# 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:**
Metacresol ..... 2.0 mg
Thioglycerol ..... 1.0 mg
Disodium edetate ..... .0.1 mg

Other excipients, q.s.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection
Yellow greenish to yellow brownish, clear solution

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Cattle and pig (sow).

### 4.2 Indications for use, specifying the 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.

Pig:
- Treatment of Postpartum Dysgalactia Syndrome –PDS- (Metritis Mastitis Agalactia Syndrome), caused by bacterial strains susceptible to marbofloxacin.

### 4.3 Contraindications

Do not use in cases where the pathogen involved is resistant to other fluoroquinolones (cross-resistance).
Do not use in animals with known hypersensitivity to marbofloxacin or any other quinolone or to any of the excipients.

### 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 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 efficacy data showed that the product has insufficient efficacy for the treatment of acute forms of mastitis induced by gram-positive 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.

## 4.6 Adverse reactions (frequency and seriousness)

Transitory inflammatory lesions can occur at the injection site, without clinical impact, when administered via the intramuscular or subcutaneous route.

Administration by the intramuscular route may cause transient local reactions such as pain and swelling at the injection site and inflammatory lesions, which may persist for at least 12 days after injection.

However, in cattle, subcutaneous route was shown to be better tolerated locally than intramuscular route. Therefore, the subcutaneous route is recommended in heavy cattle.

## 4.7 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 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 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 accordingly to the benefit/risk assessment by the responsible veterinarian.

In case of use in lactating cow, see section 4.11.

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

None known.

## 4.9 Amounts to be administered and administration route

Cattle:
**Respiratory infections:**
The recommended dosage is 8 mg marbofloxacin/kg body weight (2 ml product/25 kg BW) in a single injection by 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 product/50 kg BW), in a single daily injection for 3 to 5 consecutive days, by 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 product/50 kg BW) in a single daily injection for 3 consecutive days by intramuscular or subcutaneous route. The first injection may also be given by the intravenous route.

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

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

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

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

## 4.11 Withdrawal periods

Cattle**:**
8 mg/kg on a single occasion (IM)
Meat and offal: 3 days
Milk: 72 hours

2 mg/kg for 3 to 5 days (IV/SC/IM)
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):

Meat and offal: 4 days.

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, Fluoroquinolones,
ATCvet code: QJ01MA93

### 5.1 Pharmacodynamic properties

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

Strains with MIC ≤ 1 µg/ml are susceptible to marbofloxacin, while strains with MIC ≥ 4 µg/ml are resistant to marbofloxacin.

Resistance to fluoroquinolones occurs from chromosomal mutation by means of three mechanisms: diminution of permeability of bacterial wall, expression of efflux pumps or mutation of enzymes responsible of molecular union.

### 5.2 Pharmacokinetic particulars

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 (t½β = 5-9 hours) but faster in ruminant cattle (t½β = 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 (t½ 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 (t½β = 8-10 hours) predominantly in the active form in urine (2/3) and faeces (1/3).

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Metacresol

Thioglycerol
Disodium edetate
Gluconolactone
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

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

### 6.5 Nature and composition of immediate packaging

50 ml, 100 ml and 250 ml type II amber glass vials with type I bromobutyl stopper and flip-off aluminium cap.

Pack sizes:
- Box with 1 vial of 50 ml
- Box with 1 vial of 100 ml
- Box with 1 vial of 250 ml
- Box with 10 vials of 50 ml
- Box with 10 vials of 100 ml
- Box with 10 vials of 250 ml

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

SP VETERINARIA S.A.
Ctra. Reus-Vinyols, km 4,1
43330 Riudoms (SPAIN)

## 8. MARKETING AUTHORISATION NUMBER(S)

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

Date of first authorisation: {DD/MM/YYYY}

## 10 DATE OF REVISION OF THE TEXT

{DD/MM/YYYY}

## PROHIBITION OF SALE, SUPPLY AND/OR USE

Dispensing conditions: Veterinary medicinal product subject to veterinary prescription.

Administration conditions: Administration by a veterinarian surgeon (in case of intravenous route) or under their direct responsibility.

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE**
Labels for 100 ml and 250 ml vials
Individual boxes for 50 ml, 100 ml and 250 ml vials
Boxes with 10 vials of 50 ml, 100 ml or 250 ml

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## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:

Marbofloxacin ..... 100.0 mg
Metacresol ..... 2.0 mg
Thioglycerol ..... 1.0 mg
Disodium edetate ..... .0.1 mg
Other excipients, q.s.

## 3. PHARMACEUTICAL FORM

Solution for injection
Yellow greenish to yellow brownish, clear solution

## 4. PACKAGE SIZE

Vial of 100 ml
Vial of 250 ml
Boxes containing 10 vials of 50 ml
Boxes containing 10 vials of 100 ml
Boxes containing 10 vials of 250 ml

## 5. TARGET SPECIES

Cattle and pig (sow).

## 6. INDICATIONS

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.

Pig:

- Treatment of Postpartum Dysgalactia Syndrome –PDS- (Metritis Mastitis Agalactia Syndrome), caused by bacterial strains susceptible to marbofloxacin.

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

Cattle: IM, SC or IV use
Pigs (sows): IM use
Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD

Withdrawal period:

Cattle**:**
8 mg/kg on a single occasion (IM)
Meat and offal: 3 days
Milk: 72 hours

2 mg/kg for 3 to 5 days (IV/SC/IM)
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days.

## 9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

## 10. EXPIRY DATE

EXP {month/year}
PL: Termin ważności (EXP)
Once opened, use by 28 days

## 11. SPECIAL STORAGE CONDITIONS

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

## 12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

## 13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.
PL: Wyłącznie dla zwierząt - Wydawany z przepisu lekarza – Rp.
Do podawania pod nadzorem lekarza weterynarii

## 14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

## 15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

SP VETERINARIA S.A.
Ctra. Reus-Vinyols, km 4,1
43330 Riudoms (SPAIN)

## 16. MARKETING AUTHORISATION NUMBER(S)

## 17. MANUFACTURER'S BATCH NUMBER

Lot
PL: Nr serii (Lot)

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

Label for 50 ml vials

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## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 2. QUANTITY OF THE ACTIVE SUBSTANCE

100 mg/ml

## 3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

50 ml

## 4. ROUTES OF ADMINISTRATION

Intramuscular, subcutaneous and intravenous

## 5. WITHDRAWAL PERIOD

Withdrawal period:

Cattle**:**
8 mg/kg on a single occasion (IM)
Meat and offal: 3 days
Milk: 72 hours

2 mg/kg for 3 to 5 days (IV/SC/IM)
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days.

## 6. BATCH NUMBER

<Batch><Lot> {number}

## 7. EXPIRY DATE

EXP {month/year}
Once opened, use by 28 days

## 8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

# B. PACKAGE LEAFLET

**PACKAGE LEAFLET FOR:**

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

## 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:

SP VETERINARIA S.A.
Ctra. Reus-Vinyols, km 4,1
43330 Riudoms (SPAIN)

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

Each ml contains:

**Active substance:**
Marbofloxacin ..... 100.0 mg

**Excipients:**
Metacresol ..... 2.0 mg
Thioglycerol ..... 1.0 mg
Disodium edetate ..... .0.1 mg
Other excipients, q.s.

## 4. INDICATIONS

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.

Pig:
- Treatment of Postpartum Dysgalactia Syndrome –PDS- (Metritis Mastitis Agalactia Syndrome), caused by bacterial strains susceptible to marbofloxacin.

## 5. CONTRAINDICATIONS

Do not use in cases where the pathogen involved is resistant to other fluoroquinolones (cross-resistance).
Do not use in animals with known hypersensitivity to marbofloxacin or any other quinolone or to any of the excipients.

## 6. ADVERSE REACTIONS

Transitory inflammatory lesions can occur at the injection site, without clinical impact, when administered via the intramuscular or subcutaneous route.

Administration by the intramuscular route may cause transient local reactions such as pain and swelling at the injection site and inflammatory lesions, which may persist for at least 12 days after injection.

However, in cattle, subcutaneous route was shown to be better tolerated locally than intramuscular route. Therefore, the subcutaneous route is recommended in heavy cattle.

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

## 7. TARGET SPECIES

Cattle and pig (sow).

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Cattle:

Respiratory infections:
The recommended dosage is 8 mg marbofloxacin/kg body weight (2 ml product/25 kg BW) in a single injection by 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 product/50 kg BW), in a single daily injection for 3 to 5 consecutive days, by 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 product/50 kg BW) in a single daily injection for 3 consecutive days by intramuscular or subcutaneous route. The first injection may also be given by the intravenous route.

Pig (sow):

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

## 9. ADVICE ON CORRECT ADMINISTRATION

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

## 10. WITHDRAWAL PERIOD

Cattle**:**
8 mg/kg on a single occasion (IM)
Meat and offal: 3 days
Milk: 72 hours

2 mg/kg for 3 to 5 days (IV/SC/IM)
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days.

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.
Do not use this veterinary medicinal product after the expiry date which is stated on the label.
Shelf life after first opening the container: 28 days.

## 12. SPECIAL WARNINGS

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 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 efficacy data showed that the product has insufficient efficacy for the treatment of acute forms of mastitis induced by gram-positive 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.

Pregnancy and lactation:
Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.
Safety of the 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 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

accordingly to the benefit/risk assessment by the responsible veterinarian.
In case of use in lactating cow, see section 10.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose (symptons, emergency procedures, antidotes):
No clinical signs have been observed after administration of 3 times the recommended dose. Signs as acute neurological disorders may occur when the dose is exceeded. This signs should be treated symptomatically.
Do not exceed the recommended dose.

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

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

## 15. OTHER INFORMATION

Pack sizes:
- Box with 1 vial of 50 ml
- Box with 1 vial of 100 ml
- Box with 1 vial of 250 ml
- Box with 10 vials of 50 ml
- Box with 10 vials of 100 ml
- Box with 10 vials of 250 ml

Not all pack sizes may be marketed.

For animal treatment only. To be supplied only on veterinary prescription.

Administration conditions: Administration by a veterinarian surgeon (in case of intravenous route) or under their direct responsibility.