[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marfloquin 100 mg/ml solution for injection for cattle and pigs (sows) (AT, BE, FR, DE, EL, IT, PT)
Quiflox 100 mg/ml solution for injection for cattle and pigs (sows) (CZ, HU, LV, LT, SK)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Marbofloxacin 100 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Disodium edetate	0.10 mg
Monothioglycerol	1 mg
Metacresol	2 mg
Monothioglycerol	
Water for injections	

Clear, greenish yellow to brownish yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and pigs (sows).

3.2 Indications for use for each target species

In cattle:
- treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni*.
- treatment of acute forms of mastitis induced by marbofloxacin-sensitive *Escherichia coli* strains, during lactation.

In pigs:
- treatment of the Metritis Mastitis Agalactia syndrome caused by marbofloxacin-sensitive bacterial strains.

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 marbofloxacin or any other quinolone or to any of the excipients.

3.4 Special warnings

None.

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 on susceptibility testing.
Use of the veterinary medicinal 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 veterinary medicinal 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.
In case of accidental self injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Accidental self-injection can induce a slight irritation.
In case of contact with skin or eyes, rinse with plenty of water.
Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle and pigs:

Undetermined frequency (cannot be estimated from the available data):	Injection site oedema[1], injection site pain[1], injection site inflammation[1]

[1]Transient, may persist for at least 12 days after injection.

Fluoroquinolones are known to induce arthropathies. Nevertheless, this effect has never been observed with marbofloxacin in cattle.

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 the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

Studies in laboratory animals (rats, rabbits) have not produced any evidence of a teratogenic, embryotoxic or maternotoxic effect associated with the use of marbofloxacin.
The safety of marbofloxacin has been demonstrated at treatment of animal with daily dose 2 mg/kg in pregnant cattle. Its safety has also been demonstrated in piglets and suckling calves when used in sows and cows. Can be used during pregnancy and lactation.

Safety of the veterinary medicinal product at 8 mg/kg has not been determined in pregnant cows or in suckling calves when used in cows. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cattle: intramuscular (the neck area may be preferred), subcutaneous or intravenous injection
Pigs: intramuscular injection (the neck area may be preferred)

Cattle:
Respiratory infections:
- *Intramuscular use:*
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.
Acute mastitis:
- *Intramuscular or subcutaneous use:*
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.

Pigs (sows):
- *Intramuscular use:*
The recommended dosage is 2 mg/kg i.e. 1 ml/50kg bodyweight in a single daily injection, for 3 days.

The cap may be safely punctured up to 25 times. The user should choose the most appropriate vial size according to the target species to treat.

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

No sign of overdosage has been observed with the veterinary medicinal product after administration of 3 times the recommended dose.
Overdosage symptoms of marbofloxacin are acute neurological disorders that 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:
8 mg/kg single dose:
Meat and offal: 3 days
Milk: 72 hours

2 mg/kg single daily injection, for 3 days:
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01MA93

4.2 Pharmacodynamics

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 (*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 ≥ 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.

4.3 Pharmacokinetics

After subcutaneous or intramuscular administration in cattle and intramuscular administration in pigs at the recommended dose of 2 mg/kg, 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 bw, 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).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product.

5.2 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.

5.3 Special precautions for storage

Store in the original package in order to protect from light.
Do not freeze.

5.4 Nature and composition of immediate packaging

Bottle (amber glass type II), bromobutly rubber stopper, aluminium closure: 50 ml solution for injection, in a box.
Bottle (amber glass type II), bromobutly rubber stopper, aluminium closure: 100 ml solution for injection, in a box.
Bottle (amber glass. type II), bromobutly rubber stopper, aluminium closure: 250 ml solution for injection, in a box.

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

KRKA, d.d., Novo mesto

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

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

{Box}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marfloquin 100 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 100 mg of marbofloxacin.

3. PACKAGE SIZE

50 ml
100 ml
250 ml

4. TARGET SPECIES

Cattle and pigs (sows)

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Cattle: **i.m./s.c.**
Pigs: **i.m.**

7. WITHDRAWAL PERIODS

Withdrawal period:
Cattle:
8 mg/kg single dose:
Meat and offal: 3 days
Milk: 72 hours
2 mg/kg single daily injection, for 3 days:
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days

8. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

9. SPECIAL STORAGE PRECAUTIONS

Store in the original package in order to protect from light.
Do not freeze.

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

Marketing authorisation holder:
KRKA, d.d., Novo mesto

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{Label for 100 ml and 250 ml}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marfloquin 100 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 100 mg of marbofloxacin.

3. TARGET SPECIES

Cattle and pigs (sows)

4. ROUTES OF ADMINISTRATION

Cattle: **i.m./s.c.**
Pigs: **i.m.**

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:
Cattle:
8 mg/kg single dose:
Meat and offal: 3 days
Milk: 72 hours
2 mg/kg single daily injection, for 3 days:
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days

6. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

7. SPECIAL STORAGE PRECAUTIONS

Store in the original package in order to protect from light.
Do not freeze.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Marketing authorisation holder:
KRKA, d.d., Novo mesto

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{Label for 50 ml}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marfloquin

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

100 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Marfloquin 100 mg/ml solution for injection for cattle and pigs (sows) (AT, BE, FR, DE, EL, IT, PT)
Quiflox 100 mg/ml solution for injection for cattle and pigs (sows) (CZ, HU, LV, LT, SK)

2. Composition

Each ml contains:

Active substances:
Marbofloxacin 100 mg

Excipients:
Disodium edetate 0.10 mg
Monothioglycerol 1 mg
Metacresol 2 mg

Clear, greenish yellow to brownish yellow solution.

3. Target species

Cattle and pigs (sows).

4. Indications for use

In cattle:
- treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida, Mannheimia haemolytica,* and *Histophilus somni.*
- treatment of acute forms of mastitis induced by marbofloxacin-sensitive *Escherichia coli* strains, during lactation.

In pigs:
- treatment of the Metritis Mastitis Agalactia syndrome caused by marbofloxacin-sensitive bacterial strains.

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 marbofloxacin or any other quinolone or to any of the excipients.

6. Special warnings

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 on susceptibility testing.
Use of the veterinary medicinal 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 veterinary medicinal 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.
In case of accidental self injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Accidental self-injection can induce a slight irritation.
In case of contact with skin or eyes, rinse with plenty of water.
Wash hands after use.

Pregnancy and lactation:
Studies in laboratory animals (rats, rabbits) have not produced any evidence of a teratogenic, embryotoxic or maternotoxic effect associated with the use of marbofloxacin.
The safety of marbofloxacin has been demonstrated at treatment of animal with daily dose 2 mg/kg in pregnant cattle. Its safety has also been demonstrated in piglets and suckling calves when used in sows and cows. Can be used during pregnancy and lactation.
Safety of the veterinary medicinal product at 8 mg/kg has not been determined in pregnant cows or in suckling calves when used in cows. Use only according to the benefit-risk assessment by the responsible veterinarian.

Overdose:
No sign of overdosage has been observed with the veterinary medicinal product after administration of 3 times the recommended dose.
Overdosage symptoms of marbofloxacin are acute neurological disorders that should be treated symptomatically.

Major incompatibilities:
Do not mix with any other veterinary medicinal product.

7. Adverse events

Cattle and pigs:

Undetermined frequency (cannot be estimated from the available data):	Injection site oedema[1], injection site pain[1], injection site inflammation[1]

[1]Transient, may persist for at least 12 days after 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:

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

Cattle: intramuscular (the neck area may be preferred) (**i.m.**), subcutaneous (**s.c.**) or intravenous (**i.v.**) injection
Pigs: intramuscular injection (the neck area may be preferred) (**i.m.**)

Cattle:
Respiratory infections:
- *Intramuscular use:*
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.
Acute mastitis:
- *Intramuscular or subcutaneous use:*
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.

Pigs (sows):
- *Intramuscular use:*
The recommended dosage is 2 mg/kg i.e. 1 ml/50kg bodyweight in a single daily injection, for 3 days.

The cap may be safely punctured up to 25 times. The user should choose the most appropriate vial size according to the target species to treat.

9. Advice on correct administration

None.

10. Withdrawal periods

Cattle:
8 mg/kg single dose:
Meat and offal: 3 days
Milk: 72 hours
2 mg/kg single daily injection, for 3 days:
Meat and offal: 6 days
Milk: 36 hours

Pigs (sows):
Meat and offal: 4 days

11. Special storage precautions

Keep out of the sight and reach of children.

Store in the original package in order to protect from light.
Do not freeze.

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

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

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.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Package sizes:
Box with 1 bottle of 50 ml, 100 ml or 250 ml.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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 and contact details to report suspected adverse reactions:
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Manufacturer responsible for batch release:
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
Virbac, 1ere Avenue, 2065 M, LID, 06510 Carros Cedex, France *(for Marfloquin only)*

Local representatives and contact details to report suspected adverse reactions:
To be completed nationally.

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