SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enrofloxacin WDT 150 mg Flavour tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:
Enrofloxacin 150 mg

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
Round slightly biconvex, cream to light brownish tablets with possible visible white or darker spots, one side scored and bevel-edged. The tablets can be divided into equal parts.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

In dogs:
Treatment of infections caused by strains of *Staphylococcus* spp., *E. coli, Haemophilus* spp. *Pasteurella* spp., and *Salmonella* spp. susceptible to enrofloxacin.

The product is indicated for treatment of mono or mixed bacterial infections of the respiratory, digestive and urinary tract, otitis externa, skin and wound infections.

4.3 Contraindications

Do not use in dogs less than 1 year of age or in exceptionally large breeds of dog with a longer growth period less than 18 months of age, as articular cartilage may be affected during the period of rapid growth.
Do not use in cases of hypersensitivity to the active substance, to any other quinolone or to any of the excipients.
Do not use in dogs having seizure disorders, since enrofloxacin may cause CNS stimulation.
Do not use in cases of known resistance to (fluoro)quinolones, as there exists almost complete cross resistance to other quinolones and complete cross resistance to other fluoroquinolones.
Please, see section 4.7.

4.4 Special warnings for each target species

None known.

4.5 Special precautions for use

i) Special precautions for use in animals

Flouroquinolones should be reserved for the treatment of clinical conditions that 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. Official and local antimicrobial policies should be taken into account when the product is used. Use of the product deviating from the 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 cross resistance.
If there is no clinical improvement within three days, further susceptibility testing and possibly a change in antimicrobial therapy should be considered.
Use the product with caution in dogs with severe renal or hepatic impairment.
Pyoderma is mostly secondary to an underlying disease. It is advisable to determine the underlying cause and to treat the animal accordingly.
The product is flavoured. To avoid accidental ingestion, the tablets should be stored out of reach of animals.

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

People with known hypersensitivity to fluoroquinolones should avoid contact with the veterinary medicinal product.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Avoid contact with the eyes. In case of contact with the eyes, wash immediately with water.
Wash hands after use.
Do not smoke, eat or drink while handling the product.

4.6 Adverse reactions (frequency and seriousness)

Occasionally gastrointestinal disturbances may occur. Hypersensitivity reactions and CNS disturbances may be observed.
Possible joint cartilage alterations in growing puppies (see 4.3 contraindications).

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Do not use in pregnant or lactating bitches.

4.8 Interaction with other medicinal products and other forms of interaction

Do not combine with tetracyclines, phenicols or macrolides because of potential antagonistic effects.
Do not combine with theophylline as this could lead to a prolonged elimination of this substance.
Do not use simultaneously with NSAIDs (convulsions may occur).
Concurrent use of flunixin and enrofloxacin should be under careful veterinary monitoring, as the interactions between these drugs may lead to adverse events related to delayed elimination.
Concurrent administration of magnesium, calcium or aluminum containing substances may be followed by retarded absorption of enrofloxacin.
Excessive alkalinisation of the urine should be avoided in animals subjected to rehydration.

4.9 Amounts to be administered and administration route

For oral use.
Tablets may be given directly into the mouth or masked in food.
The dosage rate of enrofloxacin is 5 mg/kg/day (i.e. one 150 mg tablet per 30 kg per day), for 5 days. In chronic and severe cases, treatment duration can be extended to 10 days.
To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.
Do not exceed recommended dose.
Treatment should be re-evaluated if no improvement is seen. It is commonly advised to re-evaluate the treatment if no clinical improvement is observed within 3 days.

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

In case of overdose, sickness, vomiting, diarrhoea, and CNS/behavioural changes may occur and the treatment must be suspended.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use. Fluoroquinolones.
ATCvet code: QJ01MA90

5.1 Pharmacodynamic properties

Enrofloxacin is an antibiotic that belongs to the chemical class of fluoroquinolones. The compound exerts bactericidal activity via mechanism of action based on the inhibition of the A subunit of DNA gyrase (topoisomerase II). In Gram positive bacteria the primary target is topoisomerase IV instead of topoisomerase II. With this mechanism enrofloxacin blocks the replication, transcription and recombination of bacterial DNA.

Fluoroquinolones also act on bacterial cells during stationary phase by changing the permeability in the phospholipid cellular membranes. These mechanisms explain the rapid loss of viability of

the bacteria exposed to enrofloxacin. Inhibitory and bactericidal concentrations of enrofloxacin are strongly correlated. They are either equal, or differ in 1-2 dilution steps.
Antibacterial spectrum: *Staphylococcus* spp, *Escherichia coli, Haemophilus* spp., *Pasteurella* spp., *Salmonella* spp.

The enrofloxacin *in vitro* activity against pathogens isolated from canine respiratory, urinary and soft tissue infections in Europe, is good: MIC50 values are comprised between 0.03 and 0.12 µg/ml for *Escherichia coli*, 0.015 µg/ml for *Pasteurella* spp., and 0.12 µg/ml for *Staphylococcus* spp.
Susceptibility breakpoints for enrofloxacin used in Enterobacteriaceae and *Staphylococcus* spp. (in dogs and cats) have been determined as ≤ 0,5 µg/ml for sensitive, 1-2 µg/ml for intermediate and ≥ 4 µg/ml for resistant bacterial strains (CLSI, 2013).

Several Susceptibility pan-European surveillances to investigate the susceptibility to enrofloxacin of bacterial strains isolated to several pathologies in target species have been conducted. See main results below.

Susceptibility of dogs respiratory pathogens

Bacteria	Resistant (%)	MIC50 (µg/ml)	MIC90 (µg/ml)
S. intermedius	4.1	0.12	0.5
E. coli	12.5	0.06	>8
P. multocida	NA	0.015	0.015

NA: No breakpoints were available; standardised agar dilution methodology (Morrisey et al., 2016)

Susceptibility of dogs urinary tract pathogens

Bacteria	Resistant (%)	MIC50 (µg/ml)	MIC90 (µg/ml)
E. coli	3.9	0.03	0.06
S. intermedius	3.0	0.12	0.25

Standardized agar dilution methodology (Moyaert et al., 2017)

Susceptibility of dogs pathogens involved in skin infections.

Bacteria	Resistant (%)	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)
S. pseudointermedius	5.2	0.12	0.5
S. aureus	2.2	0.12	0.25
E. coli	3.7	0.06	0.12
Pasteurella spp.	NA	0.015	0.015

NA: No breakpoints were available (Ludwig et al., 2016)

Resistance to fluoroquinolones occurs by chromosomal mutation with following mechanisms: decrease of the bacterial cell wall permeability, expression change of genes coding for efflux pumps or mutations in genes encoding enzymes responsible for molecule binding. Plasmid-mediated resistance to fluoroquinolones confer only decreased susceptibility of bacteria, however, it can facilitate development of mutations in genes of target enzymes and can be transferred horizontally. Depending on the underlying resistance mechanism cross-resistance to other (fluoro)quinolones and co-resistance to other antimicrobial classes can occur.

5.2 Pharmacokinetic particulars

Enrofloxacin has relatively high bioavailability after oral administration in almost all of the species studied. In dogs, orally dosed with enrofloxacin, the maximum plasma concentration of enrofloxacin is reached after 1 hour, and the antibacterial activity is still maintained after 24 hours. Concomitant administration of compounds containing multivalent cations (antacids, milk or milk replacers) decreases the oral bioavailability of fluoroquinolones.
Fluoroquinolones are characterized by extensive distribution to body fluids and tissues, reaching in some concentrations higher than those found in plasma. Fluoroquinolones are widely distributed in skin, bone and semen as well as in the anterior and posterior chambers of the eye; they cross the placenta and brain barrier. High levels are found in phagocytic cells (alveolar macrophages, neutrophils); therefore fluoroquinolones are effective against intracellular microorganisms.
The degree of metabolism varies between species and is around 50-60%. Enrofloxacin is biotransformed in the liver, to an active metabolite ciprofloxacin. In general, metabolism occurs via hydroxylation and oxidation reactions. Other reactions involved are N-dealkylation and glucuronic acid conjugation.
Excretion occurs via the bile and kidney, the latter being predominant. The renal excretion is by glomerular filtration and tubular excretion.
In dogs, orally administered 5 mg / kg enrofloxacin rapid absorption was observed and concentrations of enrofloxacin after 4 h were 0.3 µg / ml in plasma, 3.3 µg / ml in alveolar macrophages and 4.8 µg / ml in lung epithelial fluid. The bioavailability was approximately 80%.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Maize starch
Sodium starch glycolate (type A)
Meat flavour 10022
Sodium laurilsulphate
Basic butylated methacrylate copolymer
Dibutyl sebacate
Croscarmellose sodium
Silica, colloidal anhydrous
Talc
Magnesium stearate

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Return any halved tablet to the opened strip-pack and use within 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

Polyamide/Aluminium/Polyvinyl chloride film (OPA/Al/PVC), heat sealed with aluminium foil containing 10 tablets / blister.

Package sizes:
Cardboard carton with 10 blister packs (100 tablets)
Cardboard carton with 1 blister pack (10 tablets)

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

7. MARKETING AUTHORISATION HOLDER

To be completed nationaly.

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

- *To be supplied only on veterinary prescription.*
- *Administration by a veterinary surgeon or under their direct responsibility*