

SIMPLICEF- cefpodoxime proxetil tablet
Zoetis Inc.

SIMPLICEF®
(cefpodoxime proxetil)

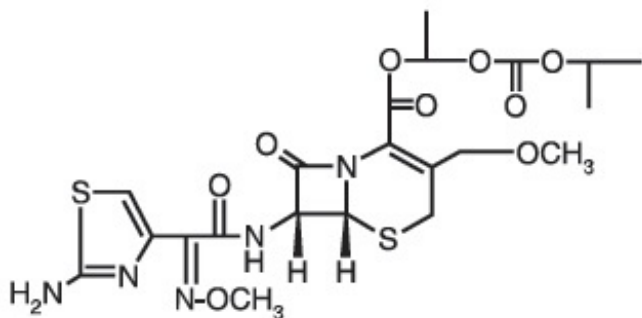
For Oral Use In Dogs Only

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, 7Z-(Z)- (Omethylloxime), isopropyl carbonate (ester) [87239-81-4].

Cefpodoxime proxetil Chemical Structure:



Cefpodoxime proxetil is a prodrug; its active metabolite is cefpodoxime. All doses of SIMPLICEF (cefpodoxime proxetil) tablets are expressed in terms of the active cefpodoxime moiety. SIMPLICEF is available as:

100 mg Tablet, each reddish-orange, elliptical, scored tablet contains cefpodoxime proxetil equivalent to 100 mg of cefpodoxime.

200 mg Tablet, each light orange, round rectangle, scored tablet contains cefpodoxime proxetil equivalent to 200 mg of cefpodoxime.

INDICATION

SIMPLICEF tablets are indicated for the treatment of skin infections (wounds and abscesses) in dogs caused by susceptible strains of *Staphylococcus intermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, β hemolytic), *Escherichia coli*, *Pasteurella multocida*, and *Proteus mirabilis*.

DOSAGE AND ADMINISTRATION

Dose range: The dose range of SIMPLICEF (cefpodoxime proxetil) tablets 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: SIMPLICEF tablets 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 SIMPLICEF at 5 mg/kg (Table 1) and 10 mg/kg (Table 2).

Table 1. Dose Table for SIMPLICEF Tablets 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 SIMPLICEF Tablets 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 β -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*

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

* Dogs may have experienced more than one of the observations during the study.

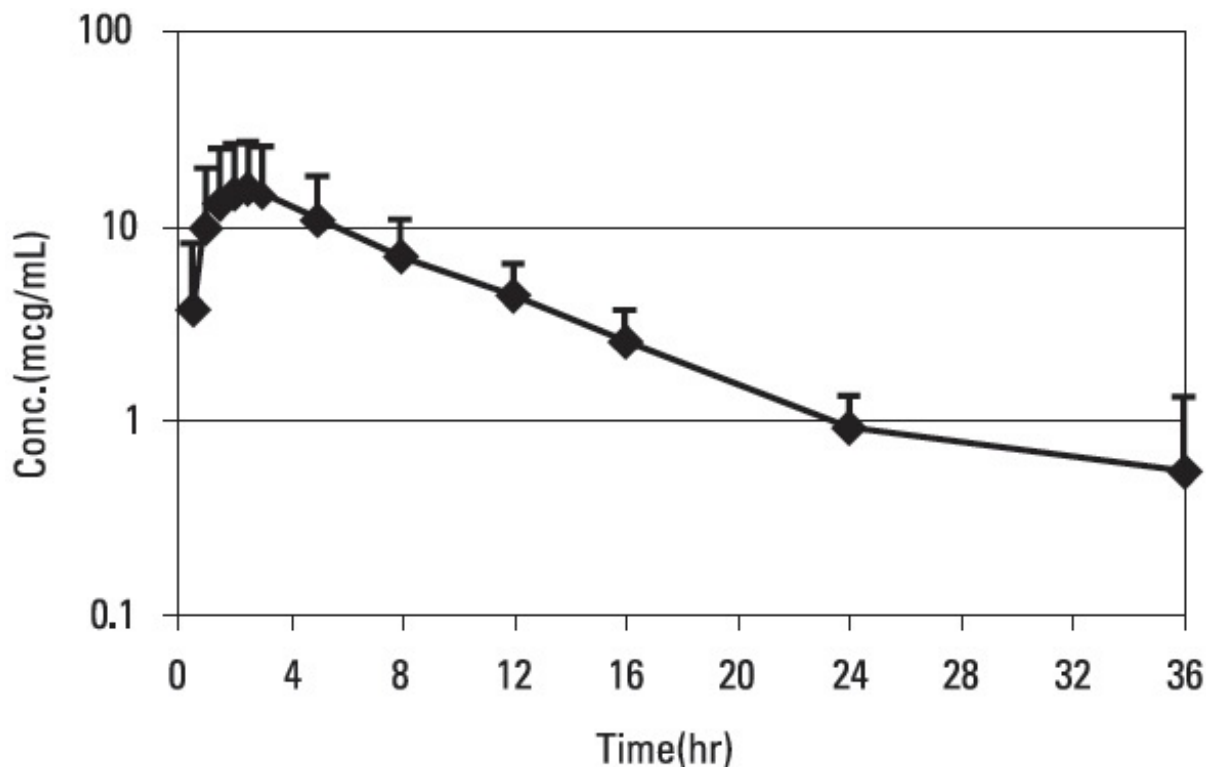
To report a suspected adverse reaction call 1-888-963-8471.

To request a material safety data sheet (MSDS) for SIMPLICEF tablets, call 1-888-963-8471.

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 $63.1 \pm 5.3\%$.

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-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
<i>Staphylococcus intermedius</i>	118	0.12	0.50	0.12->32.0
<i>Streptococcus canis</i> (group G, β hemolytic)	33	≤0.03	≤0.03	≤0.03 [†]
<i>Escherichia coli</i>	41	0.25	0.50	0.12->32.0
<i>Pasteurella multocida</i>	32	≤0.03	≤0.03	≤0.03-0.12
<i>Proteus mirabilis</i>	14	≤0.03	0.06	≤0.03-0.06
<i>Staphylococcus aureus</i>	19	2.0	2.0	0.12-2.0

* Veterinary specific interpretive criteria have not been established for the above listed canine pathogens by the NCCLS at this time.

† No Range, all isolates yielded the same value.

Table 6. Acceptable Quality Control Ranges for Cefpodoxime

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

* 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.

† 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 SIMPLICEF (cefpodoxime proxetil) was established in a multi-location (23 site) field study. In this study, 216 dogs with infected wounds or abscesses were treated with either SIMPLICEF (n=118) once daily at 5 mg/kg (2.3 mg/lb) body weight or with a active control antibiotic (n=98) administered twice daily for 5-7 days. In this study, SIMPLICEF was considered noninferior to the active control (88.7% versus 88.4% respectfully) in the treatment of canine skin infections (wounds and abscesses) caused by susceptible strains of *Staphylococcus intermedius*, *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 tablets at controlled room temperature 20° to 25°C (68° to 77°F). Replace cap securely after each opening.

HOW SUPPLIED

SIMPLICEF tablets are available in the following strengths (cefpodoxime equivalent), colors, and sizes:

100 mg (reddish-orange, elliptical, scored, debossed with 5228)

Bottles of 100

Bottles of 250

200 mg (light orange, round rectangle, scored, debossed with 5229)

Bottles of 100

Bottles of 250

NADA # 141-232, Approved by FDA

Manufactured by:

Sandoz

Kundl, Austria

Product of India

Distributed by:

Zoetis Inc.

Kalamazoo, MI 49007

Revised June 2013

46104787

PRINCIPAL DISPLAY PANEL - 100 mg Tablet Bottle Label

SIMPLICEF[®]
(cefpodoxime proxetil)

100 mg

100 TABLETS

Antimicrobial For Oral Use
in Dogs Only

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

NADA# 141-232, Approved by FDA

zoetis

SIMPLICEF[®]
(cefpodoxime proxetil)

100 mg

100 TABLETS
Antimicrobial For Oral Use
in Dogs Only

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

NADA# 141-232, Approved by FDA

zoetis

Dosage: 5 - 10 mg/kg
(2.3 - 4.5 mg/lb) body weight,
administered orally, once daily.
**See package insert for
complete product information.**
Warning: Not for human use.
Keep this and all drugs out of
reach of children. Store at
controlled room temperature
20° to 25°C (68° to 77°F).
Dispense in tight, light-
resistant container. Replace
cap securely after each
opening.

Each tablet contains:
cefpodoxime proxetil
equivalent to 100 mg
cefpodoxime.

Manufactured by:
Sandoz
Kundl, Austria

Product of India

Distributed by:
Zoetis Inc.
Kalamazoo, MI 49007

FPO: UPC

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EXP LOT

PRINCIPAL DISPLAY PANEL - 200 mg Tablet Bottle Label

SIMPLICEF[®]
(cefpodoxime proxetil)

200 mg

100 TABLETS

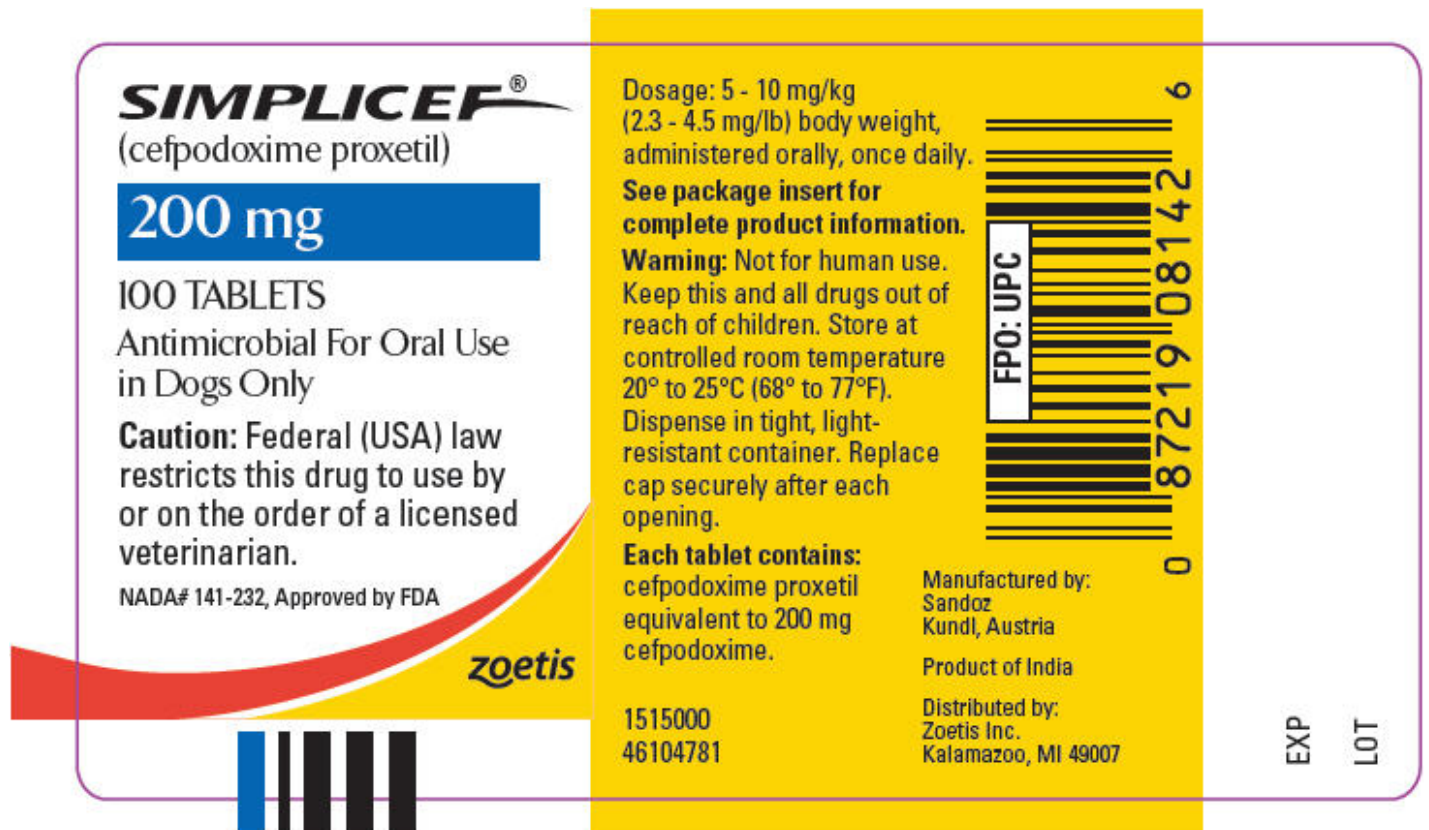
Antimicrobial For Oral Use
in Dogs Only

Caution: Federal (USA) law
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veterinarian.

NADA# 141-232, Approved by FDA

zoetis



SIMPLICEF[®]
(cefpodoxime proxetil)

200 mg

100 TABLETS
Antimicrobial For Oral Use
in Dogs Only

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

NADA# 141-232, Approved by FDA

zoetis

Dosage: 5 - 10 mg/kg (2.3 - 4.5 mg/lb) body weight, administered orally, once daily. See package insert for complete product information.

Warning: Not for human use. Keep this and all drugs out of reach of children. Store at controlled room temperature 20° to 25°C (68° to 77°F). Dispense in tight, light-resistant container. Replace cap securely after each opening.

Each tablet contains: cefpodoxime proxetil equivalent to 200 mg cefpodoxime.

Manufactured by: Sandoz Kundl, Austria
Product of India
Distributed by: Zoetis Inc. Kalamazoo, MI 49007

1515000
46104781

FPO: UPC
0 87219 08142 6

EXP
LOT

SIMPLICEF

cefpodoxime proxetil tablet

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:54771-5228
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
cefpodoxime proxetil (UNII: 2TB00A1Z7N) (cefpodoxime - UNII:7R4F94TVGY)	cefpodoxime	100 mg

Product Characteristics

Color	ORANGE (reddish-orange)	Score	2 pieces
Shape	OVAL (elliptical)	Size	11mm
Flavor		Imprint Code	5228
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54771-5228-1	100 in 1 BOTTLE		
2	NDC:54771-5228-2	250 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141232	07/22/2004	

SIMPLICEF

cefepodoxime proxetil tablet

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:54771-5229
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
cefepodoxime proxetil (UNII: 2TB00A1Z7N) (cefepodoxime - UNII:7R4F94TVGY)	cefepodoxime	200 mg

Product Characteristics

Color	ORANGE (reddish-orange)	Score	2 pieces
Shape	OVAL (elliptical)	Size	15mm
Flavor		Imprint Code	5228
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54771-5229-1	100 in 1 BOTTLE		
2	NDC:54771-5229-2	250 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141232	07/22/2004	

Labeler - Zoetis Inc. (828851555)

Establishment

Name	Address	ID/FEI	Business Operations
Sandoz GmbH		300220969	MANUFACTURE

Establishment

Name	Address	ID/FEI	Business Operations
Sandoz Private Limited		676190116	API MANUFACTURE

Revised: 3/2014

Zoetis Inc.