

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Forcyl 160 mg/ml solution for injection for cattle veterinary

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:

Active ingredient(s):

Marbofloxacin 160 mg

Excipients:

Benzyl alcohol 15 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear yellow greenish to yellow brownish solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle.

4.2 Indications for use, specifying the target species

In cattle:

- Therapeutic treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida* and *Mannheimia haemolytica*.

In lactating cows:

- Treatment of acute mastitis caused by sensitive strains of *Escherichia coli*.

4.3 Contraindications

Do not use in animals with known 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).

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings

The efficacy of the product has not been tested on mastitis caused 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 this 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. Wherever possible, use of the product should only be based on susceptibility testing.

Use of the product deviating from the instructions given in this 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 (fluoro)quinolones should avoid using this product.
- In case of contact with skin or eyes, rinse with plenty of water. Care should be taken to avoid accidental self-injection.
- Accidental self-injection can induce a slight irritation.
- In case of accidental self-injection, seek medical advice immediately and show the label or the package leaflet to the physician.
- Wash hands after use.

Other precautions

None

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, administration by the intramuscular route may cause transient local reactions such as pain and swelling at the injection site which may persist up to 7 days after injection.

Fluoroquinolones are known to induce arthropathies. In cattle, such lesions were observed after a three days treatment with the 16% marbofloxacin solution. These lesions did not induce clinical signs and should be reversible, particularly if they were to be observed after a single administration.

In very rare cases, anaphylactic-type reactions with a potentially fatal outcome might occur.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal

product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

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 10 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.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

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

Where there is slight cloudiness or visible particles present, such cloudiness or particles disappear when the bottle is shaken before use.

- Therapeutic treatment of respiratory infections

10 mg/kg body weight i.e. 10 ml /160 kg body weight in a single intramuscular injection.

- Treatment of acute mastitis caused by sensitive strains of *Escherichia coli*

10 mg/kg body weight i.e. 10 ml/160 kg body weight in a single intramuscular or intravenous injection.

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

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

Lesions of the joint cartilage were observed in some animals treated at 10 mg/kg or 30 mg/kg for three times the recommended treatment duration, but did not induce clinical signs. Moreover, no other signs of overdosage was observed throughout this study.

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

4.11 Withdrawal period(s)

Meat and offal: 5 days

Milk: 48 hours

5. PHARMACOLOGICAL PROPERTIES

ATC Vet code: QJ01MA93

Pharmacotherapeutic group: antibacterials for systemic use, Fluoroquinolones

5.1 Pharmacodynamic properties

Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the fluoroquinolone group, which acts by inhibition of DNA gyrase. The *in vitro* activity of marbofloxacin has been demonstrated towards *Pasteurella multocida*, *Mannheimia haemolytica* and *Escherichia coli*.

The marbofloxacin *in vitro* activity against pathogens isolated in 2007 from bovine respiratory diseases is good: MIC values are comprised between 0.008 and 0.5 µg/ml for *M. haemolytica* (MIC₉₀ = 0.139 µg/ml; MIC₅₀ = 0.021 µg/ml), between 0.004 and 0.5 µg/ml for *P. multocida* (MIC₉₀ = 0.028 µg/ml; MIC₅₀ = 0.012 µg/ml).

In 2008, the marbofloxacin MIC₅₀ for *E. coli* isolated from bovine mastitis was 0.021 µg/ml and the MIC₉₀ was 0.038 µg/ml.

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.

5.2 Pharmacokinetic particulars

After a single intramuscular administration in cattle at the recommended dose of 10 mg/kg body weight, the maximum plasma concentration of marbofloxacin (C_{max}) is 7.915 µg/ml reached in 1.28 h (T_{max}) for an exposure (AUC_{INF}) of 52.7 µg.h/mL. Bioavailability after intramuscular injection is complete (more than 90%). Marbofloxacin is extensively distributed. Binding to plasma proteins is about 30%.

After intravenous or intramuscular administration, marbofloxacin concentrations in milk increase rapidly and the AUC_{INF}, T_{max} and C_{max} values obtained in plasma and milk after both administration routes are similar.

Marbofloxacin is eliminated slowly (T_{1/2λz} = 17.50 h) predominantly as the active form in urine and faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glucono-delta-lactone

Benzyl alcohol

Water for injection

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

The expiry date of the product is indicated on the packaging materials.

6.4. Special precautions for storage

Store at room temperature - below 25°C.

After first opening the product should be used within 28 days.
Keep out of the reach and sight of children.

6.5 Nature and composition of immediate packaging

Details of the primary packaging:

Brown type II glass vials
Chlorobutyl rubber closure

Pack sizes:

Cardboard box containing one 50 ml vial
Cardboard box containing one 100 ml vial
Cardboard box containing one 250 ml vial

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product 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. MANUFACTURER

Vetoquinol, Magny Vernois 70200 Lure, France.

8. REGISTRATION HOLDER

Linevitz Eliezer
25 Haela St., Even-Yehuda 40500

9. REGISTRATION NUMBER

151-94-33855

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription.

Administration by a veterinary surgeon or under their direct responsibility.

This leaflet format has been determined by the Ministry of Health and the content has been checked and approved in March 2019