SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Quinoflox 100 mg/ml solution for use in drinking water for chickens and rabbits

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of the product contains:
Active substance:
Enrofloxacin 100 mg
Excipients:
Benzyl alcohol (E 1519) 14.6 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for use in drinking water.
Clear yellow solution.

4. CLINICAL PARTICULARS

4.1. Target species

Chickens (Broilers, replacement chickens, broiler breeders) and rabbits

4.2. Indications for use

Chickens (Broilers, replacement chickens, broiler breeders):
Treatment of infections caused by the following bacteria susceptible to enrofloxacin:

Mycoplasma gallisepticum,
Mycoplasma synoviae,
Avibacterium paragallinarum,
Pasteurella multocida

Rabbits: Treatment of respiratory infections caused by *P. multocida* susceptible to enrofloxacin.

Where clinical experience, supported where possible by sensitivity testing of the causal organism, indicates enrofloxacin as the drug of choice.

4.3. Contraindications

Do not use in case of renal and hepatic failure.
Do not treat animals with cartilaginous growth disturbance.
Do not use in case of known hypersensitivity to the active substance, other (fluoro)quinolones or to any of the excipients.

Do not use for prophylaxis.
Do not use when resistance/ cross-resistance to (fluoro)quinolones is known to occur in the flock intended for treatment.

See section 4.11

4.4. Special warnings for each target species

Treatment of *Mycoplasma spp* infections may not eradicate the organism.

4.5. Special precautions for use

i) Special precautions for use in animals

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.
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.
Wherever possible, fluoroquinolones should 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 quinolones due to the potential for cross resistance.
After the end of treatment, the watering system should be cleaned appropriately to prevent the intake of remaining subtherapeutic doses of the drug, which may lead to resistance

Before use, header tanks should be emptied, thoroughly cleaned and then filled with a known volume of clean water before adding the required amount of product. The resulting mixture should be stirred.

Before use, header tanks should be inspected at regular intervals for presence of dust, algae formation and sedimentation.

If there is no clinical improvement within two to three days susceptibility testing should be repeated and therapy should be changed, if appropriate.

ii) Special precautions to be taken by the person administering the product to the animals

This product is an alkaline solution; personal protective equipment, including impervious gloves, should be worn when handling the product.
Direct contact with the skin should be avoided because of sensitisation, contact dermatitis and possible hypersensitivity reactions.

In the event of eye or skin contact, rinse the affected area with clean water and if irritation occurs, seek medical attention.

People with known hypersensitivity to (fluoro)quinolones should avoid contact with the product.

Wash hands and exposed skin after use.

Do not eat, drink or smoke whilst using the product.

4.6. Adverse reactions

In very rare cases adverse reactions appear in young animals at articular level, at the central nervous system and urinary and digestive tracts.

In very rare cases, during the period of rapid growth, enrofloxacin may affect articular cartilage.

The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment).
- Common (more than 1 but less than 10 animals in 100 animals).
- Uncommon (more than 1 but less than 10 animals in 1,000 animals).
- Rare (more than 1 but less than 10 animals in 10,000 animals).
- Very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7. Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation in rabbits. Laboratory studies in rabbits have not produce any evidence of a teratogenic, foetoxic or maternotoxic effects. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.
Do not use within 14 days before start of the laying period.

4.8. Interaction with other medicinal products and other forms of interaction

Concurrent use of enrofloxacin with other antimicrobials, tetracyclines and macrolide antibiotics, may result in antagonistic effects.

Absorption of enrofloxacin may be reduced if the product is administered together with substances containing magnesium or aluminium.
Enrofloxacin may alter the hepatic metabolism of co-administered products.
Do not administer with non steroidal anti-inflammatory products.

4.9. Amount to be administered and administration route

In drinking water use.

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 and rabbits. If no clinical improvement is achieved within 2-3 days, alternative antimicrobial therapy should be considered based on susceptibility testing.

For the preparation of medicated water the body weight of the animals to be treated and their actual daily water consumption should be taken into account. Consumption may vary depending on factors like age, state of health, breed, husbandry system. To provide the required amount of veterinary medicinal product in ml per litre drinking water the following calculation should be made:

$$\frac{\text{0.1ml of the product per kg bodyweight daily} \times \text{average bodyweight (kg) of the animals to be treated} \times \text{number of animals}}{\text{Total water consumption (l) of the herd at the previous day}} = \text{ml of the product per litre drinking water}$$

Sufficient access to the system of water supply should be available for the animals to be treated to ensure adequate water consumption. No other source of drinking water should be available during the medication period. Care should be taken that the intended dose is completely ingested. Use appropriate and properly calibrated dosing equipment.

If there is no clinical improvement within 3 days the treatment approach should be reconsidered. After the end of the medication period the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance which might support development of resistance.
Medicated drinking water should be replaced every 24 hours.

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

At the dosage of 20mg/kg b.w. (twice the recommended dosage) administered in rabbits for 15 days (3 times the recommended duration of treatment) adverse reactions were not observed. In case of overdosage, the symptoms would be convulsions and the treatment should be ceased.
In case of considerable overdose in chickens intoxication by fluoroquinolones may cause nausea, vomiting and diarrhoea .
In accidental overdose there is no antidote and treatment should be symptomatic.

4.11. Withdrawal period

Meat and offal: Chickens : Meat and offal: 7 days
Rabbits: 2 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 PROPERTIES

Pharmacotherapeutic group: quinolone and quinoxaline antibacterials, fluoroquinolones.

ATCvet Code: QJ01MA90.

5.1. Pharmacodynamic properties

Enrofloxacin is a synthetic, broad spectrum antimicrobial substance, belonging to the fluoroquinolone group of antibiotics. It is bactericidal in action with activity against a range of Gram positive and Gram negative bacteria and mycoplasmas. The quinolones act primarily to inhibit bacterial DNA gyrase, an enzyme responsible for controlling the supercoiling of bacterial DNA during replication. Resealing of the double standard helix is inhibited resulting in irreversible degradation of the chromosomal DNA. The fluoroquinolones also possess activity against bacteria in the stationary phase by an alteration of the permeability of the outer membrane phospholipid cell wall.

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 properties

Enrofloxacin has a high bioavailability by oral, intramuscular and subcutaneous routes in almost all studied species.

After oral administration of enrofloxacin to chickens and rabbits, the maximum concentration is achieved between 0.5 and 2.5 hours. Maximum concentration after the administration of a therapeutic dosage ranges between 1-2.5 µg/ml.

Fluoroquinolones distribute into body fluids and tissues, achieving higher concentrations than those found in plasma. Moreover they are widely distributed in skin, bones and semen, and reach the anterior and posterior eye chambers; they cross the placenta and the brain barrier. They also accumulate in phagocytes (alveolar macrophages, neutrophils) and this explains their efficacy against intracellular microorganisms.

Metabolism varies between species and around 50-60% of the dose is metabolised. Biotransformation of enrofloxacin in the liver gives rise to an active metabolite which is ciprofloxacin.

Excretion occurs via bile and urine, with the latter being the main route . Renal excretion is carried out by glomerular filtration and also by active tubular secretion through organic anion pumps.

CHICKENS

After oral administration of 10 mg/kg a maximum concentration of 2,5 µg/ml was observed at 1.6 h post-administration, with a bioavailability of around 64%. The plasma half-life was 14 h and the mean residence time was 15 h.The protein binding was 20%.

RABBITS

Administration of 10 mg enrofloxacin/kg b.w. /day, for 5 consecutive days, in drinking water, resulted ina Cmax of around 350 ng/ml . 26.5% of the dose was metabolised to ciprofloxacin.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Benzyl alcohol (E 1519)
Purified water
Potassium hydroxide

6.2. Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.
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Increased influx of the air (admixing CO_2 from the air) into medicated drinking water may result in precipitation of enrofloxacin.
Precipitation of the salt of enrofloxacin and alkalis may occur at higher concentration of calcium and magnesium in the water system during intermediate dilution in the dosage devices.

6.3. Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 4 years
Shelf life after dilution according to directions: 24 hours
Shelf life after first opening the container: 3 months

6.4. Special precautions for storage

Protect from light

6.5. Nature and composition of immediate packaging

1 litre and 5 litre white high density polyethylene containers, provided with green screw seal cap
of the same material, with an aluminium disk sealed by induction.

Presentations: 12 x 1 L in cardboard box and 4 x 5 L in cardboard box.
1 L
5 L
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

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

Global Vet Health S.L.
c/Capçanes
No 12-bajos
Polígon Agro-Reus
43206 – REUS
(Tarragona)
Spain

8. MARKETING AUTHORISATION NUMBER

Vm 36167/4001

9. DATE OF FIRST AUTHORISATION

15 August 2011

10. DATE OF REVISION OF THE TEXT

July 2018

ADDITIONAL INFORMATION

Prohibition of sale, supply and/or use.

Approved 04 July 2018