

Ceva Animal Health Ltd
Telephone: 01494 781510
Website: www.ceva.com
Email: cevauk@ceva.com

Therios 300 mg and 750 mg Palatable Tablets for Dogs

Species:	Dogs
Therapeutic indication:	Pharmaceuticals: Antimicrobials: Oral preparations: Tablets
Active ingredient:	Cefalexin
Product:	Therios 300 mg and 750 mg Palatable Tablets for Dogs
Product index:	Therios 300 & 750 mg Tablets for Dogs

Qualitative and quantitative composition

Each Therios 300 mg tablet contains: Cefalexin (as cefalexin monohydrate) 300 mg

Each Therios 750 mg tablet contains: Cefalexin (as cefalexin monohydrate) 750 mg

Pharmaceutical form

Round scored beige palatable tablets. The tablets can be divided into equal halves and quarters

Clinical particulars

Target species

Dogs

Indications for use

For the treatment of bacterial skin infections in dogs (including deep and superficial pyoderma) caused by organisms sensitive to cefalexin.

For the treatment of urinary tract infections in dogs (including nephritis and cystitis) caused by organisms sensitive to cefalexin.

Contra-indications

Do not use in animals which are known to be hypersensitive to penicillins.

Do not use in case of severe renal failure

Do not use in rabbits, guinea pigs, hamsters and gerbils.

Special warnings for each target species

None

Special precautions for use

Whenever possible, the use of the product should be based on susceptibility testing and take into account official and local antimicrobial policies.

As with other antibiotics which are excreted mainly by the kidneys, systemic accumulation may occur when renal function is impaired. In case of known renal insufficiency the dose should be reduced.

The product is not recommended for use in dogs less than 2.5 kg bodyweight.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cefalexin and may decrease the effectiveness of treatment with other beta-lactam antibiotics due to the potential for cross-resistance.

Safety of the excipient, ammonium glycyrrhizate, has not been established in dogs less than 1 year old.

Adverse reactions

Vomiting and diarrhoea have been observed in dogs. In rare cases hypersensitivity can occur.

Use during pregnancy or lactation

Do not use in pregnant or lactating bitches.

Interactions

In order to ensure efficacy, the product should not be used in combination with bacteriostatic antibiotics.

Concurrent use of first generation cephalosporins with aminoglycoside antibiotics or some diuretics such as furosemide can enhance nephrotoxicity risks

Amounts to be administered and administration route

For oral administration. 15 mg cefalexin per kg body weight twice daily (equivalent to 30 mg per kg body weight per day) for duration of:

- 14 days in cases of urinary tract infection
- At least 15 days in cases of superficial infectious dermatitis
- At least 28 days in cases of deep infectious dermatitis

In severe or acute conditions the dose may be safely doubled to 30 mg/kg twice daily. To allow for accuracy of dosing, tablets can be halved or quartered.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid under dosing.

Therios tablets are well accepted by dogs but may be crushed or added to a small quantity of food immediately prior to feeding if necessary

Overdose

Trials performed on animals with up to 5 times the recommended twice daily dosage of 15 mg/kg demonstrated that cefalexin was well tolerated.

Pharmacological particulars

Pharmacodynamic properties

Cefalexin acts by inhibiting the nucleopeptide synthesis of the bacterial wall. Cephalosporins interfere with transpeptidation by acylating the enzyme making it unable to cross-link muramic acid-containing peptidoglycan strands. The inhibition of the biosynthesis of the material required to build the cell wall results in a defective cell wall and consequently osmotically unstable to protoplasts. The combined action results in cell lysis and filament formation.

Cefalexin is active against Gram positive pathogens such as *Streptococcus* spp. and *Staphylococcus* spp. (including penicillin-resistant strains) and Gram negative pathogens such as *Proteus mirabilis* and some strains of *Escherichia coli* and *Klebsiella* spp.

Cefalexin is active against Methicillin-susceptible staphylococci including penicillin-resistant strains not against Methicillin-resistant staphylococci.

Cefalexin is active against most beta-lactamase-producing Gram positive bacteria and has moderate activity against certain non-transferable (chromosomal) beta-lactamase-producing Gram negative Enterobacteriaceae and fastidious Gram negatives..

Resistance is plasmid-mediated or transmitted by chromosomal route.

Cefalexin has a time-dependent bactericidal activity against *Staphylococcus* spp and *Pasteurella multocida*.

CLSI cefalexin veterinary breakpoints are available for dogs in *Staphylococcus aureus*, *Staphylococcus pseudintermedius*, *Streptococci*- β -hemolytic group and *Escherichia coli* in skin and soft tissue infections. [CLSI, July 2013].

- Susceptible: $\leq 2 \mu\text{g/mL}$

- Resistant: $\geq 8 \mu\text{g/mL}$

Resistance to cefalexin may be due to one of the following mechanisms of resistance. Firstly, the production of various beta-lactamases (cephalosporinase), that inactivate the antibiotic, is the most prevalent mechanism among gram-negative bacteria. Secondly, a decreased affinity of the PBPs (penicillin-binding proteins) for beta-lactam drugs is frequently involved for beta -lactam resistant gram-positive bacteria. Lastly, efflux pumps, extruding the antibiotic from the bacterial cell, and structural changes in porins, reducing passive diffusion of the drug through the cell wall, may contribute to improve the resistant phenotype of a bacterium.

Well-known cross-resistance (involving the same resistance mechanism) exists between antibiotics belonging to the beta -lactam group due to structural similarities. It occurs with b-lactamases enzymes, structural changes in porins or variations in efflux pumps. Co-resistance (different resistance mechanisms involved) has been described in *E.coli* due to a plasmid harbouring various resistance genes.

Pharmacokinetic particulars

After single oral administration of the recommended dosage of 15 mg cefalexin per kg bodyweight to Beagle dogs, plasma concentrations were observed within 30 minutes. The plasma peak was observed at 1.33 h with a plasma concentration of 21.2 $\mu\text{g/ml}$. The bioavailability of the active was over 90%. Cefalexin was detected until 24 hours after the administration. The first urine specimen was collected within 2 to 12 hours with peak concentrations of cefalexin measured at 430 to 2758 $\mu\text{g} / \text{ml}$ within 12 hours.

After repeated oral administration of the same dosage, twice a day for 7 days, plasma peaks occurred 2 hours later with a concentration of 20µg/ml. Over the treatment period concentrations were maintained above 1 µg/ml. The mean elimination half life is 2 hours. Skin levels were around 5.8 to 6.6 µg /g 2 hours after treatment.

Pharmaceutical particulars

Excipients

Croscarmellose sodium, Silica [colloidal anhydrous], Magnesium stearate, Yeast dried, Biscuit flavour F07012, Ammonium glycyrrhizate, Macrogol 6000.

Major incompatibilities

None known

Shelf life

Therios 300 mg and 750 mg: 3 years

Shelf-life after first opening the immediate packaging: 48 hours. Any divided tablet portions remaining after 48 hours should be discarded.

Special precautions for storage

Do not store above 25 °C. Divided tablets should be stored in the blister pack.

Immediate packaging

Therios 300 mg Tablets: Polyvinylchloride blister heat sealed with an aluminium cover foil.

Pack sizes: Cardboard box with 1 blister of 10 tablets; Cardboard box with 20 blisters of 10 tablets.

Therios 750 mg Tablets: Polyvinylchloride blister heat sealed with an aluminium cover foil.

Pack sizes: Cardboard box with 1 blister of 10 tablets; Cardboard box with 20 blisters of 10 tablets.

Not all pack sizes may be marketed.

Disposal

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

Marketing Authorisation Number

Therios 300 mg Palatable Tablets for Dogs: Vm 15052/4119

Therios 750 mg Palatable Tablets for Dogs: Vm 15052/4120

Significant changes

Date of the first authorisation or date of renewal

Therios 30 mg and 750 mg: 27 February 2009

Date of revision of the text

March 2018

Any other information

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

Cephalosporins may cause sensitization (allergy) following injection, inhalation, ingestion or skin contact. Sensitivity to penicillins may lead to cross sensitivity to cephalosporin and vice versa. Allergic reactions to these substances may occasionally be serious.

1. Do not handle this product if you know you are sensitized or if you have been advised not to work with such preparations.
2. Handle this product with great care to avoid exposure, taking all recommended precautions. Wash hands after use.
3. If you develop symptoms following exposure such as skin rash you should seek medical advice and show the doctor this warning. Swellings of the face, lips or eyes or difficulty breathing are more serious symptoms and require urgent medical attention.

In the event of accidental ingestion, particularly by a child, seek medical attention and show the doctor the leaflet

Legal category

Legal category: POM-V

GTIN

GTIN description: Therios 300mg Palatable Tablets

GTIN: 03411112276004

GTIN description: Therios 750mg Palatable Tablets

GTIN: 03411112276028