Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Marbofloxacin ..... 100.0 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear yellow solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle and pigs (sows).

4.2 Indications for use, specifying the target species

Cattle:
Therapeutic treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida, Mannheimia haemolytica* and *Histophilus somni*.
Therapeutic treatment of acute mastitis caused by *E. coli* strains sensitive to marbofloxacin during the lactation period.

Sows:
Treatment of Metritis Mastitis Agalactia Syndrome caused by bacterial strains sensitive to marbofloxacin.

4.3 Contraindications

Do not use in case of known hypersensitivity to the active substance or other (fluoro)quinolones or to any of the excipients.
Do not use in case of confirmed or suspected resistance to fluoroquinolones (cross resistance).

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Use of the product should be based on susceptibility testing and has to take into account official and local antimicrobial policies.
It is prudent to reserve the fluoroquinolones for the treatment of clinical conditions that have responded poorly, or are expected to respond poorly, to other classes of antibiotics.
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.
As the vial cannot be broached more than 45 times, the user should choose the most appropriate vial size according to the target species to treat.
For the injections, the neck should be preferred in cattle and pigs.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
People with known hypersensitivity to (fluoro)quinolones should avoid any contact with the product.
If the product comes into contact with the skin or eyes, rinse with copious amounts of water.
Take care to avoid accidental self-injection since it can induce a slight irritation.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet to the physician.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Administration by the intramuscular route may cause in cattle transient local reactions such as pain at the injection site and slight muscular inflammatory lesions (resulting in fibrosis). The process of cicatrisation starts rapidly (varying from fibrosis to synthesis of extracellular matrice and collagen) and may persist for at least 15 days after injection.

Administration by the subcutaneous route may induce slight to moderate oedema at the injection site. A moderate pain on palpation of the injection site occurred in some animals.

In pigs, administration by the intramuscular route may induce very transient slight oedema and mild inflammatory lesions at the injection site persisting for 12 days after injection.

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals (rats, rabbits) did not show any evidence of a teratogenic, embryotoxic or maternotoxic effect associated with the use of marbofloxacin.
Safety of the product at 2 mg/kg has been shown in cows during gestation and in suckling pigs and calves when used in sows and cows.
Safety of the product at 8 mg/kg has not been determined in pregnant cows or in suckling calves when used in cows. Use therefore according to the benefit/risk assessment carried out by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Cattle:
Intramuscular use:
- *Respiratory infections:*
The recommended dosage is 8 mg/kg bodyweight i.e. 2 ml/25 kg bodyweight in a single injection.
If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.
Subcutaneous use:
- *Acute mastitis:*
The recommended dosage is 2 mg/kg i.e. 1 ml/50 kg bodyweight in a single daily injection, for 3 days.
The first injection may also be given by the intravenous route too.

Sows:
Intramuscular use:
The recommended dosage is 2 mg/kg i.e.1 ml/50kg bodyweight in a single daily injection by intramuscular route, for 3 days.

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

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

No sign of overdosage has been observed in cattle 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:
Intramuscular: Meat and offal: 3 days - Milk : 72 hours
Subcutaneous**:** Meat and offal: 6 days - Milk: 36 hours

Sows:
Intramuscular: Meat and offal: 4 days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: anti-infectives for systemic use, fluoroquinolones class
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 has a broad-spectrum activity in vitro against Gram-negative bacteria (*Pasteurella multocida*, *Mannheimia haemolytica*, *Histophilus somni*, *E. coli*) and against Gram-positive bacteria (in particular *Staphylococcus)*.
Resistance to *Streptococcus* may occur.

Strains with MIC ≤ 1 µg/ml are sensitive to marbofloxacin whereas strains with MIC > 2 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 properties

Cattle - Intramuscular route
After a single intramuscular administration at the recommended dose of 8 mg/kg, the maximum plasma concentration of marbofloxacin (Cmax) is 8 µg/ml reached in approximatively 1 hour (Tmax). Marbofloxacin is eliminated slowly (terminal $t_{½}$ = 9.5 h), predominantly in the active form in urine and faeces.

Cattle - Subcutaneous route
After subcutaneous administration at the recommended dose of 2 mg/kg, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.7 µg/ml in approximately 1 hour. The terminal elimination half-life ($t_{½}$) of marbofloxacin is 5.6 hours.

Pigs - Intramuscular route
After intramuscular administration at the recommended dose of 2 mg/kg, marbofloxacin is readily absorbed and reaches maximal plasma concentrations of 1.7 µg/ml in approximately 1 hour. The terminal elimination half-life ($t_{½}$) of marbofloxacin is 8.7 hours.

Its bioavailability is close to 100 %.
Marbofloxacin 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) it achieves higher concentrations than in plasma.
Marbofloxacin is eliminated predominantly in the active form in urine and faeces.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glucono-delta-lactone
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: 3 years.
Shelf-life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Primary packaging:
Amber PP/Ethylene vinyl alcohol/PP multi-layer plastic vials.
Type II chlorobutyl rubber stopper.
Aluminium and plastic flip capsule.

Pack size
Cardboard box containing one 50 ml vial
Cardboard box containing one 100 ml vial
Cardboard box containing one 250 ml vial
Cardboard box containing one 500 ml vial

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

Ceva Sante Animale
10, avenue de La Ballastiere
33500 Libourne
France

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10815/014/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th December 2010

Date of last renewal: 2nd October 2015

10 DATE OF REVISION OF THE TEXT