# ANNEX I

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Colmyc 100 mg/ml solution for injection for cattle, pigs, sheep and goat.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

**Active substance:**
Enrofloxacin 100.0 mg

**Excipients:**

| Qualitative composition of excipients and other constituents | Quantitative composition if that information is essential for proper administration of the veterinary medicinal product |
|---|---|
| n-Butyl alcohol | 30 mg |
| Potassium hydroxide | |
| Water for injections | |

Clear yellow solution

## 3. CLINICAL INFORMATION

Cattle, goat, pig, sheep

### 3.2 Indications for use for each target species

**Cattle**
Treatment of infections of the respiratory tract caused by strains of *Pasteurella multocida*, *Mannheimia haemolytica* and *Mycoplasma* spp.

Treatment of acute severe mastitis caused by strains of *Escherichia coli.*

Treatment of infections of the alimentary tract caused by strains of *Escherichia coli*.

Treatment of septicaemia caused by strains of *Escherichia coli*.

Treatment of acute mycoplasma-associated arthritis caused by strains of *Mycoplasma bovis* in cattle less than 2 years old.

**Sheep**

Treatment of infections of the alimentary tract caused by strains of *Escherichia coli*.
Treatment of septicaemia caused by strains of *Escherichia coli*.
Treatment of mastitis caused by strains of *Staphylococcus aureus* and *Escherichia coli*.

**Goats**

Treatment of infections of the respiratory tract caused by strains of *Pasteurella multocida* and *Mannheimia haemolytica.*
Treatment of infections of the alimentary tract caused by strains of *Escherichia coli*.
Treatment of septicaemia caused by strains of *Escherichia coli.*
Treatment of mastitis caused by strains of *Staphylococcus aureus* and *Escherichia coli*.

**Pigs**

Treatment of infections of the respiratory tract caused by strains of *Pasteurella multocida, Mycoplasma* spp. and *Actinobacillus pleuropneumoniae.*

Treatment of infections of the urinary tract caused by strains of *Escherichia coli.*

Treatment of post-partum dysgalactiae syndrome, PDS (MMA syndrome) caused by strains of *Escherichia coli* and *Klebsiella* spp.

Treatment of infections of the alimentary tract caused by strains of *Escherichia coli*.

Treatment of septicaemia caused by strains of *Escherichia coli.*

### 3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or other fluoroquinolones or to any of the excipients.

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

### 3.4 Special warnings

Cross-resistance within the fluoroquinolone class of antimicrobials is common.
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### 3.5 Special precautions for use

Special precautions for safe use in the target species:
Use of the product should be based on identification and susceptibility testing on the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level. 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.
Use of the product should be in accordance with official, national and regional antimicrobial policies.
Use of the product including use deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to enrofloxacin and may decrease the effectiveness of treatment with all 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.

Avoid skin and eye contact. In case of accidental spillage onto skin or eyes, wash them immediately with water
Wash hands after use. Do not eat, drink or smoke whilst handling 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.
Special precautions for the protection of the environment:

Not applicable

Other precautions:

In countries where feeding of fallen stock to scavenger bird populations is permitted as a conservation measure (see Commission Decision 2003/322/EC), the possible risk to hatching success should be considered before feeding carcasses of livestock recently treated with this product.

### 3.6 Adverse events

Cattle:

| | |
|---|---|
| Very rare (<1 animal / 10,000 animals treated, including isolated reports): | Digestive tract disorders (e.g. diarrhoea) (generally mild and transient), circulatory shock (intravenous treatment can cause shock reactions, presumably as a result of circulatory impairment.) |

Sheep and goats:

| | |
|---|---|
| Very rare (<1 animal / 10,000 animals treated, including isolated reports): | Digestive tract disorders (e.g. diarrhoea) (generally mild and transient). |

Pigs:

| | |
|---|---|
| Very rare (<1 animal / 10,000 animals treated, including isolated reports): | Digestive tract disorders (e.g. diarrhoea) (generally mild and transient), application site disorders (may persist up to 28 days after the injection) |

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See also the last section of the package leaflet for respective contact details.

### 3.7 Use during pregnancy, lactation or lay

Cattle
The safety of the veterinary medicinal product has been established in pregnant cows during the 1st quarter of pregnancy. The product can be used in pregnant cows during the 1st quarter of pregnancy.
The use of the product in cows during the 3 last quarters of pregnancy should be based on a benefit-risk assessment by the responsible veterinarian.

The product can be used in cows during lactation.

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

Pigs
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.
The product can be used in sows during lactation

### 3.8 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.
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### 3.9 Administration routes and dosage

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.

**Sheep and goats**
5 mg of enrofloxacin/kg bw, corresponding to 1 ml/20 kg bw, once daily by subcutaneous injection for 3 days.
Not more than 6 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.

### 3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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

In pigs, no adverse effects were reported after the administration of 5 times the recommended dose.

In cattle, sheep and goat, overdose has not been documented.

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

### 3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

For administration only by **a veterinarian**

### 3.12 Withdrawal periods

Cattle:

Following intravenous injection:

Meat and offal: 5 days.
Milk: 3 days.

Following subcutaneous injection:

Meat and offal: 12 days.

Milk: 4 days.

Sheep:
Meat and offal: 4 days.
Milk: 3 days.

Goats:
Meat and offal: 6 days.
Milk: 4 days.

Pigs:

Meat and offal: 13 days.

## 4 PHARMACOLOGICAL INFORMATION

### 4.1 ATCvet code:

QJ01MA90

**4.2 Pharmacodynamics**

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.

### 4.3 Pharmacokinetics

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 ruminants and less than 10% in pigs.
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.
In milk, most of drug activity consists on ciprofloxacin. Overall drug concentrations peak at 2 hours after treatment showing an approximately 3-fold higher total exposure over the 24 hours dosing interval compared to plasma.

| | Pigs | Pigs | Cattle | Cattle |
|---|---|---|---|---|
| Dose rate (mg/kg bw) | 2.5 | 5 | 5 | 5 |
| Route of administration | im | im | iv | sc |
| $T_{max}$ (h) | 2 | 2 | / | 3.5 |
| $C_{max}$ (µg/ml) | 0.7 | 1.6 | / | 0.733 |
| AUC (µg·h/ml) | 6.6 | 15.9 | 9.8 | 5.9 |
| Terminal half-life (h) | 13.12 | 8.10 | / | 7.8 |
| Elimination half-life (h) | 7.73 | 7.73 | 2.3 | |
| F (%) | 95.6 | / | / | 88.2 |

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major incompatibilities

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

### 5.2 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.

### 5.3.Special precautions for storage

Do not freeze.
Store in the original package in order to protect from light.

### 5.4 Nature and composition of immediate packaging

Amber polypropylene vials of 50, 100 and 250 ml provided with a grey (50 ml and 100 ml) or pink (250 ml) rubber-butyl stopper and aluminium capsule with a green Flip-Off sealing.

Package sizes:
1 vial of 50 ml
1 vial of 100 ml
1 vial of 250 ml

Not all pack sizes may be marketed.

### 5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or <household waste>.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

## 6. NAME OF THE MARKETING AUTHORISATION HOLDER

SP VETERINARIA SA

## 7. MARKETING AUTHORISATION NUMBER(S)

## 8. DATE OF FIRST AUTHORISATION

Date of first authorisation: DD/MM/YYYY

## 9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{MM/YYYY}

## 10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

ES: Dispensing conditions: Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database.