

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrofloxacin Krka 100 mg/ml oral solution for chickens and turkeys

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of oral solution contains:

Active substance:

Enrofloxacin 100 mg

Excipients:

Benzyl alcohol 14 mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

Clear, yellow solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Chicken and Turkey.

4.2 Indications for use, specifying the target species

Treatment of infections caused by the following bacteria susceptible to enrofloxacin:

Chickens

Mycoplasma gallisepticum

Mycoplasma synoviae

Avibacterium paragallinarum

Pasteurella multocida.

Turkey

Mycoplasma gallisepticum

Mycoplasma synoviae

Pasteurella multocida.

4.3 Contraindications

Do not use for prophylaxis.

Do not use when resistance / cross-resistance to (fluoro)quinolones is known to occur in the flock intended for treatment.

Do not use in case of hypersensitivity to the active substance, other (fluoro)quinolones or to any of the excipients.

4.4 Special warnings for each target species

Treatment of *Mycoplasma* spp. infections may not eradicate the organism.

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.

Since enrofloxacin was first authorised for use in poultry, there has been widespread reduction in susceptibility of *E. coli* to fluoroquinolones and emergence of resistant organisms. Resistance has also been reported in *Mycoplasma synoviae* in the EU.

Before use, header tanks should be emptied, thoroughly cleaned and then filled with a known volume of clean water before adding the required amount of the product. The resulting mixture should be stirred. Before use, header tanks should be inspected at regular intervals for presence of dust, algae formation and sedimentation.

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 this product.

Avoid contact with skin and eyes.

Rinse any splashes from skin or eyes immediately with water.

Wash hands and exposed skin after use.

Do not eat, drink or smoke whilst using the product.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

Do not use in laying hens producing eggs for human consumption.

Do not administer to layer replacement birds within 14 days of coming into lay.

4.8 Interaction with other medicinal products and other forms of interaction

In vitro, an antagonism was shown, when combining fluoroquinolones with bacteriostatic antimicrobial agents such as macrolides or tetracyclines and phenicols. The simultaneous application of substances containing aluminium or magnesium can impair the absorption of enrofloxacin.

4.9 Amounts to be administered and administration route

Dosage:

Chickens and turkeys

10 mg enrofloxacin/kg bodyweight per day for 3–5 consecutive days.

Treatment for 3–5 consecutive days; for 5 consecutive days in mixed infections and chronic progressive forms. If no clinical improvement is achieved within 2–3 days, alternative antimicrobial therapy should be considered based on susceptibility testing.

Via the drinking water. Always make sure that the entire dose offered has been consumed. The medicated water should be made up fresh each day just before it is offered to the animals. The drinking water must be medicated throughout the treatment period, and no other water source should be available. Determine the bodyweight of the birds as accurately as possible in order to avoid underdosing.

Use only fresh pre-solutions, prepared every day before start of treatment. Pumping systems should be checked constantly to assure proper medication. Empty the water system and fill it with medicated water before starting the treatment. Calculate the daily quantity (ml) of the product required for treatment period as follows:

Total number of birds x Average body weight in kg x 0.1 = Total volume (ml) per day

The product may be put directly into the header tank or introduced via a water proportioner pump.

Care should be taken that the intended dose is completely ingested.

Use appropriate and properly calibrated dosing equipment.

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

No adverse clinical symptoms were observed in chickens and turkeys treated respectively with doses up to 10 and 6 times higher than the therapy dose. The use of fluoroquinolones during the growth phase combined with a marked and prolonged increase in the intake of drinking water, and hence active ingredient, possibly due to high temperatures, may potentially be associated with damage of the articular cartilage.

4.11 Withdrawal period(s)

Chickens: Meat and offal: 7 days.

Turkeys: Meat and offal: 13 days.

Not authorised for use in birds producing eggs for human consumption.

Do not administer to layer replacement birds within 14 days of coming into lay.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: quinolone and quinoxaline antibacterials, fluoroquinolones.

ATCvet code: QJ01MA90

5.1 Pharmacodynamic properties

Mode of action

Two enzymes essential in DNA replication and transcription, DNA gyrase and topoisomerase IV, have been identified as the molecular targets of fluoroquinolones. They modulate the topological state of DNA through cleaving and resealing reactions. Initially, both strands of the DNA double helix are cleaved. Then, a distant segment of DNA is passed through this break before the strands are resealed. Target inhibition is caused by non-covalent binding of fluoroquinolone molecules to an intermediate state in this sequence of reactions, in which DNA is cleaved, but both strands are retained covalently attached to the enzymes. Replication forks and translational complexes cannot proceed beyond such enzyme-DNA-fluoroquinolone complexes, and inhibition of DNA and mRNA synthesis triggers events resulting in a rapid, drug concentration-dependent killing of pathogenic bacteria.

Antibacterial spectrum

Enrofloxacin is active against many Gram-negative bacteria, against Gram-positive bacteria and *Mycoplasma* spp. *In vitro* susceptibility has been shown in strains of (i) Gram-negative species such as *Pasteurella multocida* and *Avibacterium (Haemophilus) paragallinarum* and (ii) *Mycoplasma gallisepticum* and *Mycoplasma synoviae*. (See section 4.5)

Types and mechanisms of resistance

Resistance to fluoroquinolones has been reported to arise from five sources, (i) point mutations in the genes encoding for DNA gyrase and/or topoisomerase IV leading to alterations of the respective enzyme, (ii) alterations of drug permeability in Gram-negative bacteria, (iii) efflux mechanisms, (iv) plasmid mediated resistance and (v) gyrase protecting proteins. All mechanisms lead to a reduced susceptibility of the bacteria to fluoroquinolones. Cross-resistance within the fluoroquinolone class of antimicrobials is common.

5.2 Pharmacokinetic particulars

Enrofloxacin administered via drinking water to poultry is rapidly and very well absorbed with a bioavailability of approx. 90 %. Maximum plasma concentrations of 2 mg/L are reached within 1.5 hours after a single bolus dose rate of 10 mg/kg body weight with a total systemic availability of 14.4 mg·hr/L. Enrofloxacin is eliminated from the body with a total body clearance of 10.3 mL/min·kg. If dosed as continuous drinking water medication (multiple dosing) steady-state concentrations of 0.5 mg (turkeys) to 0.8 mg (chicken) enrofloxacin per litre are achieved. A high mean volume of distribution (5 L/kg) indicates good tissue penetration of enrofloxacin.

Concentrations in target tissues like lungs, liver, kidney, intestine and muscle tissue, exceed plasma concentrations by far. In poultry enrofloxacin is poorly metabolized to its active metabolite ciprofloxacin (approximately 5 %). Enrofloxacin is eliminated from the body at a half-life of 6 hours. Protein binding in poultry is approximately 25%.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose
Benzyl alcohol
Potassium Hydroxide
Purified, Water

6.2 Major 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: 5 years

Shelf-life after first opening the immediate packaging: 3 months

Shelf-life after dilution according to directions: 24 hours

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

- Carton box containing 100 ml amber type III glass vial with HDPE cap and LDPE sealing liner.

A 25 ml polypropylene dosing cup is included.

- 1 litre HDPE bottle with HDPE screw cap. A 50 ml polypropylene dosing cup is included.

- 5 litre HDPE bottle with HDPE screw cap.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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(S)

VPA 10774/024/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 7th September 2012

Date of last renewal: 6th September 2017

10 DATE OF REVISION OF THE TEXT

July 2018