LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Boflox, 100 mg/ml solution for injection for cattle and pigs
Marbofloxacin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Active substance:
Marbofloxacin 100 mg/ml
Excipients:
Disodium edetate
Monothioglycerol
Metacresol

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

100 ml
250 ml
6 x 100 ml
6 x 250 ml
10 x 100 ml
10 x 250 ml
12 x 100 ml
12 x 250 ml

5. TARGET SPECIES

Cattle, pigs (sows)

6. INDICATION(S)

Read the package leaflet before use.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Cattle: IM, SC or IV use
Pigs (sows): IM use
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Cattle:
8 mg/kg on a single occasion (IM)

Meat and offal: 3 days
Milk: 72 hours

2 mg/kg for 3 to 5 days (IV/SC/IM)
Meat and offal: 6 days
Milk: 36 hours

Pig (sows):
Meat and offal: 4 days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP
Shelf-life after first opening the container: 28 days.
Once broached, use by…

11. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Industrial Veterinaria, S.A.
Esmeralda, 19
E-08950 Esplugues de Llobregat (Barcelona) Spain

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch:

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING UNITS

LABEL 100 – 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Boflox, 100 mg/ml solution for injection for cattle and pigs
Marbofloxacin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Active substance:
Marbofloxacin 100 mg/ml
Excipients:
Disodium edetate
Monothioglycerol
Metacresol

3. PHARMACEUTICAL FORM

4. PACKAGE SIZE

100 ml – 250 ml

5. TARGET SPECIES

Cattle, pigs (sows)

6. INDICATION(S)

Read the package leaflet before use

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Cattle: IM, SC or IV use
Pigs (sows): IM use

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Cattle:
8 mg/kg on a single occasion (IM)
Meat and offal: 3 days
Milk : 72 hours

2 mg/kg for 3 to 5 days (SC/IM)
Meat and offal: 6 days
Milk: 36 hours

Pig (sows):

Meat and offal: 4 days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP
Shelf-life after first opening the container: 28 days.
Once broached, use by

11. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Industrial Veterinaria, S.A.
Esmeralda, 19
E-08950 Esplugues de Llobregat (Barcelona) Spain

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch:

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Boflox 100 mg/ml solution for injection for cattle and pigs
Marbofloxacin

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Industrial Veterinaria, S.A.
Esmeralda, 19
E-08950 Esplugues de Llobregat (Barcelona) Spain

Manufacturer responsible for batch release:
KELA N.V., St. Lenaartseweg 48, 2320 Hoogstraten, Belgium

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Boflox, 100 mg/ml solution for injection for cattle and pigs
Marbofloxacin

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Per ml

Active substance:
Marbofloxacin 100 mg

Excipients:
Disodium edetate 0.10 mg
Monothioglycerol 1 mg
Metacresol 2 mg

Yellow greenish to yellow brownish, clear solution

4. INDICATION(S)

In cattle:
- treatment of respiratory infections caused by strains of *Histophilus somni, Mannheimia haemolytica, Mycoplasma bovis, Pasteurella multocida* susceptible to marbofloxacin.
- treatment of acute mastitis caused by strains of *Escherichia coli* susceptible to marbofloxacin during the lactation period.

In pigs:
- treatment of Postpartum Dysgalactia Syndrome –PDS- (Metritis Mastitis Agalactia syndrome) caused by bacterial strains susceptible to marbofloxacin.

5. CONTRAINDICATIONS

Do not use in cases where the pathogen involved is resistant to other fluoroquinolones (cross resistance).
Do not use in animals with known hypersensitivity to the active substance or to any other quinolone or to any of the excipients.

6. ADVERSE REACTIONS

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 in cattle 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.
If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle, pigs (sows)

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Cattle:
Respiratory infections:
The recommended dosage is 8 mg marbofloxacin/kg body weight (2 ml product/25 kg body weight) in a single injection by 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 product/50 kg body weight), in a single daily injection for 3 to 5 consecutive days, by intramuscular or subcutaneous route. The first injection may be given by the intravenous route.

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

Pigs (sows):
- Intramuscular use:
The recommended dosage is 2 mg marbofloxacin/kg body weight (1 ml product/50 kg body weight) in a single daily injection, for 3 consecutive days.

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 30 times. The user should choose the most appropriate vial size according to the target species to treat.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD

Cattle:
8 mg/kg on a single occasion (IM)
Meat and offal: 3 days
Milk : 72 hours

2 mg/kg for 3 to 5 days (IV/SC/IM)
Meat and offal: 6 days
Milk: 36 hours

Pig (sows):
Meat and offal: 4 days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store in the original package in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label.
Shelf-life after first opening the container: 28 days.

12. SPECIAL WARNING(S)

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.
The efficacy data showed that the product has insufficient efficacy for the treatment of acute forms of mastitis induced by gram-positive bacteria.

User warnings:

People with known hypersensitivity to (fluoro)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 with plenty of water.
Wash hands after use.

Pregnancy and lactation:

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

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

In case of use in lactating cow, see section “Withdrawal period”.

Interaction with other medicinal products and other forms of interaction:

None known.

Overdose (symptoms, emergency procedures, antidotes):

No signs of overdosage have been observed after administration of 3 times the recommended dose.
Signs as acute neurological disorders may occur when the dose is exceeded. This signs should be treated symptomatically. Do not exceed the recommended dose.

Incompatibilities:

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.
Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

DD month YYYY

15. OTHER INFORMATION

Vials of 100 ml and 250 ml.
Vials are individually packed in a carton box.
Six, ten or twelve vials are grouped as a clinical pack.

Not all pack sizes may be marketed.

Pharmacodynamics properties

Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the fluoroquinolone group which acts by inhibition of DNA gyrase. It has a broad-spectrum activity in vitro against Gram-negative bacteria (*E. coli*, *Histophilus somni, Mannheimia haemolytica and Pasteurella multocida*) and against Mycoplasma (*Mycoplasma bovis*). Resistance to *Streptococcus* may occur.

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.

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 h) but faster in ruminant cattle ($t_{½\beta}$ = 4-7 h) predominantly in the active form in urine (3/4 in pre-ruminating calves, ½ in ruminants) and faeces (1/4 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 (Cmax) is 7.3 µg/ml reached in 0.78 hours (Tmax). Marbofloxacin is eliminated slowly (T1/2 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 (Cmax after the first administration) after 2.5 hours (Tmax after the first administration).

In pigs, marbofloxacin is eliminated slowly ($t_{½\beta}$ = 8-10 h) predominantly in the active form in urine (2/3) and faeces (1/3).