This leaflet format has been determined by the Ministry of Health and the content has been checked and approved in January 2019

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrofloxacin Medimarket 5% Veterinary

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml solution contains:
Active substance:
Enrofloxacin: 50 mg

Excipient(s):
n-Butyl alcohol: 30 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Yellow Clear solution free from particulate matter.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (calves)

4.2 Indications for use, specifying the target species

In calves

Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of Pasteurella multocida, Mannheimia haemolytica and Mycoplasma spp.
Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of Escherichia coli.
Treatment of septicaemia caused by enrofloxacin susceptible strains of Escherichia coli.
Treatment of acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of Mycoplasma bovis.

Enrofloxacin Medimarket 5% Veterinary should be used only after the sensitivity of the bacteria has been proven and it has been found that there is no alternative treatment (proven resistance to other agents).

4.3 Contraindications

Do not use in animals with known hypersensitivity to enrofloxacin or other fluoroquinolones or to any of the excipients listed in section 6.1.
Do not use in animals that are epileptic or suffer from seizures since enrofloxacin may cause CNS stimulation.

4.4 Special warnings for each target species

None.

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 including use deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to enrofloxacin and may decrease the effectiveness of treatment with all fluoroquinolones due to the potential for cross-resistance.

Special caution should be taken when using enrofloxacin in animals with impaired renal function.

Degenerative changes of articular cartilage were observed in calves treated orally with 30 mg enrofloxacin/kg body weight during 14 days.

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

People with known hypersensitivity to fluoroquinolones should avoid any contact with the product. Avoid skin and eye contact. Wash any splashes from skin or eyes immediately with water.Wash hands after use. Do not eat, drink or smoke whilst handling the product.

Care should be taken to avoid accidental self-injection. If accidental self-injection occurs seek medical advice immediately.

Other precautions

In countries where feeding of fallen stock to scavenger bird populations is permitted as a conservation measure , the possible risk to hatching success should be considered before feeding carcasses of livestock recently treated with this product.

4.6 Adverse reactions (frequency and seriousness)

Digestive tract disorders (e.g. diarrhoea) may occur in very rare cases (less than 1 animal in 10,000 animals, including isolated reports).These signs are generally mild and transient.

Local reactions at injection site

In calves, transient local tissue reactions may occur in very rare cases and may be observed up to 14 days.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product .Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form at the following link :

https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic effects but have shown evidence of foetotoxic effects at maternotoxic doses.

Mammals

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use enrofloxacin concomitantly with antimicrobial substances acting antagonistically to quinolones (e.g. macrolides, tetracyclines or phenicols).
Do not use concurrently with theophylline as the elimination of theophylline may be delayed.

4.9 Amounts to be administered and administration route

subcutaneous use.
Repeated injections should be made at different injection sites.
To ensure a correct dosage, body weight (bw) should be determined as accurately as possible to avoid underdosing.

Calves

5 mg of enrofloxacin/kg bw, corresponding to 1 ml/10 kg bw, once daily for 3-5 days.

Acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of Mycoplasma bovis: 5 mg of enrofloxacin/kg bw, corresponding to 1 ml/10 kg bw, once daily for 5 days.

The product can be administered by slow subcutaneous administration .
Not more than 10 ml should be administered at one subcutaneous injection site.

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

In cases of accidental overdoses digestive tract disorders (e.g. vomiting, diarrhoea) and neurological disorders may occur.

In cattle, overdose has not been documented.

In accidental overdose there is no antidote and treatment should be symptomatic.

4.11 Withdrawal period(s)

Calves:

Following subcutaneous injection: Meat and offal: 12 days.
Not authorised for use in animals producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, fluoroquinolones.
ATCvet code: QJ01MA90.

5.1 Pharmacodynamic properties

Mode of action
Two enzymes essential in DNA replication and transcription, DNA gyrase and topoisomerase IV, have been identified as the molecular targets of fluoroquinolones. Target inhibition is caused by non-covalent binding of fluoroquinolone molecules to these enzymes. Replication forks and translational complexes cannot proceed beyond such enzyme-DNA-fluoroquinolone complexes, and inhibition of DNA and mRNA synthesis triggers events resulting in a rapid, drug concentration-dependent killing of pathogenic bacteria. The mode of action of enrofloxacin is bactericidal and bactericidal activity is concentration dependent .

Antibacterial spectrum
Enrofloxacin is active against many Gram-negative bacteria such as Escherichia coli, Klebsiella spp., Actinobacillus pleuropneumoniae, Mannheimia haemolytica, Pasteurella spp. (e.g. Pasteurella multocida), Bordetella spp., Proteus spp., Pseudomonas spp., against Gram-positive bacteria such as Staphylococcus spp. (e.g. Staphylococcus aureus) and against Mycoplasma spp. at the recommended therapeutic doses.

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

Enrofloxacin is rapidly absorbed after parenteral injection. Bioavailability is high (approximately 100% in cattle) with a low to moderate plasma protein binding (approximately 20 to 50%).
Enrofloxacin is metabolized to the active substance ciprofloxacin at approximately 40 % in ruminants.

Enrofloxacin and ciprofloxacin distribute well into all target tissues, e.g. lung, kidney, skin, and liver ,reaching 2- to 3-fold higher concentrations than in plasma. Parent substance and active metabolite are cleared from the body via urine and faeces . Accumulation in plasma does not occur following a treatment interval of 24 h.
In milk, most of drug activity consists on ciprofloxacin. Overall drug concentrations peak at 2 hours after treatment showing an approximately 3-fold higher total exposure over the 24 hours dosing interval compared to plasma.

	Calves
Dose rate (mg/kg bw)	5
Route of administration	sc
Tmax (h)	1.2
Cmax (µg/ml)	0.73
AUC (µg·h/ml)	3.09
Terminal half-life (h)	2.34
Elimination half-life (h)	/
F (%)	/

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

n-Butanol
Potassium hydroxide
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
Shelf life after the first opening of the immediate packaging: 28 days.

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and composition of immediate packaging

Amber glass (type I) vials with a Grey teflonised chlorobutyl rubber stopper with an aluminium cap

Pack-sizes:

100 ml in a cardboard box

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

A.L. Medi Market
Hakadar 18 St.
Netanya, 42138
Israel

8. MARKETING AUTHORISATION NUMBER(S)

161-60-34991-00

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

January 2019

10 DATE OF REVISION OF THE TEXT