SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Forcyl 160 mg/ml solution for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:
Active ingredient(s):
Marbofloxacin..... 160 mg

Excipients:
Benzyl alcohol (E 1519)..... 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).

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 ~~rare~~ 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).

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* (MIC_{90} = 0.139

µg/ml; MIC_{50} = 0.021 µg/ml), between 0.004 and 0.5 µg/ml for *P. multocida* (MIC_{90} = 0.028 µg/ml; MIC_{50} = 0.012 µg/ml).
In 2008, the marbofloxacin MIC_{50} for *E. coli* isolated from bovine mastitis was 0.021 µg/ml and the MIC_{90} 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 (Cmax) is 7.915 µg/ml reached in 1.28 h (Tmax) 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} , Tmax and Cmax values obtained in plasma and milk after both administration routes are similar.
Marbofloxacin is eliminated slowly ($T1/2\lambda z$ = 17.50 h) predominantly as the active form in urine and faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Glucono-delta-lactone
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

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 28 days

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Details of the primary packaging:
Amber type II glass vials
Chlorobutyl rubber stopper
Aluminium cap or flip cap

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. MARKETING AUTHORISATION HOLDER

Vetoquinol UK Limited
Steadings Barn
Pury Hill Business Park
Nr Alderton
Towcester
Northamptonshire
NN12 7LS

8. MARKETING AUTHORISATION NUMBER

Vm 08007/4130

9. DATE OF FIRST AUTHORISATION

25 July 2011

10. DATE OF REVISION OF THE TEXT

September 2018

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription.
Administration by a veterinary surgeon or under their direct responsibility.

Approved: 11 September 2018

D Austin