ΠΑΡΑΡΤΗΜΑ 1: ΠΕΡΙΛΗΨΗ ΤΩΝ ΧΑΡΑΚΤΗΡΙΣΤΙΚΩΝ ΤΟΥ ΠΡΟΪΟΝΤΟΣ

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NAC FLOX 10 100 mg/ml solution for injection for cattle and sows

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains:

Active substance:
marbofloxacin……..……100.0 mg

Excipients:
disodium edetate…….…….. 0.1 mg
thioglycerol…..……..……..…….…….……1.0 mg
metacresol……..2.0 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear yellow solution.

4. CLINICAL PARTICULARS

4.1. Target Species

Cattle and sows.

4.2. Indications for use specifying the target species

In cattle:
Treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia (Pasteurella) haemolytica* and *Mycoplasma bovis*.
Treatment of acute mastitis caused by strains of *E. coli* sensitive to marbofloxacin during the lactation period.

In sows:
Treatment of Metritis-Mastitis-Agalactia syndrome caused by bacterial strains sensitive to marbofloxacin.

4.3. Contraindications

Bacterial infections resistant to other fluoroquinolones (cross-resistance).
Do not administer to animals in which hypersensitivity to marbofloxacin or to other quinolones or to any of the excipients has previously been found.

4.4. Special warnings for each target species

Do not administer in cases where the pathogen involved is resistant to other fluoroquinolones (cross resistance).

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.
Use of fluoroquinolones must be limited to the treatment of clinical conditions which have responded, or which are expected to respond poorly to other classes of antimicrobial products.
If possible, fluoroquinolones should be used exclusively on the basis of the results of a susceptibility test.
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.
The efficacy data for the product have demostrated a level of efficacy which is insufficient for therapy of acute mastitis caused by Gram-positive bacteria.

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

People with known hypersensitivity to marbofloxacin must avoid contact with the medicinal product. Avoid contact of the product with the skin and/or eyes.
In case of contact with the skin and/or the eyes rinse with plenty of water or normal saline solution.
Wash hands after use.
Avoid accidental self-injection since this can cause mild irritation.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6. Adverse reactions (frequency and severity)

Intramuscular administration can cause transitory local reactions such as pain and swelling to the injection site and inflammatory lesions, which can even persist for 12 days after inoculation.
In cattle, subcutaneous administration is better tolerated locally than intramuscular inoculation. Therefore, in very heavy cattle subcutaneous administration is recommended. In cattle and swine, the injection site of choice is the neck.

4.7. Use during pregnancy, lactation or lay

Studies conducted in laboratory animals (rats, rabbits) have not highlighted any teratogenic, embryotoxic or maternotoxic effects of marbofloxacin.
The safety of the product has been demonstrated in cows at the dose of 2 mg/ kg b.w. during pregnancy and in piglets and calves when consume milk from treated mothers. The safety of the product, at a dose of 8 mg / kg, has not been demonstrated in cows during pregnancy and in calves when consume milk from treated mothers. Use only according to the risk-benefit assessment of the responsible veterinarian.
In case of use in lactating cows, see paragraph 4.11. "Withdrawal periods".

4.8. Interactions with other medicinal products and other forms of interaction

Do not use in combination with tetracyclines or macrolides owing to the potential antagonistic effect. Concomitant administration of fluoroquinolones
can potentiate the action of oral anticoagulants. Concomitant oral administration of substances containing magnesium, aluminium, calcium and iron can reduce absorption of the fluoroquinolones

4.9. Amounts to be administered and administration route

Cattle:

Treatment of respiratory infections:
Treatment of respiratory infection caused by sensible strains of *Pasteurella multocida* and *Mannheimia haemolytica*: the recommended dose is 8 mg of marbofloxacin/kg b.w. (equivalent to 2 ml of NAC FLOX 10 / 25 kg b.w.) in a single injection by intramuscular route.

Treatment of respiratory infection caused by sensible strains of *Mycoplasma bovis*: the recommended dose is 2 mg of marbofloxacin / kg b.w. (equivalent to 1 ml of NAC FLOX 10 / 50 kg b.w.) in a single daily injection by the subcutaneous or intramuscular route for 3-5 consecutive days. The first administration can also be performed by the intravenous route.

Treatment of acute mastitis:
The recommended dose is 2 mg of marbofloxacin/kg b.w. (equivalent to 1 ml of NAC FLOX 10 / 50 kg b.w.) in a single daily injection by the subcutaneous or intramuscular route for 3 consecutive days. The first administration can also be performed by the intravenous route.

Sows:

The recommended dose is 2 mg of marbofloxacin/kg b.w. (equivalent to 1 ml of NAC FLOX 10 / 50 kg b.w.) in a single daily injection by the intramuscular route for 3 consecutive days.

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

No signs of overdose have been observed following administrations of marbofloxacin at a dose 3 times higher than the recommended.
Overdose can cause an acute neurological symptomatology which must be treated symptomatically.

4.11. Withdrawal periods

Cattle

Indication	**Respiratory infection**		**Mastitis**
Dose	2 mg/kg for 3-5 days (IV/IM/SC)	8 mg/kg in single injection (IM)	2 mg/kg for 3 days (IV/IM/SC)
Meat and offal	6 days	3 days	6 days
Milk	36 hours	72 hours	36 hours

Sows:

Meat and offal: 4 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-infective agent for systemic use. Fluoroquinolones. Marbofloxacin
ATC Vet code: QJ01MA93

5.1. Pharmacodynamic properties

Marbofloxacin is a synthetic bactericidal antimicrobial agent belonging to the fluoroquinolones group, which acts through inhibition of DNA gyrase. It is efficacious *in vitro* against numerous Gram-positive bacteria, in particular *Staphylococcus*, Gram-negative bacteria (*Escherichia coli*, *Pasteurella* spp.) and Mycoplasma (*Mycoplasma bovis*).
Resistance to *Streptococcus* may appear.

5.2. Pharmacokinetic particulars

After subcutaneous or intramuscular administration in cattle and in pigs at the recommended dose of 2 mg/kg b.w., marbofloxacin is rapidly absorbed and reaches a maximum plasma concentration of 1.5 µg/ml within less than one hour.
Its bioavailability is close to 100%.
Marbofloxacin binds weakly to plasma proteins (less than 10% in swine and less than 30% in cattle) and distributes extensively throughout the organism. In most tissues (liver, kidneys, skin, lungs, bladder, uterus) it reaches concentrations greater than those in the plasma.
Following intramuscular administration in lactating cows, marbofloxacin reaches in milk maximum concentrations of 1.02 µg/ml (C_{max} after the first administration) in 2.5 hours (T_{max} after the first administration).
Marbofloxacin is eliminated slowly in preruminant calves ($t_{½}$ = 5-9 hours) and in swine ($t_{½}$ = 8-10 hours), more rapidly in ruminant cattle ($t_{½}$ = 4-7 hours), principally in active form in the urine and in the faeces.

After a single intramuscular administration in cattle, at the recommended dose of 8 mg/kg, marbofloxacin reaches a maximum plasma concentration (C_{max}) of 7.3 µg / ml after about 0.78 h (T_{max}). Plasma protein binding is approximately 30%.
Marbofloxacin is slowly eliminated ($t_{1/2\,ß}$ = 15.6 h), mainly in active form via the urine and the faeces.

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: 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 temperature storage conditions.
Protect from light.

6.5 Nature and composition of the immediate packaging

Amber type II glass bottles of 100 ml, 250 ml and 500 ml, closed with a chlorobutyl type I rubber stopper, in a cardboard box. 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 product or waste materials should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

FATRO S.p.A
Via Emilia, 285, Ozzano dell' Emilia-Bologna 40064
Ιταλία

8. MARKETING AUTHORISATION NUMBERS

CY 00445V

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28/4/2014
Date of renewal:18/6/2019

10. DATE OF REVISION OF THE TEXT

18/6/2019

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

DISPENSATION REGIMEN

To be sold only upon presentation of a non-renewable veterinary medicinal prescription.