

ANNEX I: SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ENROSYVA 100 mg/ml solution for injection for cattle and pigs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Enrofloxacin 100 mg

Excipients:

Benzyl alcohol (E 1519)..... 10 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, yellow solution, free from visible particles.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pigs.

4.2 Indications for use, specifying the target species

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 the case of hypersensitivity to fluoroquinolones or to any of the excipients.

Do not use in growing horses because of possible deleterious damage on articular cartilage.

4.4 Special warnings for each target species

None.

4.5 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.

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

Use of the product including use deviating from instructions given in the SPC may increase the prevalence of bacteria resistant to the enrofloxacin and may decrease the effectiveness of treatment with other fluoroquinolones due to the potential for cross resistance.

Degenerative changes of articular cartilage were observed in calves treated orally with 30 mg enrofloxacin/kg bw during 14 days.

The use of enrofloxacin in growing lambs at the recommended dose for 15 days caused histological changes in the articular cartilage, not associated to clinical signs.

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

People with known hypersensitivity to fluoroquinolones should avoid contact with the veterinary medicinal 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.

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

Wash hands after use.

Do not eat, drink or smoke while handling the product.

4.6 Adverse reactions (frequency and seriousness)

In pigs, inflammatory reactions after intramuscular administration may occur commonly.

In cattle, inflammatory reaction of variable intensity and persistence at the administration point could be observed rarely after subcutaneously administration.

Digestive tract disorders (anorexia, vomiting and diarrhoea) may occur very rarely. These signs are generally mild and transient.

In cattle, shock reactions could be observed very rarely after intravenous administration, presumably as a result of circulatory impairment.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- *uncommon (more than 1 but less than 10 animals in 1,000 animals treated)*
- *rare (more than 1 but less than 10 animals in 10,000 animals treated)*

- very rare (less than 1 animal in 10,000 animals treated, including isolated reports)

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use enrofloxacin concomitantly with antimicrobial substances acting antagonistically to quinolones (e.g. macrolides, tetracyclines or phenicols).

Do not use concurrently with theophylline as the elimination of theophylline may be delayed.

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

In cases of accidental overdoses digestive tract disorders (e.g. vomiting, diarrhoea) and neurological disorders may occur.

In accidental overdose there is no antidote and treatment should be symptomatic.

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 PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, fluoroquinolones.

ATCvet 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 particulars

Enrofloxacin is rapidly absorbed after parenteral injection. Bioavailability is high (approximately 100% in pig and cattle) with a low to moderate plasma protein binding (approximately 20 to 50%). Enrofloxacin is metabolized to the active substance ciprofloxacin at approximately 40% in dogs and ruminants and less than 10% in pigs and cats.

Enrofloxacin and ciprofloxacin distribute well into all target tissues, e.g. lung, kidney, skin and liver, reaching 2- to 3-fold higher concentrations than in plasma. Parent substance and active metabolite are cleared from the body via urine and faeces.

Accumulation in plasma does not occur following a treatment interval of 24 h.

CATTLE:

After an intramuscular dose of 5 mg enrofloxacin per kg body weight (bw) to cattle, maximum concentration of 1µg/ml is observed and it is maintained for more than 6 hours. Distribution volume is equal to 0.6 l/kg, plasma elimination half-life is 2h and the body clearance is 210 ml/kg/h.

In cows, plasma elimination half-life was about 3h.

After i.v. administration of 2.5mg/kg to cows, enrofloxacin and ciprofloxacin in milk could be observed after 15 minutes. In dairy cattle, after intravenous administration, peak concentrations in milk are reached after 0.7 to 1.3 hours, while maximum concentrations of the active metabolite ciprofloxacin are reached after 5-8 hours from the administration. Concentrations of enrofloxacin in milk are similar to those in plasma.

PIGS

After i.v. administration of a dose of 5mg/kg of enrofloxacin, a wide volume of distribution of 3.9 l/kg was observed. After an i.v. administration of 2.5 mg/kg, plasma elimination half-life was 9.6h and the mean residence time was 12.8h.

After i.m. administration of 2.5 mg/ kg, the plasma elimination half-life was 12.1 h, the mean residence time was 17.2 h and the maximum concentration was 1.2 µg / ml.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E-1519)
Potassium hydroxide
Water for injections

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other medicinal products.

Do not mix with acid products that may precipitate the enrofloxacin.

6.3 Shelf life

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

Shelf life after first opening the immediate packaging: 28 days.

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

Type II coloured glass vials sealed with bromobutyl stoppers and aluminium cap.

Polypropylene vials sealed with bromobutyl stoppers and aluminium cap.

Pack Sizes:

Cardboard box with 1 glass vial of 100 ml.

Polypropylene vial of 250ml.

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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Laboratorios SYVA S.A.U.

Avda. Párroco Pablo Díez,

49-57 (24010) León

Spain

Tel: 0034 987800800

Fax: 0034 987802452

Email: mail@syva.es

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:> <{DD/MM/YYYY}><{DD month YYYY}.>

Date of last renewal:> <{DD/MM/YYYY}> <{DD month YYYY}.>

10 DATE OF REVISION OF THE TEXT

<{MM/YYYY}>

<{DD/MM/YYYY}>

<{DD month YYYY}>

PROHIBITION OF SALE, SUPPLY AND/OR USE