Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

MASTERFLOX 40 mg/ml solution for injection for pigs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

Active substance:
Marbofloxacin 40 mg

Excipients:
Disodium edetate 0.1 mg

For a full list of the excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.
Clear yellow solution, with no visible particles.

4 CLINICAL PARTICULARS

4.1 Target Species

Pigs (pigs for fattening).

4.2 Indications for use, specifying the target species

Treatment of respiratory infections caused by strains of *Actinobacillus pleuropneumoniae, Pasteurella multocida, Mycoplasma hyopneumoniae* susceptible to marbofloxacin.

4.3 Contraindications

Do not use in cases where the pathogen involved is resistant to marbofloxacin and other (fluoro)quinolones (cross-resistance).
Do not use in cases of hypersensivity to the active substance, to any other quinolone or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

This product does not contain an antimicrobial preservative.

Special precautions for use in animals
Official and local antimicrobial policies should be taken into account when the 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 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

(Fluoro)quinolones may cause hypersensitivity (allergy) in sensitised people. People with known hypersensitivity to (fluoro)quinolones or any of the excipients should avoid contact with the veterinary medicinal product.

Avoid contact of the skin and eyes with the product. In case of accidental spillage onto skin or eyes, rinse the affected area with large amounts of water.

Avoid accidental self-injection, since this can cause local irritation. In case of self-injection or ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Transient local reactions such as oedema, pain and swelling at the injection site and inflammatory lesions, which may persist for 6 days, may be uncommonly caused by intramuscular administration.

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

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.

Use only according to the benefit-risk assessment by the responsible veterinarian.

The product is intended only for pigs for fattening.

4.8 Interaction with other medicinal products and other forms of interactions

None known.

4.9 Amounts to be administered and administration route

For intramuscular use.

The recommended dosage is 2 mg marbofloxacin/kg body weight (equivalent to 0.5 ml of veterinary medicinal product/ 10 kg body weight) in a single daily intramuscular injection, for 3-5 consecutive days.

To ensure administration of a correct dose, body weight should be determined as accurately as possible, to avoid underdosing.

The preferred injection site is the neck area.

The vial may be broached up to 20 times.

The user should choose the most appropriate vial size according to the bodyweight and number of animals to be treated**.**

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

No signs of overdosage have been observed administering marbofloxacin at up to 3 times the recommended dose.

Overdose may cause acute signs in the form of neurological disorders which should be treated symptomatically. Do not exceed the recommended dose.

4.11 Withdrawal period(s)

Pigs

Meat and offal: 6 days.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, Fluoroquinolones.
ATC-vet code: QJ01MA93.

5.1 Pharmacodynamic properties

Marbofloxacin is a synthetic bactericidal antimicrobial belonging to the fluoroquinolone group, which acts by inhibition of DNA gyrase and topoisomerase IV. It has a broad-spectrum activity in vitro against Gram-positive bacteria, Gram-negative bacteria (*Pasteurella multocida* and *Actinobacillus pleuropneumoniae*) and against genus *Mycoplasma (Mycoplasma hyopneumoniae)*. It should be noted that some strains of Streptococci, Pseudomonas and Mycoplasma may not be sensitive to marbofloxacin. Marbofloxacin is not active against anaerobes, yeast or fungi.

Between 2015 and 2016, MICs of marbofloxacin were determined against 171 strains of *Pasteurella multocida* and 164 strains of *Actinobacillus pleuropneumoniae* isolated from pig respiratory diseases (*Morrissey*, 2019) while during the years 2010-2012 *in vitro* activity of marbofloxacin was assessed on 50 strains of *Mycoplasma hyopneumoniae* isolated from pig respiratory diseases (*Klein et al*., 2017). The results of MIC_{50}, MIC_{90} and MIC range are reported in the table below:

Target respiratory bacteria	**Number of EU strains tested**	**MIC_{50}** (µg/ml)	**MIC_{90}** (µg/ml)	**MIC range** (µg/ml)
Pasteurella multocida	171	0.015	0.03	0.004-1
Actinobacillus pleuropneumoniae	164	0.03	0.12	0.008-2
Mycoplasma hyopneumoniae	50	0.03	0.5	0.002-1

Strains with MIC ≤ 1 µg/ml are susceptible to marbofloxacin whereas strains with MIC ≥ 4 µg/ml are resistant to marbofloxacin according to the clinical breakpoints for Pasteurellaceae defined by the "Comité de l'Antibiogramme de la Société Française de Microbiologie" (= French Society of Microbiology") (CA-SFM, 2018).

Resistance to fluoroquinolones occurs by chromosomal mutations with following mechanisms: decrease of the bacterial cell wall permeability, expression change of genes coding for efflux pumps or mutations in genes encoding enzymes responsible for molecule binding. Plasmid-mediated resistance to fluoroquinolones confer only decreased susceptibility of bacteria, however, it can facilitate development of mutations in genes of target enzymes and can be transferred horizontally. Depending on the underlying resistance mechanism cross-resistance to other (fluoro)quinolones and co-resistance to other antimicrobial classes can occur.

5.2 Pharmacokinetic particulars

After intramuscular administration in swine at the recommended dose of 2 mg/kg body weight, marbofloxacin is rapidly absorbed and reaches its maximum plasma concentration of 1.5 µg/ml in less than one hour.

Marbofloxacin is readily absorbed and its bioavailability is close to 100%. It is weakly bound to plasma proteins (less than 10%), extensively distributed and in most tissues (liver, kidney, lungs, bladder, uterus, digestive tract) it achieves higher concentrations than in plasma.

Marbofloxacin is eliminated slowly ($t_{1/2}$ = 8-10 hours) predominantly in the active form in urine (2/3) and faeces (1/3).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Gluconolactone
Mannitol
Water for injections

6.2 Major 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: 2 years.
Shelf-life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Store in the original package. Protect from light.

6.5 Nature and composition of immediate packaging

50 ml, 100 ml, 250 ml amber type II glass vials, closed with chlorobutyl rubber stopper type I and aluminium collar, in a cardboard box.

Pack-sizes:
Box with 1 vial of 50 ml
Box with 1 vial of 100 ml
Box with 1 vial of 250 ml
Box with 6 vials of 100 ml

Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

FATRO S.p.A.
Via Emilia, 285 - 40064
Ozzano Emilia
Bologna
Italy

8 MARKETING AUTHORISATION NUMBER(S)

VPA10836/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23rd May 2014
Date of latest renewal: 18th April 2019

10 DATE OF REVISION OF THE TEXT

April 2019