

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Enrofloxacin 100.0 mg

Excipients:

Benzyl alcohol 0.02 ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear yellow solution.

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 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 in case of hypersensitivity to the active substance or to any of the excipients.

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

Do not use in animals with central nervous system-associated seizure disorders.

4.4 Special warnings for each target species

None known.

4.5 Special precautions for use

Special precautions for use in animals

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

Do not use in the presence of existing disorders of cartilage development or musculoskeletal damage around functionally significant or weight-bearing joints.

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.

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, fluoquinolones 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.

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.

Direct contact with the skin should be avoided because of sensitisation, contact dermatitis and possible hypersensitivity reactions to fluoroquinolones.

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 and show package leaflet to the physician.

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 product.

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.

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.

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, 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.

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, 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.

Not more than 10 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

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:

Following intravenous injection:

Meat and offal: 5 days.

Milk: 72 hours.

Following subcutaneous injection:

Meat and offal: 12 days.

Milk: 96 hours.

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 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 hours. 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
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

Environmental properties

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Lactic acid
Disodium edetate
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.

Store in the original package in order to protect from light.

6.5 Nature and composition of immediate packaging

Amber polypropylene vials of 50, 100 and 250 ml provided with a grey (50 ml and 100 ml) or pink (250 ml) rubber-butyl stopper and aluminium seal with a green Flip-Off sealing.

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 products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

GLOBAL VET HEALTH SL
c/Capcanes, nº 12-bajos
Polígono Agro-Reus
REUS 43206
Spain

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10477/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11th January 2013
Date of last renewal: 8th December 2017

10 DATE OF REVISION OF THE TEXT

December 2017