[Version 8.1,01/2017]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Greece, Bulgaria, Czech Republic, Poland	MARBOVET 100 mg/ml solution for injection for cattle and pigs.
Spain, Portugal, Romania	MARVETIN 100mg/ml solution for injection for cattle and pigs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Marbofloxacin 100.0 mg

Excipients:
Metacresol 2.0 mg
Thioglycerol 1.0 mg
Disodium edetate 0.1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Yellow greenish to yellow brownish, clear solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pig (sow)

4.2 Indications for use, specifying the target species

Cattle:
Treatment of respiratory infections caused by strains of *Pasteurella multocida*, *Mannheimia haemolytica*, *Mycoplasma bovis* and *Histophilus somni* susceptible to marbofloxacin.

Treatment of acute mastitis caused by strains of *Escherichia coli* susceptible to marbofloxacin during the lactation period.

Pigs (sows):
Treatment of Postpartum Dysgalactia Syndrome - (PDS) – (Metritis Mastitis Agalactia Syndrome) caused by bacterial strains susceptible to marbofloxacin.

4.3 Contraindications

Do not use in cases of hypersensitivity to marbofloxacin, to any other quinolone or to any of the excipients. Do not use in cases of resistance to other fluoroquinolones (cross resistance).

4.4 Special warnings for each target species

The efficacy data showed that the product has insufficient efficacy for the treatment of acute forms of mastitis induced 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 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

People with known hypersensitivity to quinolones should avoid contact with the veterinary medicinal product.
Care should be taken to avoid accidental self-injection as it can induce a slight irritation. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

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

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Transitory inflammatory lesions can occur at the injection site, without clinical impact, when administered via the intramuscular or subcutaneous route.

Administration by the intramuscular route may cause transient local reactions such as pain and swelling at the injection site and inflammatory lesions, which may persist for at least 12 days after injection.

However, in cattle, subcutaneous route was shown to be better tolerated locally than intramuscular route. Therefore, the subcutaneous route is recommended in heavy cattle.

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.

Safety of the veterinary medicinal product at 2 mg/kg body weight has been established in pregnant cows or in sucking calves and piglets when used in cows and sows. Can be used during pregnancy and lactation.

Safety of the veterinary medicinal product at 8 mg/kg body weight has not been established in pregnant cows or in sucking calves when used in cows. Therefore, this dose regimen should be used only accordingly 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

Cattle: intravenous, intramuscular or subcutaneous use
Pigs (sows): intramuscular use

Cattle:
Respiratory infections:
The recommended dosage is 8 mg marbofloxacin/kg body weight (2 ml veterinary medicinal product/25 kg body weight) in a single injection by the intramuscular route. If the volume to be injected is more than 20 ml, it should be divided between two or more injection sites.

In cases of respiratory infections caused by *Mycoplasma bovis*, the recommended dose is 2 mg marbofloxacin/kg body weight (1 ml veterinary medicinal product/50 kg body weight), in a single daily injection for 3 to 5 consecutive days, by the intramuscular or subcutaneous route. The first injection may be given by the intravenous route.

Acute mastitis:
The recommended dosage is 2 mg marbofloxacin/kg body weight (1 ml veterinary medicinal product/50 kg body weight) in a single daily injection for 3 consecutive days by the intramuscular or subcutaneous route. The first injection may also be given by the intravenous route.

Pig (sow):
The recommended dosage is 2 mg marbofloxacin/kg body weight (1 ml veterinary medicinal product/50 kg body weight) in a single daily injection for 3 consecutive days by the intramuscular route.

Cattle and Pig (sow):
To ensure administration of a correct dose, body weight should be determined as accurately as possible, to avoid underdosing.
In cattle and pig, the preferred injection site is the neck area.

The cap may be safely punctured up to 125 times in case of 100 ml bottle and up to 250 times in case of 250 ml bottle. The user should choose the most appropriate vial size according to the target species to treat.

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

No sign of overdosage has been observed after administration of 3 times the recommended dose. Overdosage may cause signs such as acute neurological disorders which should be treated symptomatically.

4.11 Withdrawal period(s)

Cattle:

Indication	**Respiratory**		**Mastitis**
Dosage	2 mg/kg for 3 to 5 days (IV/IM/SC)	8 mg/kg on a single occasion (IM)	2mg/kg for 3 days (IV/IM/SC)
Meat and offal	6 days	3 days	6 days
Milk	36 hours	72 hours	36 hours

Pigs:
Meat and offal: 4 days

5. PHARMACOLOGICAL 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-negative (*E. coli*, *Histophilus somni*, *Mannheimia haemolytica* and *Pasteurella multocida*) and Mycoplasma (*Mycoplasma bovis*). It should be noted that some strains of *Streptococci*, *Pseudomonas* and *Mycoplasma* may not be sensitive to marbofloxacin.
Strains with MIC $\leq$ 1 µg/ml are sensitive to marbofloxacin whereas strains with MIC $\geq$ 4 µg/ml are resistant to marbofloxacin according to the clinical breakpoints mentioned for *Pasteurella multocida*, *Mannheimia haemolytica* and *Histophilus somni* associated with bovine respiratory disease and *Escherichia coli* in bovine mastitis (Kroemer et al 2012) and for *Escherichia coli* in porcine metritis (El Garch et al 2017).
Resistance to fluoroquinolones occurs by chromosomal mutations with following mechanisms: diminution of permeability of bacterial cell wall, expression change of genes coding for efflux pumps or mutations in genes encoding enzymes responsible of molecular union. 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 subcutaneous or intramuscular administration in cattle and intramuscular administration in pigs at the recommended dose of 2 mg/kg body weight, 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 ($t_{½}\beta$ = 5-9 hours) but faster in ruminant cattle ($t_{½}\beta$ = 4-7 hours) predominantly in the active form in urine (3/4 in pre-ruminating calves, ½ in ruminants) and faeces (¼ in pre-ruminating calves, ½ in ruminants).

After a single intramuscular administration in cattle at the recommended dose of 8 mg/kg body weight, the maximum plasma concentration of marbofloxacin (C_{max}) is 7.3 µg/ml reached in 0.78 hours (T_{max}). Marbofloxacin is eliminated slowly ($t_{½}$ terminal = 15.60 hours).

After intramuscular administration in lactating cows, a maximum concentration in the milk of marbofloxacin of 1.02 µg/ml is reached (C_{max} after the first administration) after 2.5 hours (T_{max} after the first administration).

In pigs, marbofloxacin is eliminated slowly ($t_{½}\beta$ = 8-10 hours) predominantly in the active form in urine (⅔) and faeces (⅓).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Metacresol
Thioglycerol
Disodium edetate
Gluconolactone
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: 30 months
Shelf life after first opening the immediate packaging: 28 days

6.4 Special precautions for storage

Keep the container in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Amber Polypropylene/Ethylene vinyl alcohol/ Polypropylene multi-layer plastic vials closed with bromobutyl rubber stopper type I and aluminium and plastic flip capsule.

Package sizes:
Cardboard box with 1x100 ml vial
Cardboard box with 1x250 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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Vet-Agro Multi-Trade Company sp. z o.o.
Gliniana 32, 20-616 Lublin, Poland

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE