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:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Monothioglycerol	1.0 mg
Metacresol	2.0 mg
Disodium Edetate	
Gluconolactone	
Water for injections	

A clear yellow to amber solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and pigs (sows).

3.2 Indications for use for each 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.

3.3 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 or to any of the excipients.

3.4 Special warnings

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

3.5 Special precautions for use

Special precautions for safe use in the target species:

Official and local antimicrobial policies should be taken into account when the veterinary medicinal 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 veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to 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 veterinary medicinal 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 slight irritation.
In case of accidental self-injection or ingestion, seek medical advice immediately and show package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle and pigs (sows):

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site lesion[1, 2], Injection site reactions[2] (e.g. injection site pain and injection site swelling).

[1] Inflammatory.
[2] Transient. May persist for at least 12 days after intramuscular injection.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See also the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

Can be used during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cattle: intramuscular, subcutaneous or intravenous use.
Pigs: intramuscular use.

To ensure a correct dosage, body weight should be determined as accurately as possible.

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

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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

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

Pigs: Meat and offal: 4 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01MA93

4.2 Pharmacodynamics

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 1µg/ml. MIC_{50} was identified as 0.015µg/ml and MIC_{90} was 0.120µg/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 1µg/ml, MIC_{50} value of 0.03µg/ml and MIC_{90} value of 0.25µg/ml. 171 isolates of *M. bovis* were identified with 74% demonstrating susceptibility with MIC ranging from 0.5 to 1µg/ml, 25% exhibiting intermediate susceptibility with MIC of 2µg/ml and 1% demonstrating resistance with MIC of 4 µg/ml. MIC_{50} was 1µg/ml and MIC_{90} was 2µg/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 0.03µg/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 0.5µg/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.

4.3 Pharmacokinetics

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 via urine (2/3) and faeces (1/3).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 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.

5.3 Special precautions for storage

Do not store above 25 ^{o}C.
Protect from light.

5.4 Nature and composition of immediate packaging

20 ml, 50 ml, 100 ml, 250 ml and 500 ml amber type II glass vials and 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.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

DD/MM/YYYY

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton Box: 20 ml, 50 ml, 60 ml, 100 ml, 250 ml and 500 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbonor 100 mg/ml Solution for Injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Active substance:

Marbofloxacin 100.0 mg

3. PACKAGE SIZE

20 ml
50 ml
60 ml
100ml
250 ml
500 ml

4. TARGET SPECIES

Cattle and pigs (sows).

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Cattle: Intramuscular, Subcutaneous or Intravenous Use.
Pigs: Intramuscular Use.

7. WITHDRAWAL PERIODS

Withdrawal period:

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

Pigs: Meat and offal: 4 days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 28 days.
Once broached use by…..

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ^{O}C.
Protect from light.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

100 ml, 250 ml and 500 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbonor 100 mg/ml Solution for Injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Active substance:

Marbofloxacin 100.0 mg

3. TARGET SPECIES

Cattle and pigs (sows)

4. ROUTES OF ADMINISTRATION

Cattle: Intramuscular, Subcutaneous or Intravenous use.
Pigs: Intramuscular use.

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:

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

Pigs: Meat and offal: 4 days.

6. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days.
Once broached use by…..

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ^{o}C.
Protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

20 ml, 50 ml, 60ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marbonor

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

100 mg/ml Marbofloxacin

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days.

Once broached use by…..

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

Each ml contains:

Active Substance:

Marbofloxacin 100.0 mg

Excipients:

Monothioglycerol 1.0 mg
Metacresol 2.0 mg

A clear yellow to amber solution.

3. Target species

Cattle and pigs (sows).

4. Indications for use

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

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

6. Special warnings

Special warnings:

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

Special precautions for safe use in the target species:

Official and local antimicrobial policies should be taken into account when the veterinary medicinal 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 veterinary medicinal product deviating from the instructions given in the package insert may increase the prevalence of bacteria resistant to 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.
Do not drink, eat or smoke whilst using the veterinary medicinal product.
If the veterinary medicinal product comes into contact with skin or eyes, rinse with copious amounts of water.
Wash hands after use.
Accidental self-injection can induce slight irritation.
In case of accidental self-injection or ingestion, seek medical advice immediately and show package leaflet or the label to the physician.

Pregnancy and lactation:

Can be used during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:

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

Overdose:

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.

7. Adverse events

Cattle and pigs (sows):

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site lesion[1, 2], Injection site reactions[2] (e.g. injection site pain and injection site swelling)[2].

[1] Inflammatory.
[2] Transient. May persist for at least 12 days after intramuscular injection.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder <or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

8. Dosage for each species, routes and method of administration

Cattle: intramuscular, subcutaneous or intravenous use.
Pigs: intramuscular use.

To ensure a correct dosage, body weight should be determined as accurately as possible.

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

The recommended dosage is 2 mg marbofloxacin/kg bodyweight (1 ml of the product/50 kg bodyweight) 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.

9. Advice on correct administration

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.

10. Withdrawal periods

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

Pigs: Meat and offal: 4 days.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25 ^{o}C.
Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

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

When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

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.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

MM/YYYY

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder:
Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

Norbrook Laboratories Ltd
Station Works
Newry
Co. Down
BT35 6JP

Manufacturer responsible for batch release:
Norbrook Manufacturing Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information