Summary of Product Characteristics

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 substance:		
Enrofloxacin	100	mg
Excipients:		
Benzyl alcohol (E 1519)	14	mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral solution.
An aqueous, clear, yellowish solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Chickens and Turkeys.

4.2 Indications for use, specifying the target species

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,
Pasteurella multocida.

4.3 Contraindications

Do not use in birds producing eggs for human consumption.
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.
Refer to section 4.5.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

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

4.5 Special precautions for use

Special precautions for use in animals
Since enrofloxacin was first authorised for use in poultry, there has been widespread reduction in the 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 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 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 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
Wear impervious gloves when handling the 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 product.

4.6 Adverse reactions (frequency and seriousness)

None.

4.7 Use during pregnancy, lactation or lay

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

4.8 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.

4.9 Amounts to be administered and administration route

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 product should be adjusted accordingly. To ensure correct dosage, body weight should be determined as accurately as possible to avoid underdosering.
Taking into consideration that 10 mg enrofloxacin per kg body weight corresponds to 0.1 ml of the product per kg body weight; the following calculation should be made to provide the required amount of the product per litre of drinking water:

$$0.1 \times \frac{\text{Average bodyweight of birds to be treated (kg)}}{\text{Total water consumption (l) of the flock at the previous day}} \times \text{Number of birds} = \text{ml product per litre of drinking water}$$

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

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

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

4.11 Withdrawal period(s)

Meat and offal
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 administer to layer replacement birds within 14 days of coming into lay.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: quinolone and quinoxaline antibacterials, fluoroquinolones.
ATCvet code: QJ01MA90

5.1 Pharmacodynamic properties

Mode of action.
Enrofloxacin is a synthetic, broad spectrum antimicrobial substance, belonging to the fluoroquinoline 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*. (See section 4.5).

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.

5.2 Pharmacokinetic particulars

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 glucoronic acid.

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E 1519)
Potassium hydroxide
Purified water

6.2 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.

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: 3 months
Shelf-life after dilution according to directions: 24 hours

6.4 Special precautions for storage

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

6.5 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.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

VPA 10786/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12th September 2008
Date of last renewal: 1st February 2013

10 DATE OF REVISION OF THE TEXT

July 2018