SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Marbofloxacin ..... 100 mg

Excipients:

Metacresol ..... 2 mg
Monothioglycerol ..... 1 mg
Disodium edetate..... 0.1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Clear, yellowish solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pigs (sows).

4.2 Indications for use, specifying the target species

In cattle:

- Treatment of respiratory infections caused by marbofloxacin-susceptible strains of *Histophilus somni*, *Mannheimia haemolytica*, *Pasteurella multocida* and *Mycoplasma bovis*.

- Treatment of acute forms of mastitis induced by marbofloxacin-*susceptible Escherichia coli* strains, during lactation.

In pigs (sows):

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

4.3 Contraindications

Do not use in cases where the pathogen involved is resistant to other fluoroquinolones (cross resistance).

Do not use in cases of hypersensitivity to the active substance, to 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, it can induce a slight irritation.

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

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

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases:

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

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

Pregnancy and lactation:

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

Dose of 2 mg marbofloxacin/kg bodyweight

Can be used during pregnancy and lactation.

The safety of the veterinary medicinal product has been established in cows during gestation and suckling pigs and calves when used in cows and sows, respectively.

Dose of 8 mg marbofloxacion/kg bodyweight

The safety of the veterinary medicinal product has not been established in pregnant cows or in suckling calves when used in cows. Therefore, this dose regimen should be used only according 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 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, by the subcutaneous or intramuscular route, for 3 consecutive days. The first injection may be given by the intravenous route.

Pigs (sows):

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

In cattle and pigs, the preferred injection site is the neck area.

To ensure a correct dosage bodyweight should be determined as accurately as possible to avoid underdosing.

In order to reduce the risk of particulate contamination of the product, it is recommended that a draw-off needle be used to reduce the number of times the septum is punctured.

As the vial cannot be broached more than 50 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 sign of overdosage has been observed with the product after administration of 3 times the recommended dose.

Signs such as neurological disorders may occur when the dose is exceeded. Do not exceed the recommended dose. These signs would have to be treated symptomatically.

4.11 Withdrawal period(s)

Cattle:

Intramuscular use (8 mg/kg single dose):

Meat and offal: 3 days

Milk: 72 hours

Intramuscular or subcutaneous use (2 mg/kg single daily injection, for 3-5 days):

Meat and offal: 6 days

Milk: 36 hours

Pigs (sows):

Intramuscular use:

Meat and offal: 4 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, Fluoroquinolones.

ATC vet code: QJ01MA93.

5.1 Pharmacodynamic properties

Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the fluoroquinolone group which acts by inhibition of DNA gyrase. It has a broad-spectrum activity in vitro against Gram-positive bacteria (in particular *Staphylococcus*), against Gram-negative bacteria (*E. coli*, *Histophilus somni*, *Mannheimia haemolytica* and *Pasteurella multocida*) and against *Mycoplasma* (*Mycoplasma bovis*). Resistance to *Streptococcus* may occur.

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

Resistance to fluoroquinolones occurs by chromosomal mutation with three mechanisms: decrease of the bacterial wall permeability, expression of efflux pump or mutation of enzymes responsible for molecule binding.

5.2 Pharmacokinetic particulars

After subcutaneous or intramuscular administration in cattle and intramuscular administration in pigs at the recommended dose of 2 mg/kg bodyweight, 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 h) but faster in ruminant cattle ($t_{½}\beta$ = 4-7 h) 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 (C_{max}) is 7.3 µg/ml reached in 0.78 hours (t_{max}). Marbofloxacin is eliminated slowly ($t_{1/2}$ terminal = 15.60 hours).

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Metacresol
Monothioglycerol
Glucono-Delta-Lactone
Disodium edetate
Water for injections

6.2 Major incompatibilities

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

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Cardboard box containing one Type II amber glass vial of 50 ml, 100 ml or 250 ml, with a Type I bromobutyl rubber stopper and an aluminium cap.

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

8. MARKETING AUTHORISATION NUMBER

Vm 31592/4006

9. DATE OF FIRST AUTHORISATION

21 December 2012

10 DATE OF REVISION OF THE TEXT

February 2018

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

Approved 21 February 2018