

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Enroxil Max 100 mg/ml solution for injection for cattle.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance

Enrofloxacin 100 mg

Excipients

Benzyl alcohol (E1519) 20 mg

Butyl alcohol 30 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, yellow solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle.

4.2 Indications for use, specifying the target species

Treatment of bovine respiratory disease associated with *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma* spp. where clinical experience, supported where possible by sensitivity testing of the causal organism, indicates enrofloxacin as the drug of choice.

Treatment of local signs (inflammation, milk quality and yield) associated with peracute/acute mastitis in lactating dairy cattle caused by *E. coli*, where herd history and previous sensitivity testing indicate enrofloxacin as the drug of choice.

4.3 Contraindications

Do not use for prophylaxis.

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

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i) Special precautions for use in animals

Normal sterile precautions should be taken.

The safety of the product has not been established in calves when administered by the intravenous route and use of this route of administration in calves is therefore not recommended.

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.

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.

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

This product is an alkaline solution. Any spillage onto the skin should be washed off immediately with water.

In the event of accidental splash into the eye, rinse with copious amounts of clean water. If irritation occurs, seek medical advice.

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

Care should be taken to avoid accidental self-injection. In case of accidental self-injection, 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 veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

Transient local reactions may occur at injection site.

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

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

Dosage and duration of treatment:

For respiratory infections in cattle: administer by subcutaneous injection:

A single dose of 7.5 mg/kg bodyweight (7.5 ml per 100 kg bodyweight)

Not more than 15 ml should be administered at one subcutaneous injection site.

For *E. coli* mastitis in cattle: administer by slow intravenous injection.

5.0 ml per 100 kg body weight (5 mg enrofloxacin per kg bodyweight) daily for 2 days.

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

A dose of 25 mg/kg bodyweight administered for 15 consecutive days is tolerated without any clinical symptoms.

Clinical signs seen in gross overdosage include lethargy, lameness, ataxia, slight salivation and muscle tremors. In accidental overdose there is no antidote and treatment should be symptomatic.

4.11 Withdrawal Period(s)

Subcutaneous use:

Meat and Offal	14 Days
Milk	84 Hours

Intravenous use:

Meat and Offal	4 Days
Milk	72 Hours

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use

ATCvet code: QJ01MA90

5.1 Pharmacodynamic properties

It is bactericidal in action with activity against many 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 supercoiling of bacterial DNA during replication. Resealing of the double stranded 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 but are inactive against strict anaerobes.

Molecular resistance to fluoroquinolones has been observed to arise from two principal sources, (i) alteration to DNA gyrase or topoisomerase IV and (ii) alterations in drug permeability of the bacterial cell. Both mechanisms lead to a reduced susceptibility of the bacteria to fluoroquinolones. Clinical resistance is dependent on several mutations accumulating in a step-wise manner.

5.2 Pharmacokinetic properties

The pharmacokinetics of enrofloxacin is such that oral and parenteral administration leads to similar serum levels. Enrofloxacin is lipid soluble and amphoteric and possesses a high distribution volume. Tissue levels 2-3 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 the lungs, liver, kidney, skin, bone and lymphatic system. Enrofloxacin also distributes into the cerebrospinal fluid, the aqueous humour and the foetus in pregnant animals.

After subcutaneous administration of 7.5 mg/kg the mean peak plasma concentration is 0.8 µg/ml achieved within 6 hours. Enrofloxacin is partly metabolized in the liver. Approximately 45 per cent of the dose is excreted in the urine and 55 per cent in the faeces as active and metabolites.

After an intravenous dose of 5 mg enrofloxacin per kg body weight (bw) to lactating dairy cattle, the total systemic exposure over the dosing interval of 24 h was at 7.1 mg*h/L. In cattle serum, approximately 30% of drug exposure (2.31 mg*h/L) consisted of ciprofloxacin, the active metabolite of enrofloxacin. The drug was well distributed into the body compartments (V_{enro} = 1.5 L/kg, V_{cipro} = 8.51 L/kg). Total body clearance was 0.71 L/h/kg. In milk, most of drug activity consisted of ciprofloxacin. Overall drug concentrations peaked at 4.1 mg/kg two hours after treatment. Overall drug exposure over 24 h was 22.1 mg*h/L. The actives were eliminated from milk with a mean exposure half-life of 2.8 h.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Butyl alcohol
L-Arginine
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, 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 package for sale: 5 years.
Shelf-life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Keep the container in the outer carton in order to protect from light.
Do not freeze.

6.5 Nature and composition of immediate packaging

Amber glass Type 2 multi-dose vials of 100 ml with bromobutyl rubber stopper.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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(S)

VPA 10774/002/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16th November 2012

10 DATE OF REVISION OF THE TEXT

January 2013