

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Actimarbo 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

Monothioglycerol 1.0 mg

Disodium edetate (E 386) 0.1 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

A clear pale yellow to greenish–brownish yellow aqueous solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle & pigs.

4.2 Indications for use, specifying the target species

In cattle:

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

In pigs:

- Treatment of Metritis Mastitis Agalactia syndrome caused by susceptible strains of organisms.

4.3 Contraindications

Do not use in animals with known hypersensitivity to marbofloxacin, or any quinolones, or to any of the excipients.

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

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Do not use in case of confirmed or suspected resistance to fluoroquinolones (cross resistance).

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 upon 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 using this product.
- In case of contact with skin or eyes, rinse with plenty of water. Care should be taken to avoid accidental self injection.
- Accidental self-injection can induce a slight irritation.
- In case of accidental self injection, seek medical advice and show the label to the doctor.
- Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Transitory inflammatory lesions without clinical impact can occur at the injection site after intramuscular or subcutaneous injections.

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.

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

4.7 Use during pregnancy, lactation or lay

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

Dose of 2 mg/kg body weight:

Can be used during pregnancy and lactation.

The safety of the veterinary medicinal product has been established in cow during gestation and suckling pigs and calves when used in cow and sow.

Dose of 8 mg/kg body weight:

The safety of the veterinary medicinal product has not been established in pregnant cow or in suckling calves when used in cow. Therefore, this dose regimen should be use 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

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

Cattle:

Respiratory infections:

- Intramuscular use:

The recommended dosage is 8 mg / kg body weight i.e. 2 ml / 25 kg body weight in a single injection. If the volume to be injected is more than 20 ml, it should be divided between 2 or more injection sites.

Acute mastitis:

- Intramuscular or subcutaneous use:

The recommended dosage is 2 mg / kg / day (1 ml / 50 kg) in a single daily injection.

Treatment duration is 3 to 5 days.

The first injection may also be given by the intravenous route too. The subcutaneous route is recommended in heavy cattle (see section 4.6).

Pigs:

Acute mastitis:

- Intramuscular use:

The recommended dosage is 2 mg / kg / day (1 ml / 50 kg) in a single daily injection.

Treatment duration is 3 days.

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.

The septum can be punctured up to 27 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 severe side-effects are to be expected at doses up to 3 or 5 times the recommended dose in cattle and pigs respectively.

No sign of overdosage has been observed after administration of 3 times the recommended dose.

Overdosage may cause signs such as acute neurological disorders which should be treated symptomatically.

4.11 Withdrawal period(s)

Cattle:

- Respiratory infections (intramuscular use, 8 mg/kg single dose)
Meat and offal: 3 days
Milk: 72 hours
- Acute mastitis (intramuscular or subcutaneous use, 2 mg/kg single daily injection for 3 to 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
ATCvet 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 is effective against a wide range of Gram positive bacteria (in particular *Staphylococci*) and Gram negative bacteria (*Escherichia coli*, *Pasteurella spp*).

The marbofloxacin in vitro activity against pathogens isolated in 2004 from bovine respiratory diseases during a clinical field trial in France, Germany, Spain and Belgium, is good: MIC values are comprised between 0.015 and 0.25 µg/ml for *Mannheimia haemolytica* (MIC₉₀ = 0.124 µg/ml; MIC₅₀ = 0.025 µg/ml), between 0.004

and 0.12 µg/ml for *Pasteurella multocida* (MIC₉₀ = 0.022 µg/ml; MIC₅₀ = 0.009 µg/ml) and between 0.015 and 2 µg/ml for *Histophilus somni*. Strains with MIC ≤ 1 µg/ml are sensitive to marbofloxacin whereas strains with MIC ≥ 4 µg/ml are resistant to marbofloxacin.

Marbofloxacin susceptibility of bacteria, isolated between 2002 and 2008 from cattle with respiratory disease and mastitis in Europe, is good: *Pasteurella multocida* and *Mannheimia haemolytica* isolates (751 and 514 strains, respectively) were highly susceptible to marbofloxacin (MIC ≤ 0.03 µg/ml for 77.39% the strains). *Histophilus somni* isolates (73 strains) were highly susceptible to marbofloxacin (0.008 to 0.06 µg/ml). The majority of *Escherichia coli* isolates were highly susceptible to marbofloxacin (95.8% of 617 strains).

The marbofloxacin activity for the treatment of mastitis, metritis and agalactia syndrome in a controlled and randomized trial in France and the Netherlands involving 93 sows and published in 2000 is good: MIC₅₀ = 0.017 µg/ml and MIC₉₀ = 0.21 µg/ml for *Escherichia coli*; MIC₉₀ = 1.71 µg/ml for *Streptococci* and MIC₉₀ = 0.27 µg/ml for *Staphylococci*.

Resistance to fluoroquinolones occurs by chromosomal mutation with 3 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 2mg/kg, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.5µg/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 ($t_{1/2\beta}$ = 5-9h) but faster in ruminant cattle ($t_{1/2\beta}$ = 4-7h) predominantly in the active form in urine (3/4 in pre-ruminating calves, 1/2 in ruminants) and faeces (1/4 in pre-ruminating calves, 1/2 in ruminants).

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

After a single intramuscular administration in cattle at the recommended dose of 8 mg/kg, the maximum plasma concentration of marbofloxacin (C_{max}) is 7.3 µg/ml reached in = 0.78h (T_{max}). Binding to plasma proteins is about 30%. Marbofloxacin is eliminated slowly (T_{1/2β} = 15.60 h), predominantly in the active form in urine and faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate (E 386)
Monothioglycerol
Metacresol
Gluconolactone
Water for injection

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: 30 months
Shelf-life after first opening the immediate packaging: 28 days

6.4. Special precautions for storage

Store in the original package in order to protect from light.

6.5 Nature and composition of immediate packaging

Type I amber glass vials (20 ml, 50 ml and 100 ml) closed with a chlorobutyl rubber stopper with an aluminium capsule and a flip off seal.

Each vial is packaged in a cardboard box.

Not all pack sizes maybe 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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Ecuphar NV
Legeweg 157-i
8020 Oostkamp
Belgium

8. MARKETING AUTHORISATION NUMBER

Vm 32742/4008

9. DATE OF FIRST AUTHORISATION

14 August 2013

10. DATE OF REVISION OF THE TEXT

August 2013

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

Approved:  14/08/2013