ENPROSEEN 20% W/V ORAL SOLUTION

Name and Strength of Active Substance(s) Enrofloxacin 20%w/v

Product Description Colorless to clear light yellow liquid

Pharmacodynamics

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 fluroquinolone 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-fluroquinolone 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%.

Environmental Properties Not relevant

Indication

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

Chickens

Mycoplasma gallisepticum,

Mycoplasma synoviae,

Avibacterium paragallinarum,

Pasteurella multocida,

Escherichia coli.

Recommended Dosage

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 under dosing.

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) of Enproseen 20%w/v Oral Solution required for treatment period as follows:

Total number of birds x Average body weight in kg x 0.05= Total volume (ml) per day

Enproseen 20%w/v Oral Solution may be put directly into the header tank or introduced via a water proportioner pump.

Mode of Administration Orally

Contraindications

Do not use for prophylaxis.

Do not use when resistance/ cross-resistance to (fluoro)quinolones is known to occur.

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

Warnings and Precautions
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. Resistance has also been reported in Mycoplasma synovia in the EU.

Whenever possible, fluoroquinolones 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 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 the product.

To be prescribed by registered veterinarian only.

Interactions with 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.

Statement on usage during pregnancy and lactation
Do not use in laying hens producing eggs for human consumption.

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

Adverse Effects/Undesirable Effects None known.

Overdose and Treatment
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(s)
Chickens: Meat and offal: 7 days.

Not authorized for use in birds producing eggs for human consumption.

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

Storage Conditions Store below 30℃

Shelf Life
As package for sale: 2 years
After first opening of container : 5 weeks
After reconstitution or dilution with drinking water : 6 days

Dosage Forms Oral solution

Packaging available 1Liter

Name and Address of manufacturer/marketing authorization holder
Samyang Anipharm Co.Ltd.
35, Songseon-ro 265 beon-gil, Pocheon-si, Gyeonggi-do, Korea

Date of Revision of Package Insert 5th March 2019 (1903-2TS)

SAMYANG ANIPHARM
6-5, TONGIL-RO 83-GIL, EUNPYEONG-GU, SEOUL, KOREA
TEL : 82-2-388-2521 FAX : 82-2-357-8753