveal any teratogenic, embryotoxic or maternotoxic effect of marbofloxacin at the therapeutic dose.
Marbofloxacin may be used in pregnant and lactating sows.

Safety has not been demonstrated in cats and dogs during pregnancy and lactation. Use during gestation or lactation only according to the benefit/risk assessment of the veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Specific studies conducted in dogs did not show interaction between marbofloxacin and anaesthetic agents such as isoflurane and medetomidine/ketamine combination. In the absence of studies with other anaesthetic agents, interactions cannot be excluded.

4.9 Amounts to be administered and administration route

Calves:
The recommended dosage is 2 mg/kg/day (1 ml/10 kg) by a single daily injection by intramuscular, subcutaneous or intravenous route, for 3 to 5 days.

Pigs:
The recommended dosage is 2 mg/kg/day (1 ml/10 kg) by a single daily intramuscular injection, for 3-5 days.

Dogs:
Treatment of infected wounds and abscesses: 2 mg/kg/day (1 ml/10 kg) by a single subcutaneous injection. This should be followed by oral administration of marbofloxacin tablets.
Treatment of infections of lower urinary tract: 4 mg/kg/day (2 ml/10 kg) by three subcutaneous injections at intervals of 4 days.
Prevention of surgical infections: 2 mg/kg (1 ml/10 kg) by a single intravenous injection, just before the intervention.

Cats:
Treatment of infected wounds and abscesses: 2 mg/kg/day (0.5 ml/5 kg) by a single subcutaneous injection for 3 to 5 days.
Prevention of surgical infections: 2 mg/kg (0.5 ml/5 kg) by a single intravenous injection, just before the intervention.

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

The cap may be safely punctured up to 20 times (if 18 gauge needles are used) or 40 times (if 22 gauge needles are used). 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 severe side-effects to be expected at doses up to 3 to 5 times the recommended dose in calves and pigs respectively. In particular no lesions of the articular joints are encountered.
Overdosage may cause signs such as acute neurological disorders which should be treated symptomatically.
Bradycardia could also be observed in cats and dogs.

4.11 Withdrawal Period(s)

Calves
Meat and offal: 4 days.

Pigs
Meat and offal: 2 days.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, fluoroquinolones
ATC Vet 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 (*Actinobacillus pleuropneumoniae, Bordetella bronchiseptica, Enterobacter* spp., *Escherichia coli, Haemophilus* spp., *Histophilus* spp., *Klebsiella* spp., *Mannheimia haemolytica, Moraxella* spp., *Pasteurella multocida, Proteus mirabilis, Pseudomonas aeruginosa*) as well as *Mycoplasma* spp. It should be noted that some strains of Streptococci, Pseudomonas and Mycoplasma 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*.

In 2001, 100 % of small animals isolates of *P. multocida* and *S. intermedius* were susceptible to marbofloxacin (with MIC_{90} = 0.052 µg/ml and 0.219 µg/ml respectively), as well as 83 % *P. aeruginosa* (MIC_{90} = 1.357 µg/ml) and 90 % *E. coli* (MIC_{90} = 0.170 µg/ml).

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 properties

After subcutaneous or intramuscular administration in cattle and 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 higher concentrations than in plasma.
In cattle, marbofloxacin is eliminated slowly in pre-ruminating calves ($t_{1/2}$ = 5-9 h) but faster in ruminant cattle ($t_{1/2}$ = 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 ($t_{1/2}$ = 8-10 h) predominantly in the active form in urine (2/3) and faeces (1/3).
After a sub-cutaneous administration to dogs and cats at the recommended dose of 2 or 4 mg/kg, marbofloxacin is rapidly absorbed and its bioavailability is close to 100 %. Maximum plasma concentrations reached in the 2 species are about 1.5 µg/ml after sub-cutaneous administration of 2 mg/kg in dogs and cats and 3 µg/ml at the dose of 4 mg/kg.
Marbofloxacin is weakly bound to plasma proteins (less than 10 % in dogs and cats) and is widely distributed in the whole organism. In most tissues (skin, muscles, liver, kidney, lung, bladder, digestive tract), the tissue concentrations are higher than in plasma. Marbofloxacin is eliminated slowly (elimination half life of about 13 hours in cats and dogs) and mainly in its active form in urine (2/3) and faeces (1/3).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gluconolactone
Disodium edetate
Mannitol
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

20 ml, 50 ml or 100 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 10774/014/001

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