

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Marfloxin 100 mg/ml solution for injection for cattle and pigs (BG, IE, PL, RO, SI)

## 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
Gluconolactone	
Water for injections	

Clear, greenish yellow to brownish yellow solution.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cattle and pigs.

### 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 *E.coli* mastitis.

In pigs:

- treatment of Metritis Mastitis Agalactia (MMA) syndrome caused by susceptible strains of organisms.

### 3.3 Contraindications

Do not use in cases of hypersensitivity to fluoroquinolones, or to any of the excipients.

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

### 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.

#### Special precautions to be taken by the person administering the veterinary medicinal product to animals:

People with known hypersensitivity to fluoroquinolones should avoid contact with the veterinary medicinal product.

In case of contact with skin or eyes, rinse with plenty of water.

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.

#### Special precautions for the protection of the environment:

Not applicable.

### 3.6 Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data):	Injection site oedema <sup>2</sup> , injection site pain <sup>1,2</sup> , injection site inflammation <sup>1,2</sup>
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<sup>1</sup>Administration by subcutaneous route, without clinical impact.

<sup>2</sup>Administration by intramuscular route, 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 rats and rabbits have not produced any evidence of a teratogenic, embryotoxic or maternotoxic effects.

Can be used in pregnant and lactating cows and sows when administered at 2 mg/kg.

Safety of the veterinary medicinal product at 8 mg/kg has not been established during pregnancy and lactation. 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: Subcutaneous, intramuscular or intravenous use.

Pigs: Intramuscular use.

Cattle:

- treatment of acute *E. coli* mastitis: 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular, subcutaneous or intravenous routes. Treatment duration is 3 to 5 days.

- treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni*:

either 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular, subcutaneous or intravenous routes. Treatment duration is 3 to 5 days.

or 8 mg/kg i.e. 2 ml/25 kg body weight in a single intramuscular injection on a single occasion.

If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

Pigs:

- treatment of Metritis Mastitis Agalactia (MMA) syndrome caused by sensitive strains of organisms: 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular route. Treatment duration is 3 days.

In cattle and pigs, the preferred injection site is the neck area.

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

The cap may be safely punctured up to 25 times. It is recommended that a draw-off needle be used to reduce the number of times the septum is punctured.

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

No sign of overdosage has been observed after administration of 3 times the recommended dose and no severe side-effects are to be expected at doses up to 3 to 5 times the recommended dose in cattle and pigs.

Overdosage may cause signs such as acute neurological disorders which 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

2 mg/kg for 3 to 5 days (**i.m./s.c./i.v.**)

Meat and offal: 4 days.

Milk: 24 hours.

8 mg/kg on a single occasion (**i.m.**)

Meat and offal: 3 days.

Milk: 72 hours.

Pigs

Meat and offal: 2 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 is effective against a wide range of Gram positive bacteria (in particular *Staphylococci*, *Streptococci*) and Gram negative bacteria (*Citrobacter* spp., *Enterobacter* spp., *Escherichia coli*, *Histophilus somni*., *Klebsiella* spp., *Mannheimia haemolytica*, *Pasteurella multocida*). It should be noted that some strains of *Streptococci* and *Pseudomonas* may not be sensitive to marbofloxacin.

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 *M. haemolytica* (MIC<sub>90</sub> = 0.124 µg/ml; MIC<sub>50</sub> = 0.025 µg/ml), between 0.004 and 0.12 µg/ml for *P. multocida* (MIC<sub>90</sub> = 0.022 µg/ml; MIC<sub>50</sub> = 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.

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 ( $t_{1/2\beta}$  = 5-9 hrs) but faster in ruminant cattle ( $t_{1/2\beta}$  = 4-7 hrs) 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 ( $t_{1/2\beta}$  = 8-10 hrs) 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 = 0.78 hrs ( $t_{max}$ ). Binding to plasma proteins is about 30%. Marbofloxacin is eliminated slowly ( $t_{1/2}$  = 15.60 h), predominantly in the active form in urine and faeces.

## **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: 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**

50 ml or 100 ml or 250 ml amber glass vial (Ph. Eur. type II) sealed with a bromobutyl rubber stopper and aluminium closure packaged in an outer carton.

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: {DD/MM/YYYY}

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

{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 \(https://medicines.health.europa.eu/veterinary\)](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

Marfloxin 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.



### 5. INDICATIONS

### 6. ROUTES OF ADMINISTRATION

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

### 7. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:

2 mg/kg for 3 to 5 days (**i.m./s.c./i.v.**)

Meat and offal: 4 days.

Milk: 24 hours.

8 mg/kg on a single occasion (**i.m.**)

Meat and offal: 3 days.

Milk: 72 hours.

Pigs:

Meat and offal: 2 days.



<b>8. EXPIRY DATE</b>
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Exp. {mm/yyyy}

Once broached use within 28 days.

<b>9. SPECIAL STORAGE PRECAUTIONS</b>
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Store in the original package in order to protect from light.  
Do not freeze.

<b>10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”</b>
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Read the package leaflet before use.

<b>11. THE WORDS “FOR ANIMAL TREATMENT ONLY”</b>
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For animal treatment only.

<b>12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”</b>
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Keep out of the sight and reach of children.

<b>13. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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KRKA, d.d., Novo mesto

<b>14. MARKETING AUTHORISATION NUMBERS</b>
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<b>15. BATCH NUMBER</b>
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Lot {number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

{Label for 100 ml and 250 ml}

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Marfloxin 100 mg/ml solution for injection

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains 100 mg of marbofloxacin.

**3. TARGET SPECIES**

Cattle and pigs.



**4. ROUTES OF ADMINISTRATION**

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

Pigs: **i.m.**

Read the package leaflet before use.

**5. WITHDRAWAL PERIODS**

Withdrawal periods:

Cattle:

2 mg/kg for 3 to 5 days (**i.m./s.c./ i.v.**)

Meat and offal: 4 days.

Milk: 24 hours.

8 mg/kg on a single occasion (**i.m.**)

Meat and offal: 3 days.

Milk: 72 hours.

Pigs:

Meat and offal: 2 days.

**6. EXPIRY DATE**

Exp. {mm/yyyy}

Once broached use within 28 days.

<b>7. SPECIAL STORAGE PRECAUTIONS</b>
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Store in the original package in order to protect from light.  
Do not freeze.

<b>8. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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KRKA, d.d., Novo mesto

<b>9. BATCH NUMBER</b>
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Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

{Label for 50 ml}

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Marfloxin



**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

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

### 2. Composition

Each ml contains:

#### Active substances:

Marbofloxacin	100 mg
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#### 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.



### 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 *E.coli* mastitis.

In pigs:

- treatment of Metritis Mastitis Agalactia (MMA) syndrome caused by susceptible strains of organisms.

### 5. Contraindications

Do not use in cases of hypersensitivity to fluoroquinolones, or to any of the excipients.

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

### 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

People with known hypersensitivity to fluoroquinolones should avoid contact with the veterinary medicinal product.

In case of contact with skin or eyes, rinse with plenty of water.

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.

Pregnancy and lactation:

Studies in laboratory rats and rabbits have not produced any evidence of a teratogenic, embryotoxic or maternotoxic effects.

Can be used in pregnant and lactating cows and sows when administered at 2 mg/kg.

Safety of the veterinary medicinal product at 8 mg/kg has not been established during pregnancy and lactation. Use only according to the benefit/risk assessment by the responsible veterinarian.

Overdose:

No sign of overdosage has been observed after administration of 3 times the recommended dose and no severe side-effects are to be expected at doses up to 3 to 5 times the recommended dose in cattle and pigs.

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

Major incompatibilities:

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

## **7. Adverse events**

Cattle:

Undetermined frequency (cannot be estimated from the available data):	Injection site oedema <sup>2</sup> , injection site pain <sup>1,2</sup> , injection site inflammation <sup>1,2</sup>
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<sup>1</sup>Administration by subcutaneous route, without clinical impact.

<sup>2</sup>Administration by intramuscular route, 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 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 its local representative 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: Subcutaneous, intramuscular and intravenous use.

Pigs: Intramuscular use.

Cattle:

- treatment of acute *E. coli* mastitis: 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular (**i.m.**), subcutaneous (**s.c.**) or intravenous (**i.v.**) routes. Treatment duration is 3 to 5 days.

- treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni*:

either 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular, subcutaneous or intravenous routes. Treatment duration is 3 to 5 days.

or 8 mg/kg i.e. 2 ml/25 kg body weight in a single intramuscular injection on a single occasion.

If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

Pigs:

- treatment of Metritis Mastitis Agalactia (MMA) syndrome caused by sensitive strains of organisms: 2 mg/kg i.e. 1 ml/50 kg in a single daily injection by intramuscular route (**i.m.**). Treatment duration is 3 days.

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

The cap may be safely punctured up to 25 times. It is recommended that a draw-off needle be used to reduce the number of times the septum is punctured.

## **9. Advice on correct administration**

In cattle and pigs, the preferred injection site is the neck area.

## **10. Withdrawal periods**

Cattle

2 mg/kg for 3 to 5 days (**i.m./s.c./i.v.**)

Meat and offal: 4 days.

Milk: 24 hours.

8 mg/kg on a single occasion (**i.m.**)

Meat and offal: 3 days.

Milk: 72 hours.

Pigs

Meat and offal: 2 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.

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**

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**

{MM/YYYY}

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

## **16. Contact details**

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse events:

KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Local representatives and contact details to report suspected adverse events:

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