

D3 Proposed Package Leaflet

Interflox 100mg/ml Oral Solution

Composition:

Contains per ml:
Enrofloxacin100mg
Benzyl Alcohol14mg

Controlled Medicine
Keep out of reach of children
Jauhi dari kanak-kanak
MAL registration number

Product description:

Interflox 100mg/ml Oral Solution is a light yellow solution.

Pharmacodynamics:

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. They modulate the topological state of DNA through cleaving and resealing reactions. Initially, both strands of the DNA double helix are cleaved. Then, a distant segment of DNA is passed through this break before the strands are resealed. Target inhibition is caused by non-covalent binding of fluoroquinolone molecules to an intermediate state in this sequence of reactions, in which DNA is cleaved, but both strands are retained covalently attached to the 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-dependant killing of pathogenic bacteria.

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 *Escherichia coli*, *Pasteurella multocida* and *Avibacterium (Haemophilus) paragallinarum* and (ii) *Mycoplasma gallisepticum* and *Mycoplasma synoviae*.

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.

Pharmacokinetics:

Enrofloxacin administered via drinking water to poultry is rapidly and very well absorbed with a bioavailability of approx. 90 %. Maximum plasma concentrations of 2 mg/L are reached within 1.5 hours after a single bolus dose rate of 10 mg/kg body weight with a total systemic availability of 14.4 mg-hr/L. Enrofloxacin is eliminated from the body with a total body clearance of 10.3 ml/min-kg. If dosed as continuous drinking water medication (multiple dosing) steady-state concentrations of 0.5 mg (turkeys) to 0.8 mg (chicken) enrofloxacin per litre are achieved. A high mean volume of distribution (5 L/kg) indicated good tissue penetration of enrofloxacin. Concentrations in target tissues like lungs, liver, kidney, intestine and muscle tissue, exceed plasma concentrations by far. In poultry enrofloxacin is poorly metabolised to its active metabolite ciprofloxacin (approximately 5%). Enrofloxacin is eliminated from the body at a half-life of 6 hours. Protein binding in poultry is approximately 25%.

Indication:

Treatment of infections caused by the following bacteria susceptible to enrofloxacin:

Chickens

Mycoplasma gallisepticum,
Mycoplasma synoviae,
Avibacterium paragallinarum,
Pasteurella multocida.

Turkey

Mycoplasma gallisepticum,
Mycoplasma synoviae,
Pasteurella multocida.

Recommended dose:

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

Via the drinking water. Always make sure that the entire dose offered has been consumed. The medicated water should be made up fresh each day just before it is offered to the animals. The drinking water must be medicated throughout the treatment period, and no other water source should be available. Determine the bodyweight of the birds as accurately as possible in order to avoid underdosing.

Use only fresh pre-solutions, prepared every day before start of treatment. Pumping systems should be checked constantly to assure proper medication. Empty the water system and fill it with medicated water before starting the treatment.

Calculate the daily quantity (ml) required for treatment period as follows:

Total number of birds x Average body weight in kg x 0.1 = Total volume (ml) per day

The product may be put directly into the header tank or introduced via a water proportioner pump.

Contraindication:

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.

Do not use in the case of known hypersensitivity to the active substance, other (fluoro)quinolones or to any of the excipients.

Warning and Precautions:**Special warnings for each target species**

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

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.

Since enrofloxacin was first authorized for use in poultry, there has been widespread reduction in susceptibility of *E.coli* to fluoroquinolones and emergence of resistant organisms.

Whenever possible, fluoroquinolones should only be used based on susceptibility testing.

Use of the product deviating from the instructions given 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 medicinal product to animals

Those with known hypersensitivity to (fluoro)quinolones should avoid contact with this product.

Avoid contact with skin and eyes.

Rinse any splashes from skin or eyes immediately with water.

Wash hands and exposed skin after use.

Do not eat, drink or smoke while using this product.

TO BE PRESCRIBED BY REGISTERED VETERINARY SURGEONS ONLY.

Interaction of other medicaments:

In vitro, an antagonism was shown, when combining fluoroquinolones with bacteriostatic antimicrobial agents such as macrolides or tetracyclines and phenicols. The simultaneous application of substances containing aluminium or magnesium can impair the absorption of enrofloxacin.

Pregnancy and Lactation:

Do not use in birds producing eggs for human consumption.

Do not administer to layer replacement birds within 14 days of coming into lay.

Side Effects:

None known.

Symptoms and Treatment of Overdose:

No adverse clinical symptoms were observed in chickens and turkeys treated respectively with doses up to 10 and 6 times higher than the therapy dose.

The use of fluoroquinolones during the growth phase combined with a marked and prolonged increase in the intake of drinking water, and hence active ingredient, possibly due to high temperatures, may potentially be associated with damage of the articular cartilage.

Withdrawal period:**Meat and offal:**

Chickens: 7 days

Turkeys: 13 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.

Storage condition:

Store below 30°C. Store in the original package. Protect from light and moisture.

After first opening, store below 30°C.

Packaging:

HDPE bottle of 100 or 1000 ml closed with HDPE cap.

Not all pack sizes may be marketed.

Manufacturer:

Interchemie werken "De Adelaar" Eesti AS

Vanapere tee 14, Püünsi village, Viimsi municipality, Harju country, 74013 Estonia.

Marketing Authorization Holder:

Danberg (M) Sdn Bhd

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