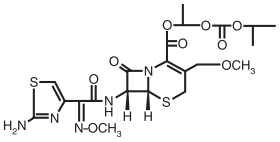
Cefpoderm®
(cefpodoxime proxetil tablets)

For Oral Use in Dogs Only

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:
Cefpodoxime proxetil is an orally administered, extended spectrum, semi-synthetic cephalosporin antibiotic.
The chemical name is: (+/-)-1-Hydroxyethyl(+)-(6R,7R)-7-[2-(2-amino-4-thiazolyl)glyoxylamido]-3-methoxymethyl)-8-oxo-5-thia -1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, 7^2-(Z)-(O-methyloxime), isopropyl carbonate (ester) [87239-81-4].

Cefpodoxime Proxetil Chemical Structure:



Cefpodoxime proxetil is a prodrug; its active metabolite is cefpodoxime. All doses of Cefpoderm (cefpodoxime proxetil tablets) are expressed in terms of the active cefpodoxime moiety.
Cefpoderm is available as:
100 mg Tablet, each yellow, elliptical, scored tablet contains cefpodoxime proxetil equivalent to 100 mg of cefpodoxime.
200 mg Tablet, each orange, oblong, tablet contains cefpodoxime proxetil equivalent to 200 mg of cefpodoxime.

INDICATION:
Cefpoderm is indicated for the treatment of skin infections (wounds and abscesses) in dogs caused by susceptible strains of *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, ß hemolytic), *Escherichia coli*, *Pasteurella multocida*, and *Proteus mirabilis*.

DOSAGE AND ADMINISTRATION:
Dose range: The dose range of Cefpoderm is 5-10 mg/kg (2.3-4.5 mg/lb) body weight, administered orally, once a day. The dose may be given with or without food. The determination of dosage for any particular patient must take into consideration such factors as the severity and nature of the infection, the susceptibility of the causative organisms, and the integrity of the patient's host-defense mechanisms. Obtain a sample of the pathogenic organism for culture and sensitivity testing prior to beginning antimicrobial therapy. Once results become available, continue with appropriate therapy.
Duration: Cefpoderm should be administered once daily for 5-7 days or for 2-3 days beyond the cessation of clinical signs, up to a maximum of 28 days.
Treatment of acute infections should not be continued for more than 3-4 days if no response to therapy is seen.
Dosing Charts: For daily oral administration of Cefpoderm at 5 mg/kg (Table 1) and 10 mg/kg (Table 2).

Table 1. Dose Table for Cefpoderm at 5 mg/kg Total Daily Dosage

Weight of Dog (lbs)						
Daily Dose		**22**	**44**	**66**	**88**	**132**
No. of 100 mg tablets		0.5	1	1.5		1
No. of 200 mg tablets					1	1
Weight of Dog (kgs)						
Daily Dose		**10**	**20**	**30**	**40**	**60**
No. of 100 mg tablets		0.5	1	1.5		1
No. of 200 mg tablets					1	1

Table 2. Dose Table for Cefpoderm at 10 mg/kg Total Daily Dosage

Weight of Dog (lbs)						
Daily Dose	**11**	**22**	**44**	**66**	**88**	**132**
No. of 100 mg tablets	0.5	1		1		
No. of 200 mg tablets			1	1	2	3
Weight of Dog (kgs)						
Daily Dose	**5**	**10**	**20**	**30**	**40**	**60**
No. of 100 mg tablets	0.5	1		1		
No. of 200 mg tablets			1	1	2	3

CONTRAINDICATIONS:
Cefpodoxime proxetil is contraindicated in dogs with known allergy to cefpodoxime or to the ß-lactam (penicillins and cephalosporins) group of antibiotics.

WARNINGS:
Not for human use. Keep this and all drugs out of reach of children. Antimicrobial drugs, including penicillins and cephalosporins, can cause allergic reactions in sensitized individuals. To minimize the possibility of allergic reactions, those handling such antimicrobials, including cefpodoxime, are advised to avoid direct contact of the product with the skin and mucous membranes.

PRECAUTIONS:
The safety of cefpodoxime proxetil in dogs used for breeding, pregnant dogs, or lactating bitches has not been demonstrated. As with other cephalosporins, cefpodoxime proxetil may occasionally induce a positive direct Coombs' test.

ADVERSE REACTIONS:
A total of 216 dogs of various breeds and ages ranging from 2 months to 15 years were included in the field study safety analysis. The following table shows the number of dogs displaying each clinical observation.

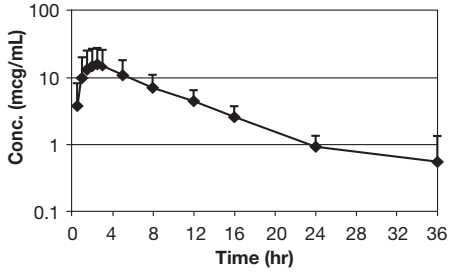
Table 3. Abnormal Health Findings in the U.S. Field Study[1]

Clinical Observation	Cefpodoxime Proxetil (n=118)	Active Control (n=98)
Vomiting	2	4
Diarrhea	1	1
Increased water drinking	0	2
Decreased appetite	1	1

[1]Dogs may have experienced more than one of the observations during the study.
To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS) contact Dechra at [866] 933-2472.
For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae

CLINICAL PHARMACOLOGY:
Pharmacokinetics/Pharmacodynamics: Cefpodoxime proxetil is a prodrug that is absorbed from and de-esterified in the gastrointestinal tract to its active metabolite, cefpodoxime. Following oral administration to fasting Beagles, oral bioavailability was 63.1 ± 5.3%.

Figure 1. Canine Plasma Concentration of Cefpodoxime After a Single Oral Dose of 10 mg/kg Cefpodoxime Proxetil Tablets



Cefpodoxime is distributed in the body with an apparent volume of distribution of 151 ± 27 mL/kg. Like other β-lactam antibiotics, cefpodoxime is eliminated from the body primarily in the urine, with an apparent elimination half-life of approximately 5-6 hours after oral administration. This is similar to the 4.7 hour apparent elimination half-life observed after intravenous dosing.
Following intravenous administration of 10 mg/kg, the average total body clearance (Cl_B) was 22.7 ± 4.19 mL/hr/kg.

Table 4. Summary of Pharmacokinetic Parameters Obtained after a Single Oral Dose of 10 mg Cefpodoxime/kg BW, Administered as a Tablet

PK Parameter	Unit	Tablet (SD)
$AUC_{0-\infty}$	mcg·hr/mL	145 (77.6)
$AUC_{0\text{-}LOQ}$	mcg·hr/mL	142 (77.5)
Maximum concentration (C_{max})	mcg/mL	16.4 (11.8)
Terminal plasma elimination half-life ($t_{1/2,z}$)	hr	5.61 (1.15)
Time of maximum concentration (t_{max})	hr	2.21 (0.542)
Mean residence time ($MRT_{0-\infty}$)	hr	9.21 (1.97)

Microbiology: Like other β-lactam antibiotics, cefpodoxime exerts its inhibitory effect by interfering with bacterial cell wall synthesis. This interference is primarily due to its covalently binding to the penicillin-binding proteins (PBPs) (i.e. transpeptidase and/or carboxypeptidase), which are essential for synthesis of the bacterial cell wall. Therefore, cefpodoxime is bactericidal. Cefpodoxime is stable in the presence of many common β-lactamase enzymes. As a result, many organisms resistant to other β-lactam antibiotics (penicillins and some cephalosporins) due to the production of β-lactamases may be susceptible to cefpodoxime.

Cefpodoxime has a broad spectrum of clinically useful antibacterial activity that includes staphylococci, streptococci, and Gram-negative species (including *Pasteurella*, *Escherichia*, and *Proteus*).
The compound is not active against most obligate anaerobes, *Pseudomonas* spp., or enterococci. The minimum inhibitory concentrations (MICs) for cefpodoxime against Gram-positive and Gram-negative pathogens isolated from canine skin infections (wounds and abscesses) in a 2002 U.S. field study are presented in Table 5. All MICs were determined in accordance with the National Committee for Clinical Laboratory Standards (NCCLS). Appropriate quality control (QC) ranges for *in vitro* susceptibility testing are presented in Table 6.

Table 5. Cefpodoxime Minimum Inhibitory Concentration Values (mcg/mL) from a 2002 Field Study Evaluating Skin Infections (wounds and abscesses) of Canines in the United States

Organism*	# of Isolates	MIC_{50}	MIC_{90}	Range
Staphylococcus pseudintermedius	118	0.12	0.50	0.12->32.0
Streptococcus canis (group G, β hemolytic)	33	≤0.03	≤0.03	≤0.03†
Escherichia coli	41	0.25	0.50	0.12->32.0
Pasteurella multocida	32	≤0.03	≤0.03	≤0.03-0.12
Proteus mirabilis	14	≤0.03	0.06	≤0.03-0.06
Staphylococcus aureus	19	2.0	2.0	0.12-2.0

†No Range, all isolates yielded the same value.
*Veterinary specific interpretive criteria have not been established for the above listed canine pathogens by the NCCLS at this time.

Table 6. Acceptable Quality Control Ranges for Cefpodoxime

QC ATCC strain	KB Disk Diffusion Method		Broth Micro-dilution Method
	Drug concentration	Zone diameter	MIC
Escherichia coli 25922	10 mcg	23-28 mm[a]	0.25-1 mcg/mL[a]
Staphylococcus aureus 25923	10 mcg	19-25 mm[a]	
Staphylococcus aureus 29213			1-8 mcg/mL[a]
Streptococcus pneumoniae 49619	10 mcg	28-34 mm[b]	0.03-0.12 mcg/mL[b]

[a] These ranges are for quality control strains used to monitor accuracy of minimum inhibitory concentrations (MICs) of non-fastidious organisms using cation-adjusted Mueller-Hinton agar or broth medium. The dilution range should encompass the QC ranges of these strains in the broth micro-dilution method.

[b] These ranges are for quality control strains used to monitor accuracy of minimum inhibitory concentrations (MICs) of fastidious organisms. When susceptibility testing is performed for *Streptococcus canis* (group G, β hemolytic), *Streptococcus pneumoniae* ATCC 49619 should be included as a QC strain in the presence of 5% lysed sheep blood (KB disk diffusion method) or 2.5% lysed horse blood (broth micro-dilution method).

EFFECTIVENESS:
The clinical effectiveness of cefpodoxime proxetil tablets was established in a multi-location (23 site) field study. In this study, 216 dogs with infected wounds or abscesses were treated with either cefpodoxime proxetil (n=118) once daily at 5 mg/kg (2.3 mg/lb) body weight or with an active control antibiotic (n=98) administered twice daily for 5-7 days. In this study, cefpodoxime proxetil was considered noninferior to the active control (88.7% versus 88.4% respectively) in the treatment of canine skin infections (wounds and abscesses) caused by susceptible strains of *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, β hemolytic), *Escherichia coli*, *Pasteurella multocida*, and *Proteus mirabilis*.

ANIMAL SAFETY:
In target animal safety studies, cefpodoxime was well tolerated at exaggerated daily oral doses of 100 mg/kg/day (10 times the maximum label dose) for 13 weeks in adult dogs and for 28 days in puppies (18-23 days of age). Therefore, once daily administration of cefpodoxime oral tablets at the maximum labeled dose of 10 mg/kg for up to 28 days was shown to be safe in adult dogs and puppies.

Blood dyscrasia including neutropenias, may be seen following high doses of cephalosporins. Cephalosporin administration should be discontinued in such cases.

STORAGE INFORMATION:
Store at controlled room temperature 68-77°F (20-25°C). Replace cap securely after each opening.

HOW SUPPLIED:
Cefpoderm (cefpodoxime proxetil tablets) is available in the following strengths (cefpodoxime equivalent), colors, and sizes:
100 mg (yellow, scored, elliptical, debossed with PV on one side, 17 on the other side) Bottles of 100
NDC 17033-431-10
200 mg (orange, oblong, debossed with PV on one side, 18 on the other side) Bottles of 100
NDC 17033-432-10

Approved by FDA under ANADA # 200-543

Manufactured for:
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