# Summary of Product Characteristics

## 1 NAME OF THE VETERINARY MEDICINAL PRODUCT

ROXACIN 100 mg/ml solution for injection for cattle and pigs

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

| | |
|---|---|
| Active substance | |
| Enrofloxacin | 100.0 mg |
| Excipients | |
| Benzyl alcohol (E1519) | 7.8 mg |
| Disodium edetate | 10.0 mg |

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for injection.

Clear slightly yellowish solution.

## 4 CLINICAL PARTICULARS

### 4.1 Target Species

Cattle and pigs.

## 4.2 Indications for use, specifying the target species

Treatment of bacterial infections caused by strains susceptible to enrofloxacin.

**Cattle**

Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mannheimia haemolytica* and *Mycoplasma* spp.
Treatment of acute severe mastitis caused by enrofloxacin susceptible strains of *Escherichia coli.*
Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of *Mycoplasma bovis* in cattle less than 2 years old.

**Pigs**
Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mycoplasma* spp. and *Actinobacillus pleuropneumoniae.*
Treatment of infections of the urinary tract caused by enrofloxacin susceptible strains of *Escherichia coli.*
Treatment of post-partum dysgalactiae syndrome, PDS (MMA syndrome) caused by enrofloxacin susceptible strains of *Escherichia coli* and *Klebsiella* spp.
Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.
Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.

## 4.3 Contraindications

Do not use in animals with central nervous system-associated seizure disorders. Do not use in the presence of existing disorders of cartilage development or musculoskeletal damage around functionally significant or weight-bearing joints. Do not use for prophylaxis. Do not use in known cases of resistance against other fluoroquinolone due to the potential for cross-resistance.

## 4.4 Special warnings for each target species

None

## 4.5 Special precautions for use

**Special precautions for use in animals**

The safety of the product has not been established in pigs or calves when administered by the intravenous route and use of this route of administration is not recommended in these animal groups.

Do not exceed the recommended dose.

Repeat injections should be administered at different sites.

Enrofloxacin should be used with caution in epileptic animals or animals affected by renal dysfunction.

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.

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

The product is an alkaline solution. Wash any splashes from skin or eyes immediately with water.

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

Care should be taken to avoid accidental self-injection. If accidental self injection occurs seek medical advice immediately.
Direct contact with the skin should be avoided because of sensitisation, contact dermatitis and possible hypersensitivity reactions. Wear gloves.
People with known hypersensitivity to (fluoro)quinolones should avoid contact with the veterinary medicinal product.

## 4.6 Adverse reactions (frequency and seriousness)

Local tissue reactions may occasionally occur at the injection site. Normal sterile precautions should be taken.
Rarely, anaphylactic reactions may occur following intravenous administration.
In cattle, gastrointestinal disturbances may occasionally occur.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

## 4.7 Use during pregnancy, lactation or lay

There is no restriction on the use of this product during pregnancy and lactation.

## 4.8 Interaction with other medicinal products and other forms of interaction

Antagonistic effects due to concurrent administration of bacteriostatic antimicrobial agents such as macrolides or tetracyclines may occur. Enrofloxacin may interfere with the metabolism of theophylline, decreasing theophylline clearance resulting in increased plasma levels of theophylline.

## 4.9 Amounts to be administered and administration route

Intravenous, subcutaneous or intramuscular use.
Repeated injections should be made at different injection sites.
To ensure a correct dosage, body weight (bw) should be determined as accurately as possible to avoid underdosing.

**Cattle**

5 mg of enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, once daily for 3 - 5 days.
Acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of *Mycoplasma bovis* in cattle less than 2 years old: 5 mg of enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, once daily for 5 days.
The product can be administered by slow intravenous or subcutaneous administration.
Acute mastitis caused by *Escherichia coli*: 5 mg enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, by slow intravenous injection once daily for two consecutive days.
The second dose may be administered by the subcutaneous route. In this case, the withdrawal period following subcutaneous injection applies.
Not more than 10 ml should be administered at one subcutaneous injection site.

**Pigs**

2.5 mg of enrofloxacin/kg bw, corresponding to 0.5 ml/20 kg bw, once daily by intramuscular injection for 3 days.
Alimentary tract infection or septicaemia caused by *Escherichia coli*: 5 mg of enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, once daily by intramuscular injection for 3 days.
In pigs, the injection should be made in the neck at the ear base.
**Not more than 3 ml should be administered at one intramuscular injection site.**

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

Do not exceed the recommended dose.
In accidental overdose (lethargy, anorexia) there is no antidote and treatment should be symptomatic.
No signs of over dosage were observed in pigs following administration of the product at five times the recommended therapeutic dose.
Degenerative changes of articular cartilage were observed in calves treated orally with 30 mg enrofloxacin/kg bw during 14 days.

## 4.11 Withdrawal Period(s)

Cattle:
Following intravenous injection:
Meat and offal: 5 days.
Milk: 3 days.

Following subcutaneous injection:
Meat and offal: 12 days.
Milk: 4 days.

Pigs:
Meat and offal: 13 days.

## 5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibiotics, fluoroquinolone group.

ATC Vet Code: QJ01MA90

## 5.1 Pharmacodynamic properties

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. Target inhibition is caused by non-covalent binding of fluoroquinolone molecules to these 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-dependent killing of pathogenic bacteria. The mode of action of enrofloxacin is bactericidal and bactericidal activity is concentration dependent.

Antibacterial spectrum
Enrofloxacin is active against many Gram-negative bacteria such as *Escherichia coli*, *Klebsiella* spp., *Actinobacillus pleuropneumoniae*, *Mannheimia haemolytica*, *Pasteurella* spp. (e.g. *Pasteurella multocida*), against Gram-positive bacteria such as *Staphylococcus* spp. (e.g. *Staphylococcus aureus*) and against *Mycoplasma* spp. at the recommended therapeutic doses.

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.

## 5.2 Pharmacokinetic properties

Enrofloxacin 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 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
Disodium edetate
Potassium hydroxide (for pH-adjustment)
Glacial acetic acid
Water for injections

## 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 packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

## 6.4 Special precautions for storage

Protect from light. Do not freeze.

## 6.5 Nature and composition of immediate packaging

Type II Amber glass vials of 250 ml capacity closed with pink bromobutyl rubber stoppers and aluminium flip-off seals. One vial of 250 ml is available in a cardboard box.
Type II Amber glass vials of 100 ml capacity closed with grey bromobutyl rubber stoppers and aluminium flip-off seals. One vial of 100 ml is available in a cardboard box.

Not all pack sizes may be marketed.

## 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

LABORATORIOS CALIER, S.A.
C/ Barcelonès, 26 (Pla del Ramassà)
LES FRANQUESES DEL VALLES (Barcelona), SPAIN.

# 8 MARKETING AUTHORISATION NUMBER(S)

VPA 10665/002/001

# 9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15th July 2011
Date of last renewal: 15th July 2016

# 10 DATE OF REVISION OF THE TEXT

October 2016