

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Enrofloxacin 100 mg

Excipient(s):

n-butyl alcohol as antimicrobial preservative 30 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear yellow solution practically free from particles.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and 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.

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 resistance against quinolones.

Do not use in cases of disturbances in growth of cartilages and/or during injury of locomotory system particularly on functionally loaded joints or due to body weight loaded joints.

Do not use in growing horses because of possible deleterious damage on articular cartilage.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

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 veterinary medicinal 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 veterinary medicinal product including use deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to enrofloxacin and may decrease the effectiveness of treatment with all fluoroquinolones due to the potential for cross-resistance.

Treatment should not be repeated if an allergic reaction occurs.

Enrofloxacin is partially excreted through the kidney. In case of the kidney's functional failure slower excretion should be taken into account.

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.

Do not re-inject into the same injection site.

The cap may be safely punctured up to 40 times. When treating groups of animals, use a draw-off needle.

Only the 50 ml vial should be used to treat small piglets.

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 veterinary medicinal product.

Avoid skin and eye contact. Wash any splashes from skin or eyes immediately with water.

Wash hands after use. Do not eat, drink or smoke whilst handling the veterinary medicinal product.

Care should be taken to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

Other precautions

In countries where feeding of fallen stock to scavenger bird populations is permitted as a conservation measure (see Commission Decision 2003/322/EC), the possible risk to hatching success should be considered before feeding carcasses of livestock recently treated with this veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Digestive tract disorders (e.g. diarrhoea) ¹ Circulatory shock ² Injection site reaction
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¹ Generally mild and transient.

² Following intravenous administration.

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Digestive tract disorders (e.g., diarrhoea) ¹
Undetermined frequency (cannot be estimated from the available data):	Injection site inflammation ²

¹ Generally mild and transient.

² May persist up to 28 days.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See also section 16 of the package leaflet for contact details.

4.7 Use during pregnancy, lactation or lay

Pregnancy:

Cattle

The safety of enrofloxacin has been established in pregnant cows during the 1st quarter of pregnancy. The veterinary medicinal product can be used in pregnant cows during the 1st quarter of pregnancy.

The use of the veterinary medicinal product in cows during the 3 last quarters of pregnancy should be based on a 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.

Lactation:

Can be used during lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use enrofloxacin concomitantly with antimicrobial substances acting antagonistically to quinolones (e. g. macrolides, tetracyclines or phenicols). Do not use concurrently with theophylline as the elimination of theophylline may be delayed.

4.9 Amounts to be administered and administration route

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

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 veterinary medicinal 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.

Cattle: Not more than 10 ml should be administered at one subcutaneous injection site.

Calves: Not more than 5 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.

If there is no clinical improvement within two to three days, further susceptibility testing and possibly a change in antimicrobial therapy should be considered.

Do not exceed the recommended dose.

Normal sterile precautions should be taken.

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

In cases of accidental overdoses digestive tract disorders (e.g. vomiting, diarrhoea) and neurological disorders may occur.

In pigs, no adverse effects were reported after the administration of 5 times the recommended dose.

In cattle, overdose has not been documented.

In accidental overdose there is no antidote and treatment should be symptomatic.

4.11 Withdrawal period(s)

Cattle

Intravenous use:

Meat and offal: 5 days.

Milk: 3 days.

Subcutaneous use:

Meat and offal: 12 days.

Milk: 4 days.

Pigs:

Meat and offal: 13 days.

5. PHARMACOLOGICAL 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. 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 pig and cattle) with a low to moderate plasma protein binding (approximately 20 to 50%). Enrofloxacin is metabolized 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 consists on 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	i.m.	i.m.	i.v.	s.c.
T _{max} (h)	2	2	/	3.5
C _{max} (µg/ml)	0.7	1.6	/	0.733
AUC (µg·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

n-butyl alcohol
Potassium hydroxide
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 veterinary medicinal product as packaged for sale: 5 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Do not store above 25 °C.
Keep the bottle in the outer carton.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 amber Type I glass bottle of 50 or 100 ml with a grey bromobutyl rubber stopper and aluminium cap.
Cardboard box with 1 amber Type II glass bottle of 50 or 100 ml with a grey bromobutyl rubber stopper and aluminium cap.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater.

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

Vm 01656/5067

9. DATE OF FIRST AUTHORISATION

15 March 2006

10. DATE OF REVISION OF THE TEXT

May 2024

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Find more product information by searching for the 'Product Information Database' or 'PID' on www.gov.uk.

Approved 18 May 2024

A handwritten signature in black ink, consisting of a stylized initial followed by the name "Hunter." with a period.