Averofectan

Cefdinir 250 mg/5 mL

Powder for oral suspension

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Averofectan for oral suspension and other antibacterial drugs, Averofectan for oral suspension should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION

Averofectan for oral suspension contain the active ingredient cefdinir, an extended-spectrum, semisynthetic cephalosporin, for oral administration. Averofectan for oral suspension, after reconstitution contains 250 mg cefdinir per 5 mL and the following inactive ingredients: Xanthan gum – Sucrose – Colloidal Silicon dioxide – Strawberry Flavor – Sodium Benzoate – Citric Acid – Magnesium stearate.

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%. Cefdinir oral suspension of 250 mg/5 mL strength was shown to be bioequivalent to the 125 mg/5 mL strength in healthy adults under fasting conditions.

Effect of Food: The C_{max} and AUC of cefdinir from the capsules are reduced by 16% and 10%, respectively, when given with a high-fat meal. In adults given the 250 mg/5 mL oral suspension with a high-fat meal, the C_{max} and AUC of cefdinir are reduced by 44% and 33%, respectively. The magnitude of these reductions is not likely to be clinically significant because the safety and efficacy studies of oral suspension in pediatric patients were conducted without regard to food intake. Therefore, cefdinir may be taken without regard to food.

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	Cmax(mcg/mL)	tmax(hr)	AUC(mcg.hr/mL)
7 mg/kg	2.30(0.65)	2.2(0.6)	8.31(2.50)
14 mg/kg	3.86(0.62)	1.8(0.4)	13.4(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) mcg/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) mcg/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) mcg/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) mcg/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) mcg/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) mcg/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 ($t_{1/2}$) 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 $t_{1/2}$ 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, $t_{1/2}$ 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 $t_{1/2}$ 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), Cmax 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 t1/2 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:

Mechanism of Action:

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.

INDICATIONS AND USAGE

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Averofectan for oral suspension and other antibacterial drugs, Averofectan for oral suspension should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Averofectan for oral suspension is 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:

1-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).

2-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).

3-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.

4-Pharyngitis/Tonsillitis:

Caused by *Streptococcus pyogenes*.

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.

5-Uncomplicated Skin and Skin Structure Infections:

Caused by *Staphylococcus aureus* (including β-lactamase producing strains) and *Streptococcus pyogenes*.

Pediatric Patients:

1-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).

2-Pharyngitis/Tonsillitis:

Caused by *Streptococcus pyogenes*.

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.

3- Uncomplicated Skin and Skin Structure Infections:

Caused by *Staphylococcus aureus* (including β-lactamase producing strains) and *Streptococcus pyogenes*.

CONTRAINDICATIONS

Averofectan is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

Hypersensitivity to the active substance, to other cephalosporins or to any of the excipients.

Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other beta-lactam medicinal products.

WARNINGS

Before Therapy with Averopreg is instituted, Careful inquiry should be made to determine whether the patent has had previous hypersensitivity reactions to cefdinir, other Cephalosporins, penicillins, or other drugs. If Averopreg 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 air way management, as clinically indicated.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including cefdinir, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

<u>hypersensitivity reactions:</u>

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with beta lactam antibiotics.

PRECAUTIONS

General:

Prescribing Averofectan for oral suspension in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

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 cefdinir should be reduced because high and prolonged plasma concentrations of cefdinir can result following recommended doses (see DOSAGE AND ADMINISTRATION).

Special caution is required to determine any other type of previous hypersensitivity reactions to penicillin or to other beta-lactam medicinal products because patients hypersensitive to these medicines may be hypersensitive to Averofectan as well (cross- allergy).

Information for Patients:

Patients should be counseled that antibacterial drugs including Averofectan for oral suspension should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When cefdinir for oral suspension is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Averofectan for oral suspension or other antibacterial drugs in the future.

Antacids containing magnesium or aluminum interfere with the absorption of cefdinir. If this type of antacid is required during cefdinir therapy, cefdinir 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 cefdinir therapy, cefdinir 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, cefdinir can be administered with iron-fortified infant formula.

Diabetic patients and caregivers should be aware that the oral suspension contains 2g of sucrose per teaspoon.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Drug Interactions:

Antacids (Aluminum- or Magnesium-Containing):

If antacids are required during cefdinir therapy, cefdinir 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 $t_{1/2}$.

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 cefdinir therapy, cefdinir 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, cefdinir can be administered with iron-fortified infant formula.

There have been reports of reddish stools in patients receiving cefdinir. In many cases, patients were also receiving iron-containing products. 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. 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.

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

ADVERSE EVENTS ASSOCIATED WITH CEFDINIR SUSPENSION	
Incidence ≥1%	Diarrhea
	Rash
	Vomiting
Incidence<1% but >0.1%	Cutaneous moniliasis
	Abdominal pain
	Leukopenia **
	Vaginal moniliasis
	Vaginitis
	Abnormal stools
	Dyspepsia
	Hyperkinesia
	Increased AST **
	Maculopapular rash
	Nausea

** Laboratory changes were occasionally reported as adverse events.

NOTE: Rates of diarrhea and rash were higher in the youngest pediatric patients.

LABORATORY VALUE CHANGES OF POSSIBLE CLINICAL SIGNIFICANCE OBSERVED WITH CEFDINIR SUSPENSION	
Incidence ≥1%	↑Lymphocytes,↓Lymphocytes
	↑Alkaline phosphatase
	↓Bicarbonate
	↑Eosinophils
	↑Lactate dehydrogenase
	↑Platelets
	↑PMNs, ↓PMNs
	↑Urine protein
Incidence <1% but >0.1%	↑Phosphorus, ↓Phosphorus
	↑Urine pH
	↓White blood cells, ↑White blood cells
	↓Calcium
	↓Hemoglobin
	↑Urine leukocytes
	↑Monocytes
	↑AST
	↑Potassium
	↑Urine specific gravity, ↓Urine specific gravity
	↓Hematocrit

Other adverse reactions:

Shock, anaphylaxis with rare cases of fatality, facial and laryngeal edema, feeling of suffocation, serum sickness-like reactions, conjunctivitis, stomatitis, Stevens -Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme, erythema nodosum, acute hepatitis, cholestasis, fulminant hepatitis, hepatic failure, jaundice, increased amylase, 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).

Skin and subcutaneous tissue disorder

Drug reaction pustulosis (AGEP), Frequency not known: Acute generalized exanthematous dermatitis, Toxic -with eosinophilia and systemic symptoms (DRESS), Bullous exfoliative stevens Johnson syndrome.

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. 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)

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, cefdinir for oral suspension should be administered twice daily in this infection. Cefdinir 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	5 to 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 infection	7 mg/kg q12h	10 days

Averopreg for oral Suspension Pediatric Dosage Chart

Weight	**250 mg/5 mL**
9 kg/20 lbs	Use 125 mg/5 mL product
18 kg/40 lbs	2.5 mL q12h or 5 mL q24h
27 kg/60 lbs	3.75 mL q12h or 7.5 mL q24h
36 kg/80 lbs	5 mL q12h or 10 mL q24h
≥43 kg */95 lbs	6 mL q12h or 12 mL q24h

* Pediatric patients who weight ≥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 (CLcr) in adult patients. For estimates to be valid, serum creatinine levels should reflect steady-state levels of renal function.

$$\text{Males: CLcr} = \frac{(\text{weight})\ (140 - \text{age})}{(72)\ (\text{serum creatinine})}$$

Females: CLcr = 0.85 x above value

Where creatinine clearance is in mL/min, age is in years, weight is in kilograms, and serum creatinine is in mg/dL.

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

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

Where K = 0.55 for pediatric patients older than 1 year and 0.45 for infants (up to 1 year).

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

Final Concentration	Final Volume(mL)	Directions
250 mg /5ml	60	Tap bottle to loosen powder, then add water in 2 portions. Shake well after each aliquot.

Storage conditions:

Store at temperature not exceeding 30 ° C in dry place, and after reconstitution to be used for 10 days and stored at temperature (2-8) ° C.

Pack:

Carton box contains (HDPE) opaque white plastic bottle marked with 60 ml contains 27.75 gm powder with (HDPE) cap and insert leaflet.

Shelf life:

3 years

Inactive ingredients:

Xanthan gum – Sucrose – Colloidal silicon dioxide – Strawberry flavor – Sodium benzoate – Citric acid – magnesium stearate

Manufactured by Shifa Medical Products (SIMCO)

For

Averroes Pharma for Pharmaceutical industries