CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: NDA 50739

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CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 50739

Trade Name: Omnicef Capsules

Generic Name: (cefdinir)

Sponsor: Parke-Davis

Approval Date: December 4, 1997

Indication: Provides for treatment of patients with community-acquired pneumonia, acute exacerbations of chronic bronchitis, acute bacterial otitis media, acute maxillary sinusitis, pharyngitis/tonsillitis, and uncomplicated skin and skin structure infections

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 50739

APPROVAL LETTER

NDA 50-739
NDA 50-749

DEC 4 1997

Parke-Davis
Attention: Drusilla Scott, Ph.D.
Director, Worldwide Regulatory Affairs
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Dr. Scott:

Please refer to your new drug applications dated September 3, 1996 (NDA 50-739) and December 30, 1996 (NDA 50-749), received September 4, 1996 and December 31, 1996, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Omnicef (cefdinir) Capsules and Powder for Oral Suspension. We note that these products are subject to the exception provisions of Section 125 (2) of Title 1 of the FDA Modernization Act of 1997.

We acknowledge receipt of your submissions dated September 24, November 13, December 16, and December 31, 1996; and January 31, February 21, March 10, March 31, April 25, May 6, May 9, June 2, June 11, June 23, June 30, July 1, July 7, July 8, July 9, July 21, July 22, August 8, August 14, August 27, August 29, September 10, September 18, September 29, October 7, October 16, October 20, October 27, November 7, November 18, November 25, and December 3, 1997. The original User Fee goal date for these applications was September 4, 1997 (NDA 50-739) and December 31, 1997 (NDA 50-749). Your submission of June 23, 1997 extended the User Fee goal date for NDA 50-739 to December 4, 1997.

These new drug applications provide for treatment of patients with community-acquired pneumonia, acute exacerbations of chronic bronchitis, acute bacterial otitis media, acute maxillary sinusitis, pharyngitis/tonsillitis, and uncomplicated skin and skin structure infections.

We have completed the review of these applications, including the submitted draft labeling, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the enclosed marked-up draft labeling. Accordingly, these applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up draft labeling. Marketing the products with FPL that is not identical to this draft labeling may render the products misbranded and unapproved new drugs.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL

PRINTED LABELING" for approved NDA's 50-739, 50-749. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drugs become available, revision of that labeling may be required.

We remind you of your Phase 4 commitments specified in your submissions dated October 20 and December 3, 1997. These commitments, along with any completion dates agreed upon, are listed below.

Protocols, data, and final reports should be submitted to your IND for these products and a copy of the cover letters sent to these NDA's. Should an IND not be required to meet your Phase 4 commitments, please submit protocol, data, and final reports to these NDA's as correspondences. In addition, we request under 21 CFR 314.81(b)(2)(vii) that you include in your annual report to these applications, a status summary of each commitment. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

In addition, please submit three copies of the introductory promotional material that you propose to use for these products. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to the Division of Anti-Infective Drug Products and two copies of both the promotional material and the package inserts directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications,
HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Beth Duvall-Miller, Project Manager, at (301) 827-2120.

Sincerely yours,

/S/

David Feigal, M.D., M.P.H.
Acting Office Director
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

ENCLOSURES

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 50739

FINAL PRINTED LABELING

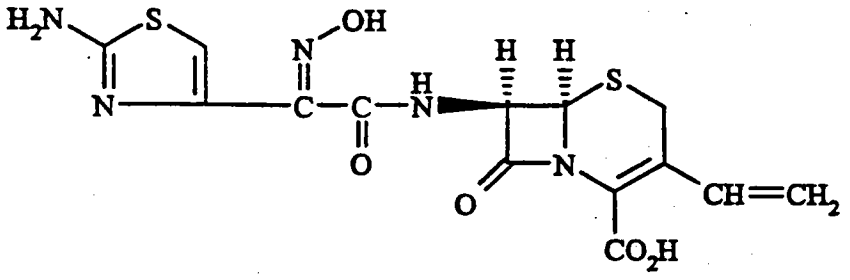
OMNICEF® (Cefdinir) CAPSULES
OMNICEF® (Cefdinir) FOR ORAL SUSPENSION
For Oral Use Only

US Package Insert

December 3, 1997

DESCRIPTION

OMNICEF® (cefdinir) Capsules and OMNICEF® (cefdinir) for Oral Suspension contain the active ingredient cefdinir, an extended-spectrum, semisynthetic cephalosporin, for oral administration. Chemically, cefdinir is [6R-[6α,7β(Z)]]-7-[[(2-amino-4-thiazolyl)-(hydroxyimino)acetyl]amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. Cefdinir is a white to slightly brownish-yellow solid. It is slightly soluble in dilute hydrochloric acid and sparingly soluble in 0.1 M pH 7.0 phosphate buffer. The empirical formula is $C_{14}H_{13}N_5O_5S_2$ and the molecular weight is 395.42. Cefdinir has the structural formula shown below:



OMNICEF Capsules contain 300 mg cefdinir and the following inactive ingredients: carboxymethylcellulose calcium, NF; polyoxyl 40 stearate, NF; magnesium stearate, NF; and silicon dioxide, NF. The capsule shells contain FD&C Blue #1; FD&C Red #40; D&C Red #28; titanium dioxide, NF; gelatin, NF; and sodium lauryl sulfate, NF.

OMNICEF for Oral Suspension, after reconstitution, contains 125 mg cefdinir per 5 mL and the following inactive ingredients: sucrose, NF; citric acid, USP; sodium citrate, USP; sodium benzoate, NF; xanthan gum, NF; guar gum, NF; artificial strawberry and cream flavors; silicon dioxide, NF; and magnesium stearate, NF.

CLINICAL PHARMACOLOGY

Pharmacokinetics and Drug Metabolism

Absorption:

Oral Bioavailability: Maximal plasma cefdinir concentrations occur 2 to 4 hours postdose following capsule or suspension administration. Plasma cefdinir concentrations increase with dose, but the increases are less than dose-proportional from 300 mg (7 mg/kg) to 600 mg (14 mg/kg). Following administration of suspension to healthy adults, cefdinir bioavailability is 120% relative to capsules. Estimated bioavailability of cefdinir capsules is 21% following administration of a 300 mg capsule dose, and 16% following administration of a 600 mg capsule dose. Estimated absolute bioavailability of cefdinir suspension is 25%.

Effect of Food: Although the rate (C_{max}) and extent (AUC) of cefdinir absorption from the capsules are reduced by 16% and 10%, respectively, when given with a high-fat meal, the magnitude of these reductions is not likely to be clinically significant. Therefore, cefdinir may be taken without regard to food.

Cefdinir Capsules: Cefdinir plasma concentrations and pharmacokinetic parameter values following administration of single 300- and 600-mg oral doses of cefdinir to adult subjects are presented in the following table:

Mean (±SD) Plasma Cefdinir Pharmacokinetic Parameter Values
Following Administration of Capsules to Adult Subjects

Dose	C_{max} (μg/mL)	t_{max} (hr)	AUC (μg·hr/mL)
300 mg	1.60	2.9	7.05
	(0.55)	(0.89)	(2.17)
600 mg	2.87	3.0	11.1
	(1.01)	(0.66)	(3.87)

Cefdinir Suspension: Cefdinir plasma concentrations and pharmacokinetic parameter values following administration of single 7- and 14-mg/kg oral doses of cefdinir to pediatric subjects (age 6 months-12 years) are presented in the following table:

Mean (±SD) Plasma Cefdinir Pharmacokinetic Parameter Values Following Administration of Suspension to Pediatric Subjects

Dose	C_{max} (μg/mL)	t_{max} (hr)	AUC (μg·hr/mL)
7 mg/kg	2.30	2.2	8.31
	(0.65)	(0.6)	(2.50)
14 mg/kg	3.86	1.8	13.4
	(0.62)	(0.4)	(2.64)

Multiple Dosing: Cefdinir does not accumulate in plasma following once- or twice-daily administration to subjects with normal renal function.

Distribution: The mean volume of distribution (Vd_{area}) of cefdinir in adult subjects is 0.35 L/kg (±0.29); in pediatric subjects (age 6 months-12 years), cefdinir Vd_{area} is 0.67 L/kg (±0.38). Cefdinir is 60% to 70% bound to plasma proteins in both adult and pediatric subjects; binding is independent of concentration.

Skin Blister: In adult subjects, median (range) maximal blister fluid cefdinir concentrations of 0.65 (0.33-1.1) and 1.1 (0.49-1.9) μg/mL were observed 4 to 5 hours following administration of 300- and 600-mg doses, respectively. Mean (±SD) blister C_{max} and AUC(0-∞) values were 48% (±13) and 91% (±18) of corresponding plasma values.

Tonsil Tissue: In adult patients undergoing elective tonsillectomy, respective median tonsil tissue cefdinir concentrations 4 hours after administration of single 300- and 600-mg doses were 0.25 (0.22-0.46) and 0.36 (0.22-0.80) μg/g. Mean tonsil tissue concentrations were 24% (±8) of corresponding plasma concentrations.

Sinus Tissue: In adult patients undergoing elective maxillary and ethmoid sinus surgery, respective median sinus tissue cefdinir concentrations 4 hours after administration of

single 300- and 600-mg doses were <0.12 (<0.12-0.46) and 0.21 (<0.12-2.0) μg/g. Mean sinus tissue concentrations were 16% (±20) of corresponding plasma concentrations.

Lung Tissue: In adult patients undergoing diagnostic bronchoscopy, respective median bronchial mucosa cefdinir concentrations 4 hours after administration of single 300- and 600-mg doses were 0.78 (<0.06-1.33) and 1.14 (<0.06-1.92) μg/mL, and were 31% (±18) of corresponding plasma concentrations. Respective median epithelial lining fluid concentrations were 0.29 (<0.3-4.73) and 0.49 (<0.3-0.59) μg/mL, and were 35% (±83) of corresponding plasma concentrations.

Middle Ear Fluid: In 14 pediatric patients with acute bacterial otitis media, respective median middle ear fluid cefdinir concentrations 3 hours after administration of single 7- and 14-mg/kg doses were 0.21 (<0.09-0.94) and 0.72 (0.14-1.42) μg/mL. Mean middle ear fluid concentrations were 15% (±15) of corresponding plasma concentrations.

CSF: Data on cefdinir penetration into human cerebrospinal fluid are not available.

Metabolism and Excretion: Cefdinir is not appreciably metabolized. Activity is primarily due to parent drug. Cefdinir is eliminated principally via renal excretion with a mean plasma elimination half-life ($t_{½}$) of 1.7 (±0.6) hours. In healthy subjects with normal renal function, renal clearance is 2.0 (±1.0) mL/min/kg, and apparent oral clearance is 11.6 (±6.0) and 15.5 (±5.4) mL/min/kg following doses of 300 and 600 mg, respectively. Mean percent of dose recovered unchanged in the urine following 300- and 600-mg doses is 18.4% (±6.4) and 11.6% (±4.6), respectively. Cefdinir clearance is reduced in patients with renal dysfunction (see **Special Populations:** *Patients with Renal Insufficiency*).

Because renal excretion is the predominant pathway of elimination, dosage should be adjusted in patients with markedly compromised renal function or who are undergoing hemodialysis (see **DOSAGE AND ADMINISTRATION**).

Special Populations:

Patients with Renal Insufficiency: Cefdinir pharmacokinetics were investigated in 21 adult subjects with varying degrees of renal function. Decreases in cefdinir elimination rate, apparent oral clearance (CL/F), and renal clearance were approximately proportional to the reduction in creatinine clearance (CL_{cr}). As a result, plasma cefdinir concentrations were higher and persisted longer in subjects with renal impairment than in those without renal impairment. In subjects with CL_{cr} between 30 and 60 mL/min, C_{max} and $t_{½}$ increased by approximately 2-fold and AUC by approximately 3-fold. In subjects with CL_{cr} <30 mL/min, C_{max} increased by approximately 2-fold, $t_{½}$ by approximately 5-fold, and AUC by approximately 6-fold. Dosage adjustment is recommended in patients with markedly compromised renal function (creatinine clearance <30 mL/min; see **DOSAGE AND ADMINISTRATION**).

Hemodialysis: Cefdinir pharmacokinetics were studied in 8 adult subjects undergoing hemodialysis. Dialysis (4 hours duration) removed 63% of cefdinir from the body and reduced apparent elimination $t_{½}$ from 16 (±3.5) to 3.2 (±1.2) hours. Dosage adjustment is recommended in this patient population (see **DOSAGE AND ADMINISTRATION**).

Hepatic Disease: Because cefdinir is predominantly renally eliminated and not appreciably metabolized, studies in patients with hepatic impairment were not conducted. It is not expected that dosage adjustment will be required in this population.

Geriatric Patients: The effect of age on cefdinir pharmacokinetics after a single 300-mg dose was evaluated in 32 subjects 19 to 91 years of age. Systemic exposure to cefdinir was substantially increased in older subjects (N = 16), C_{max} by 44% and AUC by 86%. This increase was due to a reduction in cefdinir clearance. The apparent volume of distribution was also reduced, thus no appreciable alterations in apparent elimination half-life were observed (elderly: 2.2 ± 0.6 hours vs young: 1.8 ± 0.4 hours). Since cefdinir clearance has been shown to be primarily related to changes in renal function rather than age, elderly patients do not require dosage adjustment unless they have markedly compromised renal function (creatinine clearance <30 mL/min, see *Patients with Renal Insufficiency*, above).

Gender and Race: The results of a meta-analysis of clinical pharmacokinetics (N = 217) indicated no significant impact of either gender or race on cefdinir pharmacokinetics.

Microbiology

As with other cephalosporins, bactericidal activity of cefdinir results from inhibition of cell wall synthesis. Cefdinir is stable in the presence of some, but not all, β-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins are susceptible to cefdinir.

Cefdinir has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections as described in **INDICATIONS AND USAGE.**

Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus (including β-lactamase producing strains)
NOTE: Cefdinir is inactive against methicillin-resistant staphylococci.
Streptococcus pneumoniae (penicillin-susceptible strains only)
Streptococcus pyogenes

Aerobic Gram-Negative Microorganisms:
Haemophilus influenzae (including β-lactamase producing strains)
Haemophilus parainfluenzae (including β-lactamase producing strains)
Moraxella catarrhalis (including β-lactamase producing strains)

The following *in vitro* data are available, **but their clinical significance is unknown.**

Cefdinir exhibits *in vitro* minimum inhibitory concentrations (MICs) of 1 μg/mL or less against (≥90%) strains of the following microorganisms; however, the safety and effectiveness of cefdinir in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials.

Aerobic Gram-Positive Microorganisms:
Staphylococcus epidermidis (methicillin-susceptible strains only)
Streptococcus agalactiae
Viridans group streptococci

NOTE: Cefdinir is inactive against *Enterococcus* and methicillin-resistant *Staphylococcus* species.

Aerobic Gram-Negative Microorganisms:
Citrobacter diversus
Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis

NOTE: Cefdinir is inactive against *Pseudomonas* and *Enterobacter* species.

Susceptibility Tests:
Dilution Techniques: Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a dilution method[1] (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of cefdinir powder. The MIC values should be interpreted according to the following criteria:

For organisms other than *Haemophilus* spp. and *Streptococcus* spp:

MIC (μg/mL)	Interpretation
≤1	Susceptible (S)
2	Intermediate (I)
≥4	Resistant (R)

For *Haemophilus* spp:[a]

MIC (μg/mL)	Interpretation[b]
≤1	Susceptible (S)

[a] These interpretive standards are applicable only to broth microdilution susceptibility tests with *Haemophilus* spp. using Haemophilus Test Medium (HTM).[1]

[b] The current absence of data on resistant strains precludes defining any results other than "Susceptible". Strains yielding MIC results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

For *Streptococcus* spp:

Streptococcus pneumoniae that are susceptible to penicillin (MIC ≤0.06 μg/mL), or streptococci other than *S. pneumoniae* that are susceptible to penicillin (MIC ≤0.12 μg/mL), can be considered susceptible to cefdinir. Testing of cefdinir against penicillin-intermediate or penicillin-resistant isolates is not recommended. Reliable interpretive criteria for cefdinir are not available.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentration usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of laboratory procedures. Standard cefdinir powder should provide the following MIC values:

Microorganism	MIC Range (μg/mL)
Escherichia coli ATCC 25922	0.12-0.5
Haemophilus influenzae ATCC 49766[c]	0.12-0.5
Staphylococcus aureus ATCC 29213	0.12-0.5

[c] This quality control range is applicable only to *H. influenzae* ATCC 49766 tested by a broth microdilution procedure using HTM.

Diffusion Techniques: Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure[2] requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 5-μg cefdinir to test the susceptibility of microorganisms to cefdinir.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 5-μg cefdinir disk should be interpreted according to the following criteria:

For organisms other than *Haemophilus* spp. and *Streptococcus* spp:[d]

Zone Diameter (mm)	Interpretation
≥20	Susceptible (S)
17-19	Intermediate (I)
≤16	Resistant (R)

[d] Because certain strains of *Citrobacter*, *Providencia*, and *Enterobacter* spp. have been reported to give false susceptible results with the cefdinir disk, strains of these genera should not be tested and reported with this disk.

For *Haemophilus* spp:[e]

Zone Diameter (mm)	Interpretation[f]
≥20	Susceptible

[e] These zone diameter standards are applicable only to tests with *Haemophilus* spp. using HTM.[2]

[f] The current absence of data on resistant strains precludes defining any results other than "Susceptible". Strains yielding MIC results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

For *Streptococcus* spp:
Isolates of *Streptococcus pneumoniae* should be tested against a 1-μg oxacillin disk. Isolates with oxacillin zone sizes ≥20 mm are susceptible to penicillin and can be considered susceptible to cefdinir. Streptococci other than *S. pneumoniae* should be tested with a 10-unit penicillin disk. Isolates with penicillin zone sizes ≥28 mm are susceptible to penicillin and can be considered susceptible to cefdinir.

Interpretation should be as stated above for results using dilution techniques. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for cefdinir.

As with standardized dilution techniques, diffusion methods require the use of laboratory control microorganisms to control the technical aspects of laboratory procedures. For the diffusion technique the 5-μg cefdinir disk should provide the following zone diameters in these laboratory quality control strains:

Organism	Zone Diameter (mm)
Escherichia coli ATCC 25922	24-28
Haemophilus influenzae ATCC 49766[g]	24-31
Staphylococcus aureus ATCC 25923	25-32

[g] This quality control range is applicable only to testing of *H. influenzae* ATCC 49766 using HTM.

INDICATIONS AND USAGE

OMNICEF (cefdinir) Capsules and OMNICEF (cefdinir) for Oral Suspension are indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below.

Adults and Adolescents

Community-Acquired Pneumonia caused by *Haemophilus influenzae* (including β-lactamase producing strains), *Haemophilus parainfluenzae* (including β-lactamase producing strains), *Streptococcus pneumoniae* (penicillin-susceptible strains only), and

Moraxella catarrhalis (including β-lactamase producing strains) (see **CLINICAL STUDIES**).

Acute Exacerbations of Chronic Bronchitis caused by *Haemophilus influenzae* (including β-lactamase producing strains), *Haemophilus parainfluenzae* (including β-lactamase producing strains), *Streptococcus pneumoniae* (penicillin-susceptible strains only), and *Moraxella catarrhalis* (including β-lactamase producing strains).

Acute Maxillary Sinusitis caused by *Haemophilus influenzae* (including β-lactamase producing strains), *Streptococcus pneumoniae* (penicillin-susceptible strains only), and *Moraxella catarrhalis* (including β-lactamase producing strains).

NOTE: For information on use in pediatric patients, see **Pediatric Use** and **DOSAGE AND ADMINISTRATION.**

Pharyngitis/Tonsillitis caused by *Streptococcus pyogenes* (see **CLINICAL STUDIES**)

NOTE: Cefdinir is effective in the eradication of *S. pyogenes* from the oropharynx. Cefdinir has not, however, been studied for the prevention of rheumatic fever following *S. pyogenes* pharyngitis/tonsillitis. Only intramuscular penicillin has been demonstrated to be effective for the prevention of rheumatic fever.

Uncomplicated Skin and Skin Structure Infections caused by *Staphylococcus aureus* (including β-lactamase producing strains) and *Streptococcus pyogenes*.

<u>Pediatric Patients</u>

Acute Bacterial Otitis Media caused by *Haemophilus influenzae* (including β-lactamase producing strains), *Streptococcus pneumoniae* (penicillin-susceptible strains only), and *Moraxella catarrhalis* (including β-lactamase producing strains).

Pharyngitis/Tonsillitis caused by *Streptococcus pyogenes* (see **CLINICAL STUDIES**)

NOTE: Cefdinir is effective in the eradication of *S. pyogenes* from the oropharynx. Cefdinir has not, however, been studied for the prevention of rheumatic fever following *S. pyogenes* pharyngitis/tonsillitis. Only intramuscular penicillin has been demonstrated to be effective for the prevention of rheumatic fever.

Uncomplicated Skin and Skin Structure Infections caused by *Staphylococcus aureus* (including β-lactamase producing strains) and *Streptococcus pyogenes*.

CONTRAINDICATIONS

OMNICEF (cefdinir) is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS

BEFORE THERAPY WITH OMNICEF (CEFDINIR) IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFDINIR, OTHER CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF CEFDINIR IS TO BE GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY AMONG β-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO CEFDINIR OCCURS, THE DRUG SHOULD BE DISCONTINUED. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES, INCLUDING OXYGEN, INTRAVENOUS FLUIDS, INTRAVENOUS ANTIHISTAMINES, CORTICOSTEROIDS, PRESSOR AMINES, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefdinir, and may range in severity from mild- to life-threatening.

Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis".

After the diagnosis of pseudomembranous colitis has been established, appropriate therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile*.

PRECAUTIONS

General

As with other broad-spectrum antibiotics, prolonged treatment may result in the possible emergence and overgrowth of resistant organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate alternative therapy should be administered.

Cefdinir, as with other broad-spectrum antimicrobials (antibiotics), should be prescribed with caution in individuals with a history of colitis.

In patients with transient or persistent renal insufficiency (creatinine clearance <30 mL/min), the total daily dose of OMNICEF should be reduced because high and prolonged plasma concentrations of cefdinir can result following recommended doses (see **DOSAGE AND ADMINISTRATION**).

Information for Patients

Antacids containing magnesium or aluminum interfere with the absorption of cefdinir. If this type of antacid is required during OMNICEF therapy, OMNICEF should be taken at least 2 hours before or after the antacid.

Iron supplements, including multivitamins that contain iron, interfere with the absorption of cefdinir. If iron supplements are required during OMNICEF therapy, OMNICEF should be taken at least 2 hours before or after the supplement.

Iron-fortified infant formula does not significantly interfere with the absorption of cefdinir. Therefore, OMNICEF for Oral Suspension can be administered with iron-fortified infant formula.

If the patient is diabetic, he/she/the guardian should be aware that the oral suspension contains 2.86 g of sucrose per teaspoon.

Drug Interactions

Antacids: (aluminum- or magnesium-containing): Concomitant administration of 300-mg cefdinir capsules with 30 mL Maalox® TC suspension reduces the rate (C_{max}) and extent (AUC) of absorption by approximately 40%. Time to reach C_{max} is also prolonged by 1 hour. There are no significant effects on cefdinir pharmacokinetics if the antacid is administered 2 hours before or 2 hours after cefdinir. If antacids are required during OMNICEF therapy, OMNICEF should be taken at least 2 hours before or after the antacid.

Probenecid: As with other β-lactam antibiotics, probenecid inhibits the renal excretion of cefdinir, resulting in an approximate doubling in AUC, a 54% increase in peak cefdinir plasma levels, and a 50% prolongation in the apparent elimination half-life.

Iron Supplements and Foods Fortified With Iron: Concomitant administration of cefdinir with a therapeutic iron supplement containing 60 mg of elemental iron (as $FeSO_4$) or vitamins supplemented with 10 mg of elemental iron reduced extent of absorption by 80% and 31%, respectively. If iron supplements are required during

OMNICEF therapy, OMNICEF should be taken at least 2 hours before or after the supplement.

The effect of foods highly fortified with elemental iron (primarily iron-fortified breakfast cereals) on cefdinir absorption has not been studied.

Concomitantly administered iron-fortified infant formula (2.2 mg elemental iron/6 oz) has no significant effect on cefdinir pharmacokinetics. Therefore, OMNICEF for Oral Suspension can be administered with iron-fortified infant formula.

There have been rare reports of reddish stools in patients who have received cefdinir in Japan. The reddish color is due to the formation of a nonabsorbable complex between cefdinir or its breakdown products and iron in the gastrointestinal tract.

Drug/Laboratory Test Interactions

A false-positive reaction for ketones in the urine may occur with tests using nitroprusside, but not with those using nitroferricyanide. The administration of cefdinir may result in a false-positive reaction for glucose in urine using Clinitest®, Benedict's solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix® or Tes-Tape®) be used. Cephalosporins are known to occasionally induce a positive direct Coombs' test.

Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of cefdinir has not been evaluated. No mutagenic effects were seen in the bacterial reverse mutation assay (Ames) or point mutation assay at the hypoxanthine-guanine phosphoribosyltransferase locus (HGPRT) in V79 Chinese hamster lung cells. No clastogenic effects were observed *in vitro* in the structural chromosome aberration assay in V79 Chinese hamster lung cells or *in vivo* in the micronucleus assay in mouse bone marrow. In rats, fertility and reproductive performance were not affected by cefdinir at oral doses up to 1000 mg/kg/day (70 times the human dose based on mg/kg/day, 11 times based on mg/m^2/day).

Pregnancy - Teratogenic Effects

Pregnancy Category B: Cefdinir was not teratogenic in rats at oral doses up to 1000 mg/kg/day (70 times the human dose based on mg/kg/day, 11 times based on mg/m^2/day) or in rabbits at oral doses up to 10 mg/kg/day (0.7 times the human dose based on mg/kg/day, 0.23 times based on mg/m^2/day). Maternal toxicity (decreased body weight gain) was observed in rabbits at the maximum tolerated dose of 10 mg/kg/day without adverse effects on offspring. Decreased body weight occurred in rat fetuses at ≥100 mg/kg/day, and in rat offspring at ≥32 mg/kg/day. No effects were observed on maternal reproductive parameters or offspring survival, development, behavior, or reproductive function.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

Cefdinir has not been studied for use during labor and delivery.

Nursing Mothers

Following administration of single 600-mg doses, cefdinir was not detected in human breast milk.

Pediatric Use

Safety and efficacy in neonates and infants less than 6 months of age have not been established. Use of cefdinir for the treatment of acute maxillary sinusitis in pediatric patients (age 6 months through 12 years) is supported by evidence from adequate and well-controlled studies in adults and adolescents, the similar pathophysiology of acute sinusitis in adult and pediatric patients, and comparative pharmacokinetic data in the pediatric population.

Geriatric Use

Efficacy is comparable in geriatric patients and younger adults. While cefdinir has been well-tolerated in all age groups, in clinical trials geriatric patients experienced a lower rate of adverse events, including diarrhea, than younger adults. Dose adjustment in elderly patients is not necessary unless renal function is markedly compromised (see **DOSAGE AND ADMINISTRATION**).

ADVERSE EVENTS

Clinical Trials - OMNICEF Capsules (Adult and Adolescent Patients):

In clinical trials, 4527 adult and adolescent patients (3275 US and 1252 non-US) were treated with the recommended dose of cefdinir capsules (600 mg/day). Most adverse events were mild and self-limiting in nature. No deaths or permanent disabilities were attributed to cefdinir. One hundred twenty-five of 4527 (3%) patients discontinued medication due to adverse events thought by the investigators to be possibly, probably, or definitely associated with cefdinir therapy. The discontinuations were primarily for gastrointestinal disturbances, usually diarrhea or nausea. Seventeen of 4527 (0.4%) patients were discontinued due to rash thought related to cefdinir administration.

In the US, the following adverse events were thought by investigators to be possibly, probably, or definitely related to cefdinir capsules in multiple-dose clinical trials (n = 3275 cefdinir-treated patients):

ADVERSE EVENTS ASSOCIATED WITH CEFDINIR CAPSULES US TRIALS IN ADULT AND ADOLESCENT PATIENTS (N = 3275)[a]		
Incidence ≥1%	Diarrhea	16%
	Vaginal moniliasis	5% of women
	Nausea	3%
	Headache	2%
	Abdominal pain	1%
	Vaginitis	1% of women
Incidence <1% but >0.1%	Rash	0.9%
	Dyspepsia	0.8%
	Flatulence	0.6%
	Vomiting	0.6%
	Anorexia	0.3%
	Constipation	0.3%
	Abnormal stools	0.2%
	Asthenia	0.2%
	Dizziness	0.2%
	Insomnia	0.2%
	Leukorrhea	0.2% of women
	Pruritus	0.2%
	Somnolence	0.2%

[a] 1469 males, 1806 females

The following laboratory value changes of possible clinical significance, irrespective of relationship to therapy with cefdinir, were seen during clinical trials conducted in the US:

LABORATORY VALUE CHANGES OBSERVED WITH CEFDINIR CAPSULES US TRIALS IN ADULT AND ADOLESCENT PATIENTS (N = 3275)		
Incidence ≥1%	↑ Gamma-glutamyltransferase	1%
	↑ Urine protein	1%
	↑ Urine red blood cells	1%
Incidence <1% but >0.1%	↑ Glucose, ↓ Glucose	0.9, 0.2
	↑ Alanine aminotransferase (ALT)	0.9
	↑ Urine glucose	0.9
	↑ White blood cells, ↓ White blood cells	0.8, 0.7
	↓ Lymphocytes, ↑ Lymphocytes	0.8, 0.2
	↑ Urine specific gravity	0.8
	↓ Bicarbonate	0.6
	↑ Eosinophils	0.6
	↑ Phosphorus, ↓ Phosphorus	0.6, 0.3
	↑ Aspartate aminotransferase (AST)	0.4
	↑ Urine white blood cells	0.4
	↓ Hemoglobin	0.3
	↑ Alkaline phosphatase	0.2
	↑ Blood urea nitrogen (BUN)	0.2
	↑ Bilirubin	0.2
	↑ Lactate dehydrogenase	0.2
	↑ Platelets	0.2
	↓ Polymorphonuclear neutrophils (PMNs)	0.2
	↑ Potassium	0.2
	↑ Urine pH	0.2

Clinical Trials - OMNICEF for Oral Suspension (Pediatric Patients):

In clinical trials, 1893 pediatric patients (1387 US and 506 non-US) were treated with the recommended dose of cefdinir suspension (14 mg/kg/day). Most adverse events were mild and self-limiting. No deaths or permanent disabilities were attributed to cefdinir. Thirty-nine of 1893 (2%) patients discontinued medication due to adverse events considered by the investigators to be possibly, probably, or definitely associated with cefdinir therapy. Discontinuations were primarily for gastrointestinal disturbances, usually diarrhea. Five of 1893 (0.3%) patients were discontinued due to rash thought related to cefdinir administration.

In the US, the following adverse events were thought by investigators to be possibly, probably, or definitely related to cefdinir suspension in multiple-dose clinical trials (n = 1387 cefdinir-treated patients):

ADVERSE EVENTS ASSOCIATED WITH CEFDINIR SUSPENSION US TRIALS IN PEDIATRIC PATIENTS (N = 1387)[a]		
Incidence ≥1%	Diarrhea	8%
	Rash	3%
	Cutaneous moniliasis	1%
	Vomiting	1%
Incidence <1% but >0.1%	Abdominal pain	0.9%
	Leukopenia[b]	0.4%
	Nausea	0.3%
	Vaginal moniliasis	0.3% of girls
	Vaginitis	0.3% of girls
	Dyspepsia	0.2%
	Maculopapular rash	0.2%
	Increased AST[b]	0.2%

[a] 743 males, 644 females
[b] Laboratory changes were occasionally reported as adverse events.

The following laboratory value changes of possible clinical significance, irrespective of relationship to therapy with cefdinir, were seen during clinical trials conducted in the US:

LABORATORY VALUE CHANGES OBSERVED WITH CEFDINIR SUSPENSION US TRIALS IN PEDIATRIC PATIENTS (N = 1387)		
Incidence ≥1%	↑ Lactate dehydrogenase	2%
	↑ Alkaline phosphatase	1%
	↓ Bicarbonate	1%
	↑ Eosinophils	1%
	↑ Urine pH	1%
Incidence <1% but >0.1%	↑ Lymphocytes, ↓ Lymphocytes	0.9, 0.7
	↑ Phosphorus, ↓ Phosphorus	0.9, 0.4
	↓ White blood cells, ↑ White blood cells	0.9, 0.4
	↑ Urine protein	0.9
	↑ PMNs	0.8
	↑ Platelets	0.7
	↓ Calcium	0.5
	↑ AST	0.2
	↓ Hemoglobin	0.4
	↑ Potassium	0.3
	↑ ALT	0.2
	↓ Hematocrit	0.2
	↑ Urine specific gravity	0.2
	↑ Urine white blood cells	0.2

Postmarketing Experience

The following adverse experiences and altered laboratory tests, regardless of their relationship to cefdinir, have been reported during extensive postmarketing experience, beginning with approval in Japan in 1991: Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme, erythema nodosum, conjunctivitis, stomatitis, acute hepatitis, cholestasis, fulminant hepatitis, hepatic failure, jaundice, increased amylase, shock, anaphylaxis, facial and laryngeal edema, feeling of suffocation, acute enterocolitis, bloody diarrhea, hemorrhagic colitis, melena, pseudomembranous colitis, pancytopenia, granulocytopenia, leukopenia, thrombocytopenia, idiopathic thrombocytopenic purpura, hemolytic anemia, acute respiratory failure, asthmatic attack, drug-induced pneumonia, eosinophilic pneumonia, idiopathic interstitial pneumonia, fever, acute renal failure, nephropathy, bleeding tendency, coagulation disorder, disseminated intravascular coagulation, upper GI bleed,

peptic ulcer, ileus, loss of consciousness, allergic vasculitis, possible cefdinir-diclofenac interaction, cardiac failure, chest pain, myocardial infarction, hypertension, involuntary movements, and rhabdomyolysis.

Cephalosporin Class Adverse Events

The following adverse events and altered laboratory tests have been reported for cephalosporin-class antibiotics in general:

Allergic reactions, anaphylaxis, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, false-positive test for urinary glucose, neutropenia, pancytopenia, and agranulocytosis. Pseudomembranous colitis symptoms may begin during or after antibiotic treatment (see **WARNINGS**).

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced (see **DOSAGE AND ADMINISTRATION** and **OVERDOSAGE**). If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

OVERDOSAGE

Information on cefdinir overdosage in humans is not available. In acute rodent toxicity studies, a single oral 5600-mg/kg dose produced no adverse effects. Toxic signs and symptoms following overdosage with other β-lactam antibiotics have included nausea, vomiting, epigastric distress, diarrhea, and convulsions. Hemodialysis removes cefdinir from the body. This may be useful in the event of a serious toxic reaction from overdosage, particularly if renal function is compromised.

DOSAGE AND ADMINISTRATION

(See INDICATIONS AND USAGE for Indicated Pathogens)

Capsules

The recommended dosage and duration of treatment for infections in adults and adolescents are described in the following chart; the total daily dose for all infections is 600 mg. Once-daily dosing for 10 days is as effective as BID dosing. Once-daily dosing has not been studied in pneumonia or skin infections; therefore, OMNICEF Capsules should be administered twice daily in these infections. OMNICEF Capsules may be taken without regard to meals.

Adults and Adolescents (Age 13 years and Older)

Type of Infection	Dosage	Duration
Community-Acquired Pneumonia	300 mg q12h	10 days
Acute Exacerbations of Chronic Bronchitis	300 mg q12h	10 days
	or	
	600 mg q24h	10 days
Acute Maxillary Sinusitis	300 mg q12h	10 days
	or	
	600 mg q24h	10 days
Pharyngitis/Tonsillitis	300 mg q12h	5 to 10 days
	or	
	600 mg q24h	10 days
Uncomplicated Skin and Skin Structure Infections	300 mg q12h	10 days

Powder for Oral Suspension

The recommended dosage and duration of treatment for infections in pediatric patients are described in the following chart; the total daily dose for all infections is 14 mg/kg, up to a maximum dose of 600 mg per day. Once-daily dosing for 10 days is as effective as BID dosing. Once-daily dosing has not been studied in skin infections; therefore, OMNICEF for Oral Suspension should be administered twice daily in this infection. OMNICEF for Oral Suspension may be administered without regard to meals.

Pediatric Patients (Age 6 Months Through 12 Years)

Type of Infection	Dosage	Duration
Acute Bacterial Otitis Media	7 mg/kg q12h or	10 days
	14 mg/kg q24h	10 days
Acute Maxillary Sinusitis	7 mg/kg q12h or	10 days
	14 mg/kg q24h	10 days
Pharyngitis/Tonsillitis	7 mg/kg q12h or	5 to 10 days
	14 mg/kg q24h	10 days
Uncomplicated Skin and Skin Structure Infections	7 mg/kg q12h	10 days

OMNICEF FOR ORAL SUSPENSION PEDIATRIC DOSAGE CHART

Weight	125 mg/5 mL
9 kg/20 lbs	2.5 mL (½ tsp) q12h or 5 mL (1 tsp) q24h
18 kg/40 lbs	5 mL (1 tsp) q12h or 10 mL (2 tsp) q24h
27 kg/60 lbs	7.5 mL (1½ tsp) q12h or 15 mL (3 tsp) q24h
36 kg/80 lbs	10 mL (2 tsp) q12h or 20 mL (4 tsp) q24h
≥43 kg*/95 lbs	12 mL (2½ tsp) q12h or 24 mL (5 tsp) q24h

* Pediatric patients who weigh ≥43 kg should receive the maximum daily dose of 600 mg.

Patients With Renal Insufficiency

For adult patients with creatinine clearance <30 mL/min, the dose of cefdinir should be 300 mg given once daily.

Creatinine clearance is difficult to measure in outpatients. However, the following formula may be used to estimate creatinine clearance (CL_{cr}) in adult patients. For estimates to be valid, serum creatinine levels should reflect steady-state levels of renal function.

Males:

$$CL_{cr} = \frac{(\text{weight})\ (140 - \text{age})}{(72)\ (\text{serum creatinine})}$$

Females:

$$CL_{cr} = 0.85 \times \text{above value}$$

where creatinine clearance is in mL/min, age is in years, weight is in kilograms, and serum creatinine is in mg/dL.[3]

The following formula may be used to estimate creatinine clearance in pediatric patients:

$$CL_{cr} = K \times \frac{\text{body length or height}}{\text{serum creatinine}}$$

where K = 0.55 for pediatric patients older than 1 year[4] and 0.45 for infants (up to 1 year)[5].

In the above equation, creatinine clearance is in mL/min/1.73 m^2, body length or height is in centimeters, and serum creatinine is in mg/dL.

For pediatric patients with a creatinine clearance of <30 mL/min/1.73 m^2, the dose of cefdinir should be 7 mg/kg (up to 300 mg) given once daily.

Patients on Hemodialysis

Hemodialysis removes cefdinir from the body. In patients maintained on chronic hemodialysis, the recommended initial dosage regimen is a 300-mg or 7-mg/kg dose every other day. At the conclusion of each hemodialysis session, 300 mg (or 7 mg/kg) should be given. Subsequent doses (300 mg or 7 mg/kg) are then administered every other day.

Directions for Mixing Omnicef for Oral Suspension

DIRECTIONS FOR MIXING OMNICEF FOR ORAL SUSPENSION

Final Concentration	Final Volume (mL)	Amount of Water	Directions
125 mg/5 mL	60 100	39 mL 65 mL	Tap bottle to loosen powder, then add water in 2 portions. Shake well after each aliquot.

After mixing, the suspension can be stored at room temperature (25°C/77°F). The container should be kept tightly closed, and the suspension should be shaken well before each administration. The suspension may be used for 10 days, after which any unused portion must be discarded.

HOW SUPPLIED

OMNICEF Capsules, containing 300 mg cefdinir, as lavender and turquoise capsules imprinted with the product name, are available as follows:

60 Capsules/Bottle NDC 0071-0067-20

OMNICEF for Oral Suspension is a cream-colored powder formulation that, when reconstituted as directed, contains 125 mg cefdinir/5 mL. The reconstituted suspension has a cream color and strawberry flavor. The powder is available as follows:

60-mL bottles	NDC 0071-2006-16
100-mL bottles	NDC 0071-2006-18

Store the capsules and unsuspended powder at 25°C (77°F); excursions permitted to 15 to 30°C (59-86°F) [see USP Controlled Room Temperature]. Once reconstituted, the oral suspension can be stored at controlled room temperature for 10 days.

CLINICAL STUDIES

Community-Acquired Bacterial Pneumonia

In a controlled, double-blind study in adults and adolescents conducted in the US, cefdinir BID was compared with cefaclor 500 mg TID. Using strict evaluability and microbiologic/clinical response criteria 6 to 14 days posttherapy, the following clinical cure rates, presumptive microbiologic eradication rates, and statistical outcomes were obtained (see table below):

US Community-Acquired Pneumonia Study
Cefdinir vs Cefaclor

	Cefdinir BID		Cefaclor TID		Outcome
Clinical Cure Rates	150/187	(80%)	147/186	(79%)	Cefdinir equivalent to control
Eradication Rates					
Overall	177/195	(91%)	184/200	(92%)	Cefdinir equivalent to control
S. *pneumoniae*	31/31	(100%)	35/35	(100%)	
H. influenzae	55/65	(85%)	60/72	(83%)	
M. catarrhalis	10/10	(100%)	11/11	(100%)	
H. parainfluenzae	81/89	(91%)	78/82	(95%)	

In a second controlled, investigator-blind study in adults and adolescents conducted primarily in Europe, cefdinir BID was compared with amoxicillin/clavulanate

500/125 mg TID. Using strict evaluability and clinical response criteria 6 to 14 days posttherapy, the following clinical cure rates, presumptive microbiologic eradication rates, and statistical outcomes were obtained (see table below):

European Community-Acquired Pneumonia Study
Cefdinir vs Amoxicillin/Clavulanate

	Cefdinir BID		Amoxicillin/ Clavulanate TID		Outcome
Clinical Cure Rates	83/104	(80%)	86/97	(89%)	Cefdinir not equivalent to control
Eradication Rates					
Overall	85/96	(89%)	84/90	(93%)	Cefdinir equivalent to control
S. *pneumoniae*	42/44	(95%)	43/44	(98%)	
H. influenzae	26/35	(74%)	21/26	(81%)	
M. catarrhalis	6/6	(100%)	8/8	(100%)	
H. parainfluenzae	11/11	(100%)	12/12	(100%)	

Streptococcal Pharyngitis/Tonsillitis

In four controlled studies conducted in the United States, cefdinir was compared with 10 days of penicillin in adults, adolescents, and pediatric patients. Two studies (one in adults and adolescents, the other in pediatric patients) compared 10 days of cefdinir QD or BID to penicillin 250 mg or 10 mg/kg QID. Using strict evaluability and microbiologic/ clinical response criteria 5 to 10 days posttherapy, the following clinical cure rates, microbiologic eradication rates, and statistical outcomes were obtained (see table below):

Pharyngitis/Tonsillitis Studies
Cefdinir (10 days) vs Penicillin (10 days)

Study	Efficacy Parameter	Cefdinir QD		Cefdinir BID		Penicillin QID		Outcome
Adults/ Adolescents	Eradication of *S. pyogenes*	192/210	(91%)	199/217	(92%)	181/217	(83%)	Cefdinir superior to control
	Clinical Cure Rates	199/210	(95%)	209/217	(96%)	193/217	(89%)	Cefdinir superior to control
Pediatric Patients	Eradication of *S. pyogenes*	215/228	(94%)	214/227	(94%)	159/227	(70%)	Cefdinir superior to control
	Clinical Cure Rates	222/228	(97%)	218/227	(96%)	196/227	(86%)	Cefdinir superior to control

Two studies (one in adults and adolescents, the other in pediatric patients) compared 5 days of cefdinir BID to 10 days of penicillin 250 mg or 10 mg/kg QID. Using strict evaluability and microbiologic/clinical response criteria 4 to 10 days posttherapy, the following clinical cure rates, microbiologic eradication rates, and statistical outcomes were obtained (see table below):

Pharyngitis/Tonsillitis Studies
Cefdinir (5 days) vs Penicillin (10 days)

Study	Efficacy Parameter	Cefdinir BID		Penicillin QID		Outcome
Adults/ Adolescents	Eradication of *S. pyogenes*	193/218	(89%)	176/214	(82%)	Cefdinir equivalent to control
	Clinical Cure Rates	194/218	(89%)	181/214	(85%)	Cefdinir equivalent to control
Pediatric Paients	Eradication of *S. pyogenes*	176/196	(90%)	135/193	(70%)	Cefdinir superior to control
	Clinical Cure Rates	179/196	(91%)	173/193	(90%)	Cefdinir equivalent to control

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