1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cefaseptin 300 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substances:
Cefalexin (as cefalexin monohydrate)…… 300 mg

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate
Povidone K30
Croscarmellose sodium
Microcrystalline cellulose
Porcine liver powder
Yeast
Crospovidone
Sodium stearyl fumarate

Beige oblong tablet.
The tablet can be divided into 2 or 4 equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For the treatment of bacterial skin infections (including deep and superficial pyoderma) caused by organisms**,** including *Staphylococcus* spp., susceptible to cefalexin.

For the treatment of urinary-tract infections (including nephritis and cystitis) caused by organisms, including *Escherichia coli,* susceptible to cefalexin.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance, to other cephalosporins, to other substances of the β-lactam group or to any of the excipients.

Do not use in known cases of resistance to cephalosporins or penicillins.

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

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

The need for systemic antibiotics compared with non-antibiotic alternatives for the treatment of superficial pyoderma should be carefully considered by the responsible veterinarian.

As with other antibiotics which are excreted mainly by the kidneys, systemic accumulation may occur in the body when renal function is impaired. In case of known renal insufficiency, the dose should be reduced and antimicrobials known to be nephrotoxic should not be administered concurrently.

This veterinary medicinal product should not be used to treat puppies of less than 1 kg of bodyweight.

Use of the veterinary medicinal product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about the susceptibility of the target bacteria.

Use of the veterinary medicinal 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 cephalosporins and penicillins, due to the potential for cross-resistance.

Official, national and regional antimicrobial policies should be taken into account when the veterinary medicinal product is used.

Pseudomonas aeruginosa is known for intrinsic (or natural) resistance to cefalexin.

The tablets are flavoured (presence of porcine liver powder). In order to avoid accidental ingestion, store tablets out of reach of the animals.

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

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-reactions to cephalosporin and vice versa. Allergic reactions to these substances may occasionally be serious.

1. Do not handle this veterinary medicinal product if you know you are sensitised or if you have been advised not to work with such preparations.
2. Handle this veterinary medicinal 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 immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty in breathing are more-serious symptoms and require urgent medical attention.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10 000 animals treated):	Hypersensitivity reaction[1]
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Nausea, vomiting, diarrhoea

[1] *In this case, treatment should be discontinued*

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 package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Pregnancy and lactation:

Laboratory studies have not produced any evidence of teratogenic effects in mice (up to 400 mg cefalexin/kg bw/day) and rats (up to 1200 mg cefalexin/kg bw/day). In mice, maternal effects and foetotoxicity were observed from the lowest dose tested (100 mg cefalexin/kg bw/day). In rats, there is evidence of foetotoxicity at 500 mg cefalexin/kg bw/day and maternal effects from the lowest dose tested (300 mg cefalexin/kg bw/day).

Use only according to the benefit-risk assessment by the responsible veterinarian

3.8 Interaction with other medicinal products and other forms of interaction

In order to ensure efficacy, the veterinary medicinal product should not be used in combination with bacteriostatic antibiotics (macrolides, sulfonamides and tetracyclines). Concurrent use of first generation cephalosporins with aminoglycoside antibiotics or some diuretics such as furosemide can enhance nephrotoxicity risks.
Concomitant use with such active substances should be avoided.

3.9 Administration routes and dosage

Oral use.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

15 mg of cefalexin per kg of bodyweight twice daily (equivalent to 30 mg per kg of bodyweight per day) corresponding to one tablet per 20 kg of bodyweight twice daily, for a duration of:
- 14 days in case of urinary-tract infection
- at least 15 days in case of superficial bacterial infection of the skin.
- at least 28 days in case of deep bacterial infection of the skin.

The veterinary medicinal product may be crushed or added to food if necessary.

In severe or acute conditions, except in cases of known renal insufficiency (see section 3.5), the dose may be doubled.

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

Studies on animals with up to 5 times the recommended twice daily dosage of 15 mg cefalexin/kg have been performed.

Adverse reactions that may occur at the recommended dose (nausea, vomiting, and/or diarrhea) are expected in the case of overdose. In the event of overdose, 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 periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code :

QJ01DB01

4.2 Pharmacodynamics

Cefalexin is a time-dependent bactericidal antibiotic that acts by inhibiting the nucleopeptide synthesis of the bacterial wall.
Cephalosporins interfere with the enzymes of transpeptidation making it unable to cross-link the peptidoglycans of the bacterial cell wall. The glycan cross-linking is essential for the cell to build its cell wall. Inhibition of the biosynthesis results to a weakened cell wall, which eventually ruptures to osmotic pressure. The combined action results in cell lysis and filament formation.

Cefalexin is active against a wide range of Gram-positive (e.g. *Staphylococcus* spp.) and Gram-negative (e.g. *Escherichia coli*) aerobic bacteria.

The following breakpoints are recommended by the CLSI (VET08, 4th edition, August 2019) in dogs:

In dogs for skin and soft tissue infections:

Bacterial species	Susceptible	Resistant
Staphylococcus aureus *Staphylococcus pseudintermedius*	≤ 2	≥ 4
Streptococcus spp and *E. coli*	≤ 2	≥ 8

In dogs for urinary tract infections:

Bacterial species	Susceptible	Resistant
E. coli *Klebsiella pneumoniae* *Proteus mirabilis*	≤ 16	≥ 32

MIC data for the use of Cefaseptin in dogs with skin and soft tissues infections and with urinary tract infections.
Data were collected between 2011 and 2017.

Bacterial species	***Range of MIC (mg/L)***	***MIC_{50} (mg/L)***	***MIC_{90} (mg/L)***
Dermatological infections			
***Staphylococcus* spp.**[a]	*0.25-512*	*0.993*	*12.435*
Staphylococcus aureus[b]	*1-512*	*2.160*	*153.987*
Coagulase negative staphylococcus[c]	*0.25-64*	*0.989*	*14.123*
Staphylococcus pseudintermedius[b]	*0.5-512*	*0.768*	*5.959*
***Streptococcus* spp.**[d]	*0.06-0.5*	*0.155*	*0.234*
Streptococcus canis[d]	*0.06-0.5*	*0.146*	*0.226*
Streptococcus dysgalactiae[d]	*0.25-0.5*	*0.185*	*0.354*
Escherichia coli[b]	*4-512*	*5.481*	*11.314*
Pasteurella multocida[b]	*0.12-4*	*1.373*	*1.877*
Urinary tract infections			
Proteus mirabilis[b]	*8-512*	*6.498-12.491*	*12.553-207.937*
Klebsiella pneumoniae[b]	*2-512*	*3.564*	*362.039*
E. coli[b]	*4-512*	*5.022-5.82*	*7.671-13.929*

a: period 2011-2017; b: period 2011-2015; c: period 2016-2017; d: period 2012-2015

Resistance to cefalexin can be due to one of the following mechanisms of resistance. Firstly, the production of cephalosporinases, that inactivate the antibiotic by hydrolysis of the β-lactam ring, is the most prevalent mechanism among Gram-negative bacteria. This resistance is transmitted by plasmid or chromosomally. 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 beta-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. *Pseudomonas aeruginosa* is known for resistance to cefalexin.

4.3 Pharmacokinetics

After single oral administration of the recommended dosage of 15 mg of cefalexin per kg of bodyweight to Beagle dogs, plasma concentrations were observed within 30 minutes. The plasma peak was observed at 1.3 hour with a plasma concentration of 18.2 µg/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 µg/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 20 µg/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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

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: 48 hours.

5.3 Special precautions for storage

Store in the original package.
Return any part used tablet to the opened blister-pack and use within 48 hours.

5.4 Nature and composition of immediate packaging

PVC/aluminium/OPA – PVC blister
Cardboard box of 1 blister of 10 tablets
Cardboard box of 10 blisters of 10 tablets
Cardboard box of 25 blisters of 10 tablets

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 AUTHORISATION HOLDER

Vetoquinol Ireland Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA10983/044/002

8. DATE OF FIRST AUTHORISATION

15/01/2016

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

11/05/2026

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).