IRISH MEDICINES BOARD ACT 1995

EUROPEAN COMMUNITIES (ANIMAL REMEDIES) (No. 2) REGULATIONS 2007

(S.I. No. 786 of 2007)

VPA: **10983/037/001**
Case No: 7006206

The Irish Medicines Board in exercise of the powers conferred on it by Animal Remedies (No. 2) Regulations (S.I. No. 786 of 2007) hereby grants to:

Vetoquinol Ireland Limited

10 Lad Lane, **Lower Baggot Street**, **Dublin 2**, **Ireland**

an authorisation, subject to the provisions of the said Regulations and the general conditions of the attached authorisation, in respect of the Veterinary Medicinal Product:

MARBOCYL 1% SA, powder and solvent for solution for injection

The particulars of which are set out in Part 1 and Part 2 of the said Schedule. The authorisation is also subject to any special conditions as may be specified in the said Schedule.

The authorisation,unless revoked, shall continue in force from **05/06/2009** until **29/09/2013**.

Signed on behalf of the Irish Medicines Board

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A person authorised in that behalf by the said Board.

(NOTE: This authorisation replaces any previous authorisation in respect of this product which is now null and void.)

Part II

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

MARBOCYL 1% SA, powder and solvent for solution for injection, for cats and dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Before reconstitution:	
Powder	
Marbofloxacin	198.41 mg
Disodium edetate	19.84 mg
Benzalkonium chloride	1.98 mg
Excipient to	1 g
Solvent	
Water for injections	
Reconstituted solution	
Marbofloxacin	10.00 mg
Disodium edetate	1.00 mg
Benzalkonium chloride	0.10 mg
Excipient to	1 ml

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection
Pale yellow to pale beige powder and clear, colourless solvent

4 CLINICAL PARTICULARS

4.1 Target Species

Cats and dogs.

4.2 Indications for use, specifying the target species

Treatment of Infections due to marbofloxacin susceptible bacteria.

In dogs:

- treatment of infected wounds and abscesses
- treatment of lower urinary tract infections due to *Escherichia coli* and *Proteus mirabilis*
- prevention of surgical infections due to *Staphylococcus intermedius, Escherichia coli* and *Pseudomonas aeruginosa*.

In cats:

- treatment of infected wounds and abscesses
- prevention of surgical infections due to *Staphylococcus intermedius, Escherichia coli* and *Pseudomonas aeruginosa*.

4.3 Contraindications

In growing pups of large or very large sized breeds, articular impairments (erosion of the articular cartilage) may appear during prolonged treatments with fluoroquinolones. In medium-sized growing dogs marbofloxacine is well tolerated up to doses of
4 mg/kg/day administrated during 13 weeks. However, it is not advised to administer the veterinary medicinal product to pups of large or very large breeds up to the age of 12 and 18 months respectively.

Do not use in bacterial infections with cross-resistance to other fluoroquinolones.

Do not administer to an animal previously found to be hypersensitive to marbofloxacine or other (fluoro)quinolone, or to any of the excipients of the product.

4.4 Special warnings for each target species

See section 4.5i.

4.5 Special precautions for use

i) Special precautions for use in animals

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. Official and local antimicrobial policies should be taken into account when the product is used.
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.

Some fluroquinolones at high doses may have an epileptogenic potential and a depressor effect on cardiovascular function. Before pre-surgical administration to animals with a history of seizures or cardiovascular disorders, pre-surgical examination and anaesthetic protocol should be carefully considered.

Experimentally, marbofloxacin has not led to such epileptic reactions in dogs, including in case of over-dosages.

When given IV, the product should be injected slowly.

ii) Special precautions to be taken by the person administering the medicinal product to animals

In case of contact with skin, rinse with clear water.
In case of eye contact or accidental ingestion, rinse the eye or mouth with clear water and seek medical advice.

4.6 Adverse reactions (frequency and seriousness)

On very rare occasions, neurological signs (seizures, ataxia, mydriasis, muscle tremor), digestive signs (hypersalivation, emesis) and reactions at the injection site have been recorded after treatment. In case of severe reactions, symptomatic treatment must be initiated.

4.7 Use during pregnancy, lactation or lay

Studies on laboratory animals (rats, rabbits) did not reveal any teratogenic, embryotoxic or maternotoxic effect of marbofloxacin at the therapeutic dose. Safety has not been demonstrated in cats and dogs during pregnancy and lactation. Use during gestation or lactation only according to the benefit/risk assessment of the veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Specific studies conducted in dogs did not show interaction between marbofloxacin and anaesthetic agents such as isoflurane and medetomidine/ketamine combination.
In the absence of studies with other anaesthetic agents, interactions cannot be excluded.

4.9 Amounts to be administered and administration route

Prepare the solution by introducing the total content of the solvent vial into the lyophilisate vial.

Dogs:

Treatment of infected wounds and abscesses: 2 mg marbofloxacin / kg / day by a single sub-cutaneous injection, followed by oral administration for 6 days in the form of tablets.

Treatment of infections of lower urinary tract : 4 mg of marbofloxacin / kg / day by three sub-cutaneous injections at intervals of 4 days.

Prevention of surgical infections: 2 mg of marbofloxacin / kg by a single intravenous injection, just before the intervention.

Cats:

Treatment of infected wounds and abscesses: 2 mg marbofloxacin / kg / day by a single subcutaneous injection for 3 to 5 days.

Prevention of surgical infections: 2 mg of marbofloxacin / kg by a single intravenous injection, just before the intervention.

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

Symptoms observed in case of over-dosage are neurological: hypersalivation, lacrimation, trembling, myoclonia and convulsions. In case of severe reactions, symptomatic treatment must be initiated.
Bradycardia could also be observed.

4.11 Withdrawal Period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

ATC Vet code: QJ 01 MA 93
Pharmacotherapeutic Group: anti-infective for systemic use (fluroquinolone).

5.1 Pharmacodynamic properties

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 (especially *Staphylococcus* and *Streptococcus*), and Gram negative bacteria (especially *Escherichia coli, Citrobacter freundii, Enterobacter cloacae, Serratia marcescens, Morganella morganii, Proteus sp, Klebsiella sp, Pasteurella sp, Moraxella sp, Pseudomonas sp).*
In 2001, 100% of *Pasteurella multocida* and *Staphylococcus intermedius* were susceptible to marbofloxacin (with MIC_{90} = 0.052 µg/ml and 0.219 µg/ml respectively), as well as 83 % *Pseudomonas aeruginosa* (MIC_{90} = 1.357 µg/ml) and 90 % *E. coli* (MIC_{90} = 0.170 µg/ml).

The breakpoints are : MIC sensitive strain ≤1 µg/ml ; MIC resistant strain ≥ 4µg/ml.

Intrinsic resistance to quinolones is observed in some micro-organisms (yeast, fungi, strict anaerobes, some *Pseudomonas*). Acquired resistance is due to chromosome mutation. Since 1997, sensitivity of key pathogens to marbofloxacin remains very high.

5.2 Pharmacokinetic properties

After a sub-cutaneous administration to dogs and cats at the recommended dose of 2 or 4 mg/kg, marbofloxacin is rapidly absorbed and its bioavailability is close to 100 %. Maximum plasma concentrations reached in the 2 species are about 1.5 µg/ml after sub-cutaneous administration of 2 mg/kg in dogs and cats and 3 µg/ml at the dose of 4 mg/kg.
Marbofloxacin is weakly bound to plasma proteins (less than 10% in dogs and cats) and is widely distributed in the whole organism. In most tissues (skin, muscles, liver, kidney, lung, bladder, digestive tract), the tissue concentrations are higher than in plasma.
Marbofloxacin is eliminated slowly (elimination half life of about 13 hours in cats and dogs) and mainly in its active form in urine (2/3) and faeces (1/3).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol (E421)
Sodium hydroxide (E524)
Disodium edetate
Benzalkonium chloride
Water for injection

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after reconstitution according to directions: 28 days.

6.4 Special precautions for storage

Before reconstitution: this veterinary medicinal product does not requie any special storage conditions.
After reconstitution: do not store above 25°C, keep in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Primary packaging

- Lyophilisate: colourled glass vial of type II
- Solvent: colourless glass vial of type II
- Chlorobutyl stopper
- Aluminium cap or flip cap

Sales-presentation(s) and administrative identification number(s)

- Box containing one 504 mg lyophilisate vial and 10 ml vial of solvent
- Box containing one 1008 mg lyophilisate vial and 20 ml vial of solvent

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

7 MARKETING AUTHORISATION HOLDER

Vetoquinol Ireland Limited
10 Lad Lane
Lower Baggot Street
Dublin 2
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10983/037/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30th September 2008

10 DATE OF REVISION OF THE TEXT

5th June 2009