

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrox Flavour 15 mg Tablets for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance :

Enrofloxacin 15 mg

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

Round slightly biconvex, cream to light brownish tablets with possible visible white or darker spots and bevel-edged.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and cats.

4.2 Indications for use, specifying the target species

The product is for use in dogs and cats in the treatment of bacterial infections of the alimentary, respiratory and urogenital tracts, skin, secondary wound infections and otitis externa 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 dogs less than 1 year of age or in exceptionally large breeds of dog with a longer growth period less than 18 months of age, as articular cartilage may be affected during the period of rapid growth.

Do not use in cats less than 8 weeks of age.

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

Do not use in dogs having seizure disorders, since enrofloxacin may cause CNS stimulation.

Do not use for prophylaxis.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i) Special precautions for use in animals

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, use of fluoroquinolones should be 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.

Official and local antimicrobial policies should be taken into account when the product is used.

Do not use in case of resistance to quinolones, as there exists almost complete cross resistance to other quinolones and complete cross resistance to other fluoroquinolones.

Do not exceed the recommended dosage.

Retinotoxic effects including blindness can occur in cat when the recommended dose is exceeded.

Use the product with caution in dogs with severe renal or hepatic impairment.

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

Wash hands after use.

In case of contact with the eyes, wash with plenty of clean water.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

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

4.6 Adverse reactions (frequency and seriousness)

During the period of rapid growth, enrofloxacin may affect articular cartilage development.

In very rare cases (less than 1 animal in 10,000 animals, including isolated reports) vomiting and anorexia are observed.

4.7 Use during pregnancy, lactation or lay

As enrofloxacin passes into maternal milk, use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Do not combine with tetracyclines, phenicols or macrolides because of potential antagonistic effects.

Concurrent administration of fluoroquinolones may increase the action of oral anticoagulants.

Do not combine with theophylline as this could lead to a prolonged elimination of this substance.

Concurrent administration of magnesium or aluminum containing substances may be followed by retarded absorption of enrofloxacin.

4.9 Amounts to be administered and administration route

Do not exceed the recommended dosage. The dosage rate of enrofloxacin is 5 mg/kg given orally once daily or as a divided dose twice daily for 5 to 10 days with or without food.

The duration of treatment in dogs may be extended depending on the clinical response and the judgement of the responsible veterinary surgeon.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

The daily dose is achieved as follows:

Cats and small dogs: one tablet per 3 kg body weight.

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

In accidental overdose, vomiting, diarrhoea and CNS/behavioural changes may occur.

There is no antidote and treatment should be symptomatic. If necessary, administration of aluminium- or magnesium-containing antacids or activated carbon can be used to reduce absorption of enrofloxacin.

In target animal species, cats have been shown to suffer ocular damage after receiving doses of more than 15 mg/kg once daily for 21 consecutive days. Doses of 30 mg/kg given once daily for 21 consecutive days have been shown to cause irreversible ocular damage. At 50 mg/kg given once daily for 21 consecutive days, blindness can occur.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, quinolone and quinoxaline antibacterials, fluoroquinolones.

ATCvet code: QJ01MA90

5.1 Pharmacodynamic properties

Enrofloxacin is bactericidal in action with activity against Gram positive and Gram negative bacteria and mycoplasmas. The mechanism of action of the quinolones is unique among antimicrobials – they act primarily to inhibit bacterial DNA gyrase, an enzyme responsible for controlling the super coiling 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.

Susceptibility of selected target pathogens (MIC) is as follows:

- *Pasteurella multocida*: 0.03 mg/L;
- *Escherichia coli*: 0.03-0.06 mg/L;
- *Staphylococcus pseudointermedius*: 0.125 mg/L;
- *Pseudomonas aeruginosa*: 2.0 mg/L.

Susceptibility breakpoints are: sensitive ≤ 0.5 mg/L; intermediate 1-2 mg/L; resistant ≥ 4 mg/L

Bacterial resistance to fluoroquinolones most commonly occurs by alteration of the target, DNA-gyrase, via mutation. Less commonly mutation occurs at the topoisomerase-IV target. Other mechanisms of resistance occur when bacteria decrease the ability of the drug to enter the cell or increase active transport out of the cell. Resistance is usually chromosomally developed and, therefore, remains after antimicrobial therapy ends. Cross-resistance of enrofloxacin with other

fluoroquinolones can occur. Changes in levels of resistance to fluoroquinolones over time by *Campylobacter* and *Salmonella* species are being monitored because of their possible impact on human health.

5.2 Pharmacokinetic particulars

The pharmacokinetics of enrofloxacin in dogs and cats are such that oral and parenteral administration leads to similar serum levels.

Enrofloxacin is rapidly absorbed after oral, intramuscular and subcutaneous administration. In the study performed with the product in cats, the dose of enrofloxacin administered in cats was 3.36 (± 0.30) mg/kg. The corrected maximal plasma concentration was 1654.37 ± 247.92 ng/mL and it was reached within $1.28 (\pm 0.58)$ h (T_{max}). AUC was $8433.55 (\pm 1851.80)$ ng h/mL and the value of $T_{1/2}$ was 3.75 h (harmonic mean).

Approximately 40% of the oral or intravenous enrofloxacin dose administered in dogs is metabolised to ciprofloxacin.

Maximal plasma concentration for ciprofloxacin in cats was 173.18 ± 34.08 ng/mL.

T_{max} was 2.42 ± 0.89 h and terminal half life was 4.88 h (harmonic mean).

Enrofloxacin possesses a high distribution volume. Tissue levels 2-3 times higher than that found in the serum, have been demonstrated in laboratory animals and target species. Organs in which high levels can be expected are lungs, liver, kidney, skin, bone and lymphatic system. Enrofloxacin also distributes into the cerebrospinal fluid, the aqueous humour and the foetus in pregnant animals.

The elimination of enrofloxacin is renal, primarily through glomerular filtration and tubular secretion.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Maize starch

Sodium starch glycolate (type A)

Meat flavour 10022

Sodium laurilsulphate

Basic butylated methacrylate copolymer

Dibutyl sebacate

Croscarmellose sodium

Silica, colloidal anhydrous

Talc

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years

6.4. Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Polyamide/Aluminium/Polyvinyl chloride film (OPA/Al/PVC), heat sealed with aluminium foil containing 10 tablets / blister. Each cardboard carton contains 100 tablets in 10 blister packs.

Polyamide/Aluminium/Polyvinyl chloride film (OPA/Al/PVC), heat sealed with aluminium foil containing 10 tablets / blister. Each cardboard carton contains 10 tablets in 1 blister pack.

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

KRKA, d.d., Novo mesto
Šmarješka cesta 6
8501 Novo mesto
Slovenia

8. MARKETING AUTHORISATION NUMBER

Vm 01656/4007

9. DATE OF FIRST AUTHORISATION

18 June 2009

10. DATE OF REVISION OF THE TEXT

May 2014

Approved:  **22/05/2014**