[Version 9,03/2022]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Marbofloxacin ..... 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**
Metacresol	2.0 mg
Thioglycerol	1.0 mg
Disodium edetate	0.1 mg
Gluconolactone	
Water for injections	

Yellow greenish to yellow brownish, clear solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and pigs (sows and pigs for fattening).

3.2 Indications for use for each target species

Cattle:
- Treatment of respiratory infections caused by strains of *Histophilus somni*, *Mannheimia haemolytica*, *Mycoplasma bovis* and *Pasteurella multocida* susceptible to marbofloxacin.
- Treatment of acute mastitis caused by strains of *Escherichia coli* susceptible to marbofloxacin during the lactation period.

Pigs:
- Treatment of Postpartum Dysgalactia Syndrome –PDS- (Metritis Mastitis Agalactia Syndrome), caused by bacterial strains susceptible to marbofloxacin.
- Treatment in pigs for fattening of respiratory tract infections caused by susceptible strains of *Actinobacillus pleuropneumoniae, Mycoplasma hyopneumoniae and Pasteurella multocida.*

3.3 Contraindications

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

3.4 Special warnings

The efficacy data showed that the product has insufficient efficacy for the treatment of acute forms of mastitis induced by gram-positive bacteria.
Do not use in cases of resistance to other fluoroquinolones (cross-resistance).

3.5 Special precautions for use

Special precautions for safe use in the target species:

The use of the product should be based on identification and susceptibility testing of 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.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

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 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.

The feeding of waste milk containing residues of marbofloxacin to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

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

People with known hypersensitivity to (fluoro)quinolones should avoid contact with the veterinary medicinal product. Care should be taken to avoid accidental self-injection as it can induce a slight irritation.

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

In case of contact with skin or eyes, rinse immediately with plenty of water.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle and pigs (sows and pigs for fattening):

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site disorders (e.g. injection site lesions, injection site swelling or injection site pain) *[1,2]

1. Transitory inflammatory lesions at the injection site can occur, when administered via the intramuscular or subcutaneous route. When administering by the intramuscular route which may persist for at least 18 days after injection.

2. In cattle, subcutaneous route was shown to be better tolerated locally than intramuscular route.

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

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.

Safety of the veterinary medicinal product at 2 mg/kg body weight has been established in pregnant cows or in sucking calves and piglets when used in cows and sows. Can be used during pregnancy and lactation.

Safety of the veterinary medicinal product at 8 mg/kg body weight has not been established in pregnant cows or in sucking calves when used in cows. Therefore, this dose regimen should be used only according to the benefit/risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cattle:

Respiratory infections:

The recommended dosage is 8 mg marbofloxacin/kg body weight (2 ml veterinary medicinal product/25 kg body weight) in a single injection by the intramuscular route. If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

In cases of respiratory infections caused by *Mycoplasma bovis*, the recommended dose is 2 mg marbofloxacin/kg body weight (1 ml veterinary medicinal product/50 kg body weight), in a single daily injection for 3 to 5 consecutive days, by the intramuscular or subcutaneous route. The first injection may be given by the intravenous route.

Acute mastitis:

The recommended dosage is 2 mg marbofloxacin/kg body weight (1 ml veterinary medicinal product/50 kg body weight) in a single daily injection for 3 consecutive days by the intramuscular or subcutaneous route. The first injection may also be given by the intravenous route.

Pigs:

Treatment of Postpartum Dysgalactia Syndrome –PDS– (Metritis Mastitis Agalactia Syndrome):

The recommended dosage is 2 mg marbofloxacin/kg body weight (1 ml veterinary medicinal product/50 kg body weight) in a single daily injection for 3 consecutive days by the intramuscular route.

Treatment in pigs for fattening of respiratory infections:
The recommended dosage is 2 mg marbofloxacin/kg body weight (1 ml veterinary medicinal product/50 kg body weight) in a single daily injection for 3 to 5 consecutive days by the intramuscular route.

To ensure administration of a correct dose, body weight should be determined as accurately as possible.
In cattle and pig, the preferred injection site is the neck area.
The cap may be safely punctured up to 30 times. The user should choose the most appropriate vial size according to the target species to treat.

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

No clinical signs have been observed after administration of 3 times the recommended dose.
Signs such as acute neurological disorders may occur when the dose is exceeded. These signs should be treated symptomatically.
Do not exceed the recommended dose.

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

ES: For administration only by a veterinarian (in case of intravenous route) or under their direct responsibility.

3.12 Withdrawal periods

Cattle:

Indication	**Respiratory**		**Mastitis**
Dosage	2 mg/kg for 3 to 5 days (IV/IM/SC)	8 mg/kg on a single occasion (IM)	2mg/kg for 3 days (IV/IM/SC)
Meat and offal	6 days	3 days	6 days
Milk	36 hours	72 hours	36 hours

Pigs:
Meat and offal: 4 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01MA93

4.2 Pharmacodynamic
Marbofloxacin is a synthetic, bactericidal antimicrobial with concentration-dependent activity, belonging to the fluoroquinolone group which acts by inhibition of DNA gyrase and topoisomerase IV. It has *in vitro* activity against *Histophilus somni, Mannheimia haemolytica, Pasteurella multocida, E. coli*, *Mycoplasma bovis, Actinobacillus pleuropneumoniae and Mycoplasma hyopneumoniae*. It

should be noted that some strains of Streptococci, Pseudomonas and Mycoplasma may not be sensitive to Marbofloxacin.

There are no validated breakpoints for marbofloxacin for swine and cattle target pathogens.

Resistance to fluoroquinolones occurs by chromosomal mutations with following mechanisms: diminution of permeability of bacterial cell wall, expression change of genes coding for efflux pumps or mutations in genes encoding enzymes responsible of molecular union. Plasmid-mediated resistance to fluoroquinolones confer only decreased susceptibility of bacteria, however, it can facilitate development of mutations in genes of target enzymes and can be transferred horizontally. Depending on the underlying resistance mechanism cross-resistance to other (fluoro)quinolones and co-resistance to other antimicrobial classes can occur.

4.3 Pharmacokinetic

After subcutaneous or intramuscular administration in cattle and intramuscular administration in pigs at the recommended dose of 2 mg/kg body weight, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.5 µg/ml within less than 1 hour. Its bioavailability is close to 100%.

It is weakly bound to plasma proteins (less than 10% in pigs, and 30% in cattle), extensively distributed and in most tissues (liver, kidney, skin, lung, bladder, uterus, digestive tract) it achieves a higher concentration than in plasma.

In cattle, marbofloxacin is eliminated slowly in pre-ruminating calves ($t_{½\beta}$ = 5-9 hours) but faster in ruminant cattle ($t_{½\beta}$ = 4-7 hours) predominantly in the active form in urine (3/4 in pre-ruminating calves, ½ in ruminants) and faeces (1/4 in pre-ruminating calves, ½ in ruminants).

After a single intramuscular administration in cattle at the recommended dose of 8 mg/kg body weight, the maximum plasma concentration of marbofloxacin (Cmax) is 7.3 µg/ml reached in 0.78 hours (Tmax). Marbofloxacin is eliminated slowly ($t_{½}$ terminal = 15.60 hours).

After intramuscular administration in lactating cows, a maximum concentration in the milk of marbofloxacin of 1.02 µg/ml is reached (Cmax after the first administration) after 2.5 hours (Tmax after the first administration).

In pigs, marbofloxacin is eliminated slowly ($t_{½\beta}$ = 8-10 hours) predominantly in the active form in urine (2/3) and faeces (1/3).

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 in glass vials: 3 years
Shelf life of the veterinary medicinal product as packaged for sale in PP vials: 2 years
Shelf life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Type II amber glass vials with type I bromobutyl stopper and flip-off aluminium cap.
Amber polypropylene vials with type I bromobutyl stopper and flip-off aluminium cap.

Pack sizes:
Box with 1 glass vial of 50 ml
Box with 1 glass vial of 100 ml
Box with 1 glass vial of 250 ml
Box with 10 glass vials of 50 ml
Box with 10 glass vials of 100 ml
Box with 10 glass vials of 250 ml
Box with 1 PP vial of 100 ml
Box with 1 PP vial of 250 ml
Box with 10 PP vials of 100 ml
Box with 10 PP vials 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 S.A.

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

DD/MM/YYYY

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database.