

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

KARIFLOX 100 mg/ml Oral Solution for Chickens and Turkeys

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Enrofloxacin..... 100 mg

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Benzyl alcohol (E 1519)	14 mg
Potassium hydroxide	
Purified water	

An aqueous, clear, yellowish solution.

3. CLINICAL INFORMATION

3.1. Target species

Chickens and turkeys.

3.2. Indications for use for each target species

Treatment of infections caused by the following bacteria susceptible to enrofloxacin:

Chickens

Mycoplasma gallisepticum,
Mycoplasma synoviae,
Avibacterium paragallinarum,
Pasteurella multocida,

Turkey

Mycoplasma gallisepticum,
Mycoplasma synoviae,
Pasteurella multocida,

3.3. Contraindications

Do not use for prophylaxis.

Do not use when resistance/ cross-resistance to (fluoro)quinolones is known to occur in the flock intended for treatment.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4. Special warnings

Treatment of *Mycoplasma* spp. infections may not eradicate the organism.

3.5. Special precautions for use

Special precautions for safe use in target species:

Since enrofloxacin was first authorised for use in poultry, there has been widespread reduction in susceptibility of *E. coli* to fluoroquinolones and emergence of resistant organisms. Resistance has also been reported in *Mycoplasma synoviae* in the EU.

Before use, header tanks should be emptied, thoroughly cleaned and then filled with a known volume of clean water before adding the required amount of the veterinary medicinal product. The resulting mixture should be stirred.

Before use, header tanks should be inspected at regular intervals for presence of dust, algae formation and sedimentation.

Official and local antimicrobial policies should be taken into account when the veterinary medicinal 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.

Wherever possible, fluoroquinolones should be used based on susceptibility testing.

Use of the veterinary medicinal product deviating from instructions given in the SPC may increase the prevalence of bacteria resistant to fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.

If there is no clinical improvement within two to three days susceptibility testing should be repeated and therapy should be changed, if appropriate.

Do not exceed the recommended dose.

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

Personal protective equipment consisting of impervious gloves should be worn when handling the veterinary medicinal product.

Direct contact with the skin should be avoided because of sensitisation, contact dermatitis and possible hypersensitivity reactions.

Wash any splashes from skin or eyes immediately with water.

Wash hands and exposed skin after use.
Do not eat, drink or smoke whilst using the veterinary medicinal product.

Special precautions for the protection of the environment:

Not applicable

3.6. Adverse events

None.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the label-leaflet for respective contact details.

3.7. Use during pregnancy, lactation or lay

Not for use in laying birds producing eggs for human consumption.

3.8. Interaction with other medicinal products and other forms of interaction

Concurrent use of enrofloxacin with other antimicrobials, tetracyclines and macrolide antibiotics, may result in antagonistic effects.

Absorption of enrofloxacin may be reduced if the product is administered together with substances containing magnesium or aluminium.

Do not combine enrofloxacin with steroidal anti-inflammatory products.

3.9. Administration routes and dosage

For oral administration via the drinking water. This may be put directly into the header tanks, or via water proportioner systems.

10 mg enrofloxacin/kg bodyweight per day for 3-5 consecutive days.

Treatment for 3-5 consecutive days; for 5 consecutive days in mixed infections and chronic progressive forms. If no clinical improvement is achieved within 2-3 days, alternative antimicrobial therapy should be considered based on susceptibility testing.

Medication of the water supply should be continuous during the treatment period and no other source of water should be available.

Medicated water should be made every day, immediately prior to provision. Carefully calculate the total body mass to be treated and the total daily water consumption before each treatment.

The uptake of medicated water depends on age and clinical condition of the birds, ambient temperature, and light regime. In order to obtain the correct dosage the concentration of the veterinary medicinal product should be adjusted accordingly. To ensure correct dosage, body weight should be determined as accurately as possible.

Taking into consideration that 10 mg enrofloxacin per kg body weight corresponds to 0.1 ml of the veterinary medicinal product per kg body weight; the following

calculation should be made to provide the required amount of the product per litre of drinking water:

$$\begin{array}{rcccl} 0.1 & \times & \text{Average bodyweight of} & \times & \text{Number of} \\ & & \text{birds to be treated (kg)} & & \text{birds} \\ \hline & & & & \text{ml product} \\ & & & & \text{per litre of} \\ & & & & \text{drinking} \\ & & & & \text{water} \end{array} =$$

Total water consumption (l) of the flock at the previous day

Care should be taken that the intended dose is completely ingested.
Use appropriate and properly calibrated dosing equipment.

3.10. Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Do not exceed the recommended dose. In accidental overdose there is no antidote and treatment should be symptomatic.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12. Withdrawal period

Chickens:
Meat and offal: 7 days.

Turkeys:
Meat and offal: 13 days.

Not for use in birds producing eggs for human consumption.
Do not use within 2 weeks before the start of the laying period.

4. PHARMACOLOGICAL INFORMATION

4.1. ATCvet code: QJ01MA90

4.2. Pharmacodynamics

Mode of action:

Enrofloxacin is a synthetic, broad spectrum antimicrobial substance, belonging to the fluoroquinolone group of antibiotics. It is bactericidal in action with activity against a range of Gram-positive and Gram-negative bacteria and mycoplasmas. The mechanism of action of the quinolones is unique among antimicrobials – they act primarily to inhibit bacterial DNA gyrase, an enzyme responsible for controlling the supercoiling of bacterial DNA during replication. Resealing of the double standard helix is inhibited resulting in irreversible degradation of the chromosomal DNA. The fluoroquinolones

also possess activity against bacteria in the stationary phase by an alteration of the permeability of the outer membrane phospholipid cell wall.

Antibacterial spectrum:

Enrofloxacin is active against many Gram-negative bacteria, against Gram-positive bacteria and *Mycoplasma* spp.

In vitro susceptibility has been shown in strains of (i) Gram-negative species such as *Pasteurella multocida* and *Avibacterium (Haemophilus) paragallinarum* and (ii) *Mycoplasma gallisepticum* and *Mycoplasma synoviae*.

Types and mechanisms of resistance:

Resistance to fluoroquinolones has been reported to arise from five sources: (i) point mutations in the genes encoding for DNA gyrase and/or topoisomerase IV leading to alterations of the respective enzyme, (ii) alterations of drug permeability in Gram-negative bacteria, (iii) efflux mechanisms, (iv) plasmid mediated resistance and (v) gyrase protecting proteins. All mechanisms lead to a reduced susceptibility of the bacteria to fluoroquinolones. Cross-resistance within the fluoroquinolone class of antimicrobials is common.

4.3. Pharmacokinetics

The pharmacokinetics of enrofloxacin are such that oral and parenteral administration leads to similar serum levels. Enrofloxacin possesses a high distribution volume. Tissue levels 2 – 3 times higher than that found in the serum, have been demonstrated in laboratory animals and target species. Organs in which high levels can be expected are the lungs, liver, kidney, skin, bone and lymphatic system. Enrofloxacin also distributes into the cerebrospinal fluid and the aqueous humor.

The degree of metabolism depends on the species and ranges between 50-60%. Biotransformation at hepatic level of enrofloxacin results in the active metabolite, ciprofloxacin. In general, metabolism is by hydroxylation and oxidation processes to oxofluoroquinolones. Other reactions that also occur are N-dealkylation and conjugation with glucuronic acid.

Excretion occurs by biliary and renal route, with excretion in the urine predominating.

5. PHARMACEUTICAL PARTICULARS

5.1. Major incompatibilities

Do not mix with any other veterinary medicinal product.

Increased influx of the air (admixing CO₂ from the air) into medicated drinking water may result in precipitation of enrofloxacin.

High concentrations of calcium and magnesium in the water system may result in precipitation of enrofloxacin during intermediate dilution in the dosage devices.

5.2. Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf life after first opening the immediate packaging: 3 months.

Shelf life after dilution according to directions: 24 hours.

5.3. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4. Nature and composition of immediate packaging

White high-density polyethylene containers of three capacities: 250 ml jars, 1 L bottles and 5 L barrels. Containers are closed with a seal screw cap of the same material with induction disk.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORIZATION HOLDER

LABORATORIOS KARIZOO, S.A.

7. MARKETING AUTHORISATION NUMBER

8. DATE OF FIRST AUTHORISATION

<Date of first authorisation:> <{DD/MM/YYYY}>

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

<{MM/YYYY}>

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the [Union Product Database \(https://medicines.health.europa.eu/veterinary\)](https://medicines.health.europa.eu/veterinary).

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET

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Excipients:

Benzyl Alcohol (E 1519) 14 mg

Qualitative composition of excipients and other constituents

Potassium hydroxide

Purified water

An aqueous, clear, yellowish solution.

3. PACKAGE SIZE

250 ml jars

1 L bottles

5 L barrels

4. TARGET SPECIES

Chickens and turkeys.

5. INDICATIONS FOR USE

Indications for use

Treatment of infections caused by the following bacteria susceptible to enrofloxacin:

Chickens

Mycoplasma gallisepticum,
Mycoplasma synoviae,
Avibacterium paragallinarum,
Pasteurella multocida,

Turkeys

Mycoplasma gallisepticum,
Mycoplasma synoviae,
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6. CONTRAINDICATIONS

Contraindications

Do not use for prophylaxis.

Do not use when resistance/ cross-resistance to (fluoro)quinolones is known to occur in the flock intended for treatment.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

7. SPECIAL WARNINGS

Special warnings

Special warnings:

Treatment of *Mycoplasma* spp. infections may not eradicate the organism.

Special precautions for safe use in target species:

Since enrofloxacin was first authorised for use in poultry, there has been widespread reduction in susceptibility of *E. coli* to fluoroquinolones and emergence of resistant organisms. Resistance has also been reported in *Mycoplasma synoviae* in the EU.

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If there is no clinical improvement within two to three days susceptibility testing should be repeated and therapy should be changed, if appropriate.

Do not exceed the recommended dose.

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

Personal protective equipment consisting of impervious gloves should be worn when handling the veterinary medicinal product.

Direct contact with the skin should be avoided because of sensitisation, contact dermatitis and possible hypersensitivity reactions.

Wash any splashes from skin or eyes immediately with water.

Wash hands and exposed skin after use.

Do not eat, drink or smoke whilst using the veterinary medicinal product.

Interaction with other medicinal products and other forms of interaction:

Concurrent use of enrofloxacin with other antimicrobials, tetracyclines and macrolide antibiotics, may result in antagonistic effects.

Absorption of enrofloxacin may be reduced if the veterinary medicinal product is administered together with substances containing magnesium or aluminium.

Do not combine enrofloxacin with steroidal anti-inflammatory products.

Laying birds:

Not for use in laying birds producing eggs for human consumption.

Overdose:

Do not exceed the recommended dose. In accidental overdose there is no antidote and treatment should be symptomatic.

Major incompatibilities:

Do not mix with any other veterinary medicinal product.

Increased influx of the air (admixing CO₂ from the air) into medicated drinking water may result in precipitation of enrofloxacin.

High concentrations of calcium and magnesium in the water system may result in precipitation of enrofloxacin during intermediate dilution in the dosage devices.

8. ADVERSE EVENTS

Adverse events

None.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or its local representative using the contact details on this label, or via your national reporting system:

9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration

For oral administration via the drinking water. This may be put directly into the header tanks, or via water proportioner systems.

10 mg enrofloxacin/kg bodyweight per day for 3-5 consecutive days.

Treatment for 3-5 consecutive days; for 5 consecutive days in mixed infections and chronic progressive forms. If no clinical improvement is achieved within 2-3 days, alternative antimicrobial therapy should be considered based on susceptibility testing.

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Total water consumption (l) of the flock at the previous day

Care should be taken that the intended dose is completely ingested.
Use appropriate and properly calibrated dosing equipment.

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

Before use, header tanks should be emptied, thoroughly cleaned and then filled with a known volume of clean water before adding the required amount of the veterinary medicinal product. The resulting mixture should be stirred.

11. WITHDRAWAL PERIODS

Withdrawal periods

Chickens: Meat and offal: 7 days.
Turkeys: Meat and offal: 13 days.

Not authorised for use in birds producing eggs for human consumption.
Do not use within 2 weeks before the start of the laying period.

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Keep out of the sight and reach of children.
Do not use this veterinary medicinal product after the expiry date which is stated on the label-leaflet after Exp. The expiry date refers to the last day of that month.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

EU/0/00/000/000

Pack sizes: 250 ml, 1 L and 5 L

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

<{MM/YYYY}>

Detailed information on this veterinary medicinal product is available in the Union Product Database (<https://medicines.health.europa.eu/veterinary>).

17. CONTACT DETAILS

Contact details

Marketing authorisation holder and manufacturer responsible for batch release:

LABORATORIOS KARIZOO, S.A.

Polígono Industrial La Borda

Mas Pujades, 11-12

08140 – CALDES DE MONTBUI (Barcelona)

Spain

Tel: +34 93 865 41 48

Email: pharmacovigilance@alivira.es

Local representatives and contact details to report suspected adverse events:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder:

18. OTHER INFORMATION

Other information

19. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

Once opened, use by ...

Shelf life after first opening the container: 3 months.

Shelf life after dilution according to directions: 24 hours.

21. BATCH NUMBER

Lot {number}