SUMMARY OF PRODUCT CHARACTERISTIC

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ES :Aquaflox 100 mg/ml solution for use in drinking water, chicken and rabbits

PT, RO, PL, IT, DE, FR, IK, BE: Quinoflox 100 mg/ml solution for use in drinking water, chicken and rabbits

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of the product contains:
Active substance:
Enrofloxacin 100 mg
Excipients:
Benzyl alcohol ……...14.6 mg

For a 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 *E. coli*, *Salmonella* spp and *Mycoplasma* spp.
Rabbits: Treatment of respiratory infections caused by *P. multocida* sensible 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 resistance to quinolones.

Do not administer in animals with known hypersensitivity to Enrofloxacin or any other quinolone.
or to any of the excipients
Do not use in birds producing eggs for human consumption.
Do not use for prophylaxis.
Do not use in cases of confirmed, or suspected, resistance to quinolones.

See section 4.11

4.4. Special warnings for each target species

None.

4.5. Special precautions for use

i) 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.
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

The most frequent adverse reactions appear in young animals at joint level, at the central nervous system and urinary and digestive tracts.

After administration to rabbits, no adverse reactions have been observed in animals treated at the therapeutic dosage.
During the period of rapid growth, enrofloxacin may affect articular cartilage

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.
Increased influx of the air (admixing CO2 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.

4.9. Amount to be administered and administration route

For oral administration via drinking water.

The effective dose is 10 mg enrofloxacin per kg bodyweight per day corresponding to 0.1 ml of the product per kg bodyweight per day. The duration of treatment is 3 to 5 days in chicken and 5 days in rabbits.

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:

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

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.

In case of salmonella clinical signs, mortality and excretion of the pathogens will be reduced for several weeks but the pathogens will not be eradicated

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 .
Do not exceed the recommended dose. In accidental overdose there is no antidote and treatment should be symptomatic.

4.11. Withdrawal period

Meat and offal:	Chickens	4 days
	Rabbits	2 days

Eggs:
Do not use in birds producing eggs for human consumption

5. PHARMACOLOGICAL PROPERTIES

ATC Vet code: QJ01MA90

Pharmacotherapeutic Group: Fluoroquinolones

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.

Bacterial resistance to enrofloxacin normally occurs by alteration of the DNA-gyrase (topoisomerase II) by the mutation of the Gyr-A subunit and less frequently but more important for Gram positive bacteria, by the alteration of the topoisomerase IV by mutation of subunit ParC.
Other mechanisms of resistance appear when the bacteria reduce the permeability of its membrane . Permeability changes occurs either via decreased permeability of the hydrophilic pores or through alteration of the active transport (efflux) pump, thereby decreasing the intracellular content of fluoroquinolones .
The isolated germs resistant to quinolones have shown cross reactivity against different fluoroquinolones.

Enrofloxacin has antimicrobial action at low concentrations and against the most of Gram negative bacteria and more Gram positive, aerobic and anaerobic.

Antimicrobial spectrum:
Escherichia coli
Salmonella spp.
Pasteurella spp.
Mycoplasma spp.

5.2. Pharmacokinetic properties

Enrofloxacin has a high bioavailability by oral, intramuscular and subcutaneous route 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 therapeutical dosage ranges between 1-2.5 µg/ml.

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

Metabolization varies between species and it is around 50-60%. Biotransformation of enrofloxacin at hepatic level gives raise to an active metabolite which is ciprofloxacin.

Excretion occurs by bile and kidney, being the latest the main one. Renal excretion is carried out by glomerular filtration and also by active tubular secretion through organic anions pump.

CHICKENS

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

Within the administration of the product at the recommended dosage, 10 mg enrofloxacin/kg b.w. /day, for 5 consecutive days, administered in drinking water, they were found values of Cmax around 350 ng/ml and a mean metabolization of enrofloxacin into ciprofloxacin of 26.5%.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Benzyl alcohol
Purified water
Potassium hydroxide

6.2. Incompatibilities

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: 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

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

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 products should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

GLOBAL VET HEALTH SL
C/Capçanes
nº12-bajos
Polígono Agro-Reus
REUS 43206

ADDITIONAL INFORMATION

Marketing authorisation number:

Vm 36167/4001

Date of first authorisation:

15 August 2011

Date of last revision of the text:

August 2011