Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrotron 100 mg/ml solution for use in drinking waterfor chicken, turkeys and rabbits

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:
Active substance:
Enrofloxacin 100.0 mg
Excipients:
Benzyl alcohol (E-1519) 14.0 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for use in drinking water.

Clear yellowish solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Chickens, turkeys, rabbits

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.

Turkeys
Mycoplasma gallisepticum,
Mycoplasma synoviae,
Pasteurella multocida.

Rabbits
For the treatment of infectious diseases due to *Pasteurella multocida* and bacterial enteritis due to infection with *E. coli*.

Enrofloxacin should be used where clinical experience, supported where possible by sensitivity testing of the causal organism, indicates enrofloxacin as the active substance of choice.

4.3 Contraindications

Do not use when resistance/cross-resistance to (fluoro)quinolones is known to occur in the flock intended for treatment.
Do not use in cases of known hypersensitivity to the active substance, other (fluoro)quinolones or to any of the excipients.
Do not use for prophylaxis.

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.
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.

Whenever possible fluoroquinolones should only be used based on susceptibility testing.

Use of the product deviating from instructions given in the SPC may increase the prevalence of bacteria resistant to fluoroquinolones and may decrease the effectiveness of treatment with other fluoroquinolones due to the potential for cross resistance.

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 skin and eye contact.
Direct contact with the skin should be avoided because of sensitisation, possible hypersensitivity reactions and contact dermatitis.
Wear gloves for this purpose.
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 interactions

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

Chickens and turkeys
Via the drinking water.
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.

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.

Rabbits
10 mg/kg bodyweight per day for 5 consecutive days.

Calculate the daily quantity (ml) of the product required for treatment period as follows:
Total number of rabbits x Average body weight in kg x 0.1 = Total volume (ml) per day

Medicated drinking water should be replaced every 24 hours.

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
Rabbits:
Meat and offal: 15 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

Benzyl alcohol (E-1519)
Potassium hydroxide (for pH adjustment)
Hydrochloric acid, dilute (for pH adjustment)
Purified Water

6.2 Major incompatibilities

In absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal product.

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: 3 months
Shelf life after dilution according to directions: 24 hours

6.4 Special precautions for storage

Keep the container tightly closed.
After dilution, do not expose to direct daylight.

6.5 Nature and composition of immediate packaging

100 ml and 1000 ml opaque polyethylene bottle with opaque polyethylene tamper evident screw cap and polypropylene measuring pitcher.
100 ml, 12 x 100 ml and 6 x 1000 ml are presented in a cardboard box.
Pack sizes: 1 x 100 ml, 12 x 100 ml, 1 x 1000 ml; 6 x 1000 ml.

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/national requirements.

7 MARKETING AUTHORISATION HOLDER

aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell
Germany

8 MARKETING AUTHORISATION NUMBER(S)

VPA10826/018/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 June 2013
Date of last renewal: 06 April 2018

10 DATE OF REVISION OF THE TEXT

July 2018