Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbonor 100 mg/ml Solution for Injection for cattle and pig

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Substance:
Marbofloxacin 100.0 mg

Excipients:
Monothioglycerol 1.0 mg
Metacresol 2.0 mg
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear yellow to amber solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle and Pigs (sows).

4.2 Indications for use, specifying the target species

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

Sows
Treatment of Metritis Mastitis Agalactia Syndrome (postpartum dysgalactia syndrome, PDS) caused by bacterial strains sensitive 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 cases of hypersensitivity to active substance or to any of the excipients.

4.4 Special warnings for each target species

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

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 upon susceptibility testing. Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.

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 veterinary medicinal product.
If the product comes into contact with skin or eyes, rinse with copious amounts of water.
Do not drink, eat or smoke whilst using the veterinary medicinal product.
Wash hands after use.
Accidental self-injection can induce a slight irritation.
In case of accidental self-injection or ingestion, seek medical advice immediately and show package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

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 than intramuscular route. Therefore, the subcutaneous route is recommended in heavy cattle.

4.7 Use during pregnancy, lactation or lay

May be used in pregnant and lactating cows and sows.

4.8 Interaction with other medicinal products and other forms of interactions

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.

The recommended dosage is 2 mg/kg (1 ml/50 kg) in a single daily injection by intramuscular, subcutaneous or intravenous routes in cattle and by intramuscular route in pigs. For the injections, the neck should be preferred in cattle and pigs

Treatment durations are 3 days in pigs and 3 to 5 days in cattle.

The vial may be broached up to 35 times. The user should choose the most appropriate vial size according to the target species to be treated.

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.

Signs such as neurological disorders may occur when the dose is exceeded.

Such signs should be treated symptomatically

4.11 Withdrawal period(s)

Cattle: Meat and offal: 6 days.
Milk: 36 hours

Pigs: Meat and offal: 4 days.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic Group: Antibacterials for systemic use, Flouroquinolones
ATC Vet Code: QJ01MA93

5.1 Pharmacodynamic properties

Marbofloxacin is a synthetic, broad spectrum antimicrobial, belonging to the fluoroquinolone group of antibiotics. Marbofloxacin is bactericidal with efficacy against a wide range of Gram-negative bacteria, Gram-positive bacteria and Mycoplasma species. The mechanism of action of marbofloxacin is based on the inhibition of type II topoisomerases, DNA gyrase and topoisomerase IV.
A 6 year pan European study by Kroemer, S et al 2012, reviewed marbofloxacin efficacy against indicated pathogens isolated from cases of bovine respiratory disease. In this study, 751 isolates of *P. multocida* were identified, over 99% of which were determined to be highly susceptible to marbofloxacin with MIC ranging from 0.004 to 1 µg/ml. MIC_{50} was identified as 0.015 µg/ml and MIC_{90} was 0.120 µg/ml. This study also assessed 514 isolates of *M. haemolytica* with >98% of isolates determined to be highly susceptible with a MIC range of 0.008 to 1 µg/ml, MIC_{50} value of 0.03 µg/ml and MIC_{90} value of 0.25 µg/ml. 171 isolates of *M. bovis* were identified with 74% demonstrating susceptibility with MIC ranging from 0.5 to 1 µg/ml, 25% exhibiting intermediate susceptibility with MIC of 2 µg/ml and 1% demonstrating resistance with MIC of 4 µg/ml. MIC_{50} was 1 µg/ml and MIC_{90} was 2 µg/ml; however these were deemed to be irrelevant due to the low number of isolates. This study also reviewed marbofloxacin efficacy *in E. coli* mastitis which analysed 617 isolates and demonstrated over 98% susceptibility with MIC of these susceptible organisms ranging from 0.008 to 1µg/ml. MIC_{50} and MIC_{90} were both determined to be 0.03 µg/ml. In a pan European study by El Garch *et al* 2017, 369 E. Coli isolates from porcine metritis identified 92.7% susceptibility to marbofloxacin with a MIC ranging from 0.008 to 1 µg/ml. 0.3% of isolates exhibited intermediate susceptibility with a MIC of 2 and 7% exhibited resistance with a MIC of >4. MIC_{50} was determined to be 0.03µg/ml and MIC_{90} was 0.5 µg/ml.

The pan European studies by Kroemer, S et al 2012 and El Garch, F., et al 2017, established clinical breakpoints for marbofloxacin use in *P. multocida* and *M. haemolytica* associated bovine respiratory disease and *E. Coli* in bovine mastitis and porcine metritis. Resistant strains were determined to have a MIC of ≥4 µg/ml, intermediate strains a MIC=2 µg/ml and susceptible strains, a MIC≤1 µg/ml. No clinical breakpoints have been established for *Mycoplasma* species.
Resistance to fluoroquinolones mainly occurs by chromosomal mutations with three mechanisms: decrease of the bacterial cell wall permeability, change in expression of efflux pump genes or mutation within genes coding for target enzymes. Plasmid mediated quinolone resistance is a separate mechanism by which resistance may develop. This may occur via three different mechanisms: through plasmid genes coding for proteins which protect DNA gyrase and topoisomerase IV from quinolone inhibition, through acetylation of certain quinolones by a variant of acetyltransferase AAC(6')-Ib or through plasmid genes coding for enhanced efflux pumps. Whilst the low-level resistance this confers should not exceed the clinical breakpoints for susceptibility, it may enable selection of higher level resistance.

5.2 Pharmacokinetic particulars

After subcutaneous or intramuscular administration in cattle and pigs, at the recommended dose of 2 mg/kg bodyweight, marbofloxacin is readily absorbed and reaches peak plasma concentrations of 1.5 µg/ml within 1 hour. The bioavailability of marbofloxacin is almost 100%.
Marbofloxacin is weakly bound to plasma proteins (less than 10% in pigs and 30 % in cattle), extensively distributed and achieves a higher concentration in most tissues, (liver, kidney, skin, lung, bladder, uterus and digestive tract) than in plasma
In cattle, marbofloxacin is eliminated slowly in pre-ruminant calves but faster in ruminant cattle ($t_{1/2}$ = 5-9 hours and 4 – 7 hours respectively). In pre-ruminant calves elimination of the active form is predominantly via urine, (¾ urine, ¼ faeces). In ruminant cattle the active form is eliminated equally in urine and faeces.
In pigs, the active form of marbofloxacin is eliminated slowly ($t_{1/2}$= 8 – 10 hours) predominantly urine (2/3) and faeces (1/3).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Monothioglycerol
Metacresol
Disodium Edetate
Gluconolactone
Water for injections

6.2 Major 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

Do not store above 25oC.
Protect from light.

6.5 Nature and composition of immediate packaging

The product is packaged in 20 ml, 50 ml, 100 ml 250 ml and 500 ml amber type II glass vials, 60 ml, 100 ml, 250 ml and 500 ml amber co-ex plastic (polypropylene) vials.
The vials are closed with chlorobutyl rubber stoppers sealed with aluminium caps.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA22664/100/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 February 2013
Date of last renewal: 17 November 2017

10 DATE OF REVISION OF THE TEXT

January 2019