SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrotron 100 mg/ml Solution for injection for cattle, sheep, goats and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Substance

Enrofloxacin	100.0 mg

Excipients

1-Butanol	30.0 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, slightly yellowish to yellowish orange solution.

4. CLINICAL PARTICULARS

4.1 Target Species

Cattle
Sheep
Goats
Pigs

4.2 Indications for use, specifying the target species

Cattle

Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mannheimia haemolytica* and *Mycoplasma* spp.
Treatment of acute severe mastitis caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of *Mycoplasma bovis* in cattle less than 2 years old.

Sheep

Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of mastitis caused by enrofloxacin susceptible strains of *Staphylococcus aureus* and *Escherichia coli*.

Goats
Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida* and *Mannheimia haemolytica*.
Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of mastitis caused by enrofloxacin susceptible strains of *Staphylococcus aureus* and *Escherichia coli*.

Pigs
Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mycoplasma* spp. and *Actinobacillus pleuropneumoniae*.
Treatment of infections of the urinary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of post-partum dysgalactiae syndrome, PDS (MMA syndrome) caused by enrofloxacin susceptible strains of *Escherichia coli* and *Klebsiella* spp.
Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.

4.3 Contraindications
Do not use for prophylaxis.
Do not use in cases of known hypersensitivity to fluoroquinolones or to any of the excipients.
Do not use when resistance / cross resistance to (fluoro)quinolones is known to occur.
Refer to section 4.5.
Do not use in growing horses because of possible deleterious damage on articular cartilage.

4.4 Special warnings for each target species
None.

4.5 Special precautions for use
Special precautions for use in animals

The safety of the product has not been established in pigs or calves when administered by the intravenous route and use of this route of administration is not recommended in these animal groups.
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, fluoroquinoones 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.
Enrofloxacin should be used with caution in epileptic animals or animals affected by renal dysfunction.

Degenerative changes of articular cartilage were observed in calves treated orally with 30 mg enrofloxacin/kg bw during 14 days.

The use of enrofloxacin in growing lambs at the recommended dose for 15 days caused histological changes in the articular cartilage, not associated with clinical signs.

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

The product is an alkaline solution. Direct contact with skin should be avoided due to sensitisation, contact dermatitis and possible hypersensitivity reactions to (fluoro)quinolones. Wear gloves. In case of eye or skin contact, rinse immediately with water. Do not eat, drink or smoke whilst handling the product.
Care should be taken to avoid accidental self-injection. If accidental self injection occurs seek medical advice immediately and show the package leaflet or the label to the physician.

Other precautions
None known.

4.6 Adverse reactions (frequency and seriousness)

Digestive tract disorders (e.g. diarrhoea) may occur in very rare cases. These signs are generally mild and transient.

Intravenous treatment of cattle can cause shock reactions in very rare cases, presumably as a result of circulatory impairment.

Local reactions at injection site
In pigs, after intramuscular administration of the product, inflammatory reactions may occur. They may persist up to 28 days after the injection.

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

4.7 Use during pregnancy or lactation

Cattle
The safety of the veterinary medicinal product has been established in pregnant cows during the 1st quarter of pregnancy. The product can be used in pregnant cows during the 1st quarter of pregnancy.
The use of the product in cows during the 3 last quarters of pregnancy should be based on a benefit-risk assessment by the responsible veterinarian.
The product can be used in cows during lactation.

Sheep and goats
The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only accordingly to the benefit-risk assessment by the responsible veterinarian.

Pigs
The safety of the veterinary medicinal product has not been established during pregnancy. Use only accordingly to the benefit-risk assessment by the responsible veterinarian.
The product can be used in sows during lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Antagonistic effects due to concurrent administration of macrolides, tetracyclines and phenicols may occur. Enrofloxacin may interfere with the metabolism of theophylline, decreasing theophylline clearance resulting in increased plasma levels of theophylline.

4.9 Amounts to be administered and administration route

Intravenous, subcutaneous or intramuscular use.
Repeated injections should be made at different injection sites.
To ensure a correct dosage, body weight (bw) should be determined as accurately as possible to avoid underdosing.

Cattle
5 mg of enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, once daily for 3-5 days.
Acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of *Mycoplasma bovis* in cattle less than 2 years old: 5 mg of enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, once daily for 5 days.
The product can be administered by slow intravenous or subcutaneous administration.
Acute mastitis caused by *Escherichia coli*: 5 mg enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, by slow intravenous injection once daily for two consecutive days. The second dose may be administered by the subcutaneous route. In this case, the withdrawal period following subcutaneous injection applies.
Not more than 10 ml should be administered at one subcutaneous injection site.

Sheep and goats
5 mg of enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, once daily by subcutaneous injection for 3 days. Not more than 6 ml should be administered at one subcutaneous injection site.

Pigs
2.5 mg of enrofloxacin/kg bw, corresponding to 0.5 ml/20 kg bw, once daily by intramuscular injection for 3 days.
Alimentary tract infection or septicaemia caused by *Escherichia coli*: 5 mg of enrofloxacin/kg bw,
corresponding to 1 ml/20 kg bw, once daily by intramuscular injection for 3 days.
In pigs, the injection should be made in the neck at the ear base. Not more than 3 ml should be administered at one intramuscular injection site.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary
Do not exceed the recommended dosage. In accidental overdose there is no antidote and treatment should be symptomatic.
No signs of over dosage were observed in pigs following administration of the product at five times the recommended therapeutic dose. In cattle, sheep and goats, overdose has not been documented.

4.11 Withdrawal Period(s)
Cattle:
Following intravenous injection:
Meat and offal: 5 days.
Milk: 3 days.

Following subcutaneous injection:
Meat and offal: 12 days.
Milk: 4 days.

Sheep:
Meat and offal: 4 days.
Milk: 3 days.

Goats:
Meat and offal: 6 days.
Milk: 4 days.

Pigs:
Meat and offal: 13 days.

5. PHARMACOLOGICAL OR IMMUNOLOGICAL PROPERTIES
Pharmacotherapeutic group: antibacterials for systemic use, fluoroquinolones
ATC Vet 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. Target inhibition is caused by noncovalent binding of fluoroquinolone molecules to these 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. The mode of action of enrofloxacin is bactericidal and bactericidal activity is concentration dependent.

Antibacterial spectrum
Enrofloxacin is active against many Gram-negative bacteria such as *Escherichia coli, Klebsiella* spp.*,*
Actinobacillus pleuropneumoniae, Mannheimia haemolytica, Pasteurella spp. (e.g. *Pasteurella multocida*), against Gram-positive bacteria such as *Staphylococcus* spp. (e.g. *Staphylococcus aureus*)
and against *Mycoplasma* spp. at the recommended therapeutic doses.

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 is rapidly absorbed after parenteral injection. Bioavailability is high (approximately 100% in pigs and cattle) with a low to moderate plasma protein binding (approximately 20 to 50%). Enrofloxacin is metabolised to the active substance ciprofloxacin at approximately 40% in ruminants and less than 10% in pigs.
Enrofloxacin and ciprofloxacin distribute well into all target tissues, e.g. lung, kidney, skin and liver, reaching 2- to 3-fold higher concentrations than in plasma. Parent substance and active metabolite are cleared from the body via urine and faeces. Accumulation in plasma does not occur following a treatment interval of 24 h.
In milk, most of drug activity relates to ciprofloxacin. Overall drug concentrations peak at 2 hours after treatment showing an approximately 3-fold higher total exposure over the 24 hours dosing interval compared to plasma.

	Pigs	Pigs	Cattle	Cattle
Dose rate (mg/kg bw)	2.5	5	5	5
Route of administration	IM	IM	IV	SC
T_{max} (h)	2	2	-	3.5
C_{max} (µg/ml)	0.7	1.6	-	0.733
AUC (µg x h/ml)	6.6	15.9	9.8	5.9
Terminal half-life (h)	13.12	8.10	-	7.8
Elimination half-life (h)	7.73	7.73	2.3	-
F (%)	95.6	-	-	88.2

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

1-Butanol
Potassium Hydroxide (excipient and for pH adjustment)
Hydrochloric acid (for pH adjustment)
Water for Injections

6.2 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 product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Pack Size:
100 ml clear glass vial type I with Teflon coated rubber stopper sealed with an aluminium cap.
Cartons of 1 x 100 ml or 12 x 100 ml are available.
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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

aniMedica GmbH
Im Südfeld 9
48308 Senden
Germany

8. MARKETING AUTHORISATION NUMBER

Vm 24745/4028

9. DATE OF THE FIRST AUTHORISATION

6 March 2012

10. DATE OF REVISION OF THE TEXT

October 2022

Approved 05 October 2022