

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Interflox-100, 100 mg/ml solution for injection for cattle, sheep, goats and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

Active substance:

Enrofloxacin.....100,0 mg

Excipients:

n-Butyl alcohol.....30,0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, light-yellow solution.

4. CLINICAL PARTICULARS

4.1. Target species

Cattle, sheep, goat, pig.

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 in animals with known hypersensitivity to enrofloxacin or other fluoroquinolones or to any of the excipients.

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

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 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.

Degenerative changes of articular cartilage were observed in calves treated orally with 30 mg enrofloxacin/kg body weight 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 to clinical signs.

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.

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 product.

Care should be taken to avoid accidental self-injection. If accidental self-injection occurs seek medical advice immediately.

4.6. Adverse reactions (frequency and seriousness)

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

In very rare cases intravenous treatment of cattle can cause shock reactions, 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.

4.7. Use during pregnancy, lactation or lay

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

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, sheep, goat) or intramuscular (pig) 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 per 1 kg bw, corresponding to 1 ml of product per 20 kg bw, once daily for up to 3–5 consecutive days.

Acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of *Mycoplasma bovis* in cattle less than 2 years old: 5 mg of enrofloxacin per 1 kg bw, corresponding to 1 ml of product per 20 kg bw, once daily for up to 5 consecutive days.

The product can be administered by slow intravenous or subcutaneous administration.

Acute mastitis caused by *Escherichia coli*: 5 mg enrofloxacin per 1 kg bw, corresponding to 1 ml of product per 20 kg bw, by slow intravenous injection once daily for up to 2 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 per 1 kg bw, corresponding to 1 ml of product per 20 kg bw, once daily by subcutaneous injection for up to 3 consecutive days.

Not more than 6 ml should be administered at one subcutaneous injection site.

Pigs

2.5 mg of enrofloxacin per 1 kg bw, corresponding to 0.5 ml of product per 20 kg bw, once daily by intramuscular injection for up to 3 consecutive days.

Alimentary tract infection, or septicaemia caused by *Escherichia coli*: 5 mg of enrofloxacin per 1 kg bw, corresponding to 1 ml of product per 20 kg bw, once daily by intramuscular injection for up to 3 consecutive 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

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

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

In cattle, sheep and goats, overdose has not been documented.

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

4.11. Withdrawal period(s)

Cattle:	<i>Following intravenous injection:</i> Meat and offal: 5 days. Milk: 3 days. <i>Following subcutaneous injection:</i> 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 PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, 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 non-covalent 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	im	im	iv	sc
Tmax (h)	2	2	/	3,5
Cmax (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. 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: 3 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4. Special precautions for storage

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

After first opening the immediate packaging do not store above 25°C.

6.5. Nature and composition of immediate packaging

100 ml amber glass bottles (type I) closed with brombutyl rubber stopper and aluminium cap in cardboard box.

6.6. Special precautions for the disposal of unused veterinary medicinal product 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

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8. MÜÜGILOA NUMBER (NUMBRID)

To be completed in accordance with national requirements after conclusion of the MR phase.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be completed in accordance with national requirements after conclusion of the MR phase.

10. DATE OF REVISION OF THE TEXT

To be completed in accordance with national requirements after conclusion of the MR phase.

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be completed in accordance with national requirements after conclusion of the MR phase.