Cefdinir (Omnicef®)

Classification

Third generation cephalosporin antibiotic

Pharmacology

OMNICEF® (cefdinir) capsules for oral administration contain the active ingredient, cefdinir, an extended-spectrum, semisynthetic cephalosporin. 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; it has enhanced activity against aerobic gram-negative bacteria including E. coli, Klebsiella sp. and P. mirabilis, as well as some anaerobic bacteria. It is also inactive against most strains of *Enterobacter* spp., *Pseudomonas* spp., *Enterococcus* spp., penicillin-resistant streptococci, and methicillin-resistant staphylococci [1].

Indication -FDA & literature supported non-FDA

Cefdinir is FDA approved for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated bacteria in the following conditions:

Adults and Adolescents

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

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

Pharyngitis/Tonsillitis caused by *Streptococcus pyogenes*.

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

Pediatric Patients

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

Pharyngitis/Tonsillitis caused by *Streptococcus pyogenes* [1].

Off label alternative use in the management of acute uncomplicated cystitis [2]

Pharmacokinetics [1]

Pharmacokinetic Parameter	Details
Absorption	Maximal plasma cefdinir concentrations occur 2 to 4 hours postdose following capsule administration. Suspension bioavailability is 120% relative to the capsule formulation. Absorption not significantly impacted by food.
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). 60-70% bound to plasma proteins.
Metabolism	Cefdinir is not appreciably metabolized. Activity is primarily due to parent drug.
Excretion	Cefdinir is eliminated principally via renal excretion with a mean plasma elimination half-life (t½) of 1.7 (± 0.6) hours. 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

Dosage/Administration

The total daily dose for all adult and adolescent (13 years of age and older) 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, cefdinir capsules should be administered twice daily in these infections. Cefdinir capsules may be taken without regard to meals.

The recommended dosage and duration of treatment of infections in pediatric patients (6 months through 12 years of age) is a total daily dose of 14 mg/kg, up to

a maximum of 600 mg per day. Pediatric patients 43 kg or more should receive the maximum dose of 600 mg per day.

See product labeling for additional specific dosage information based on age group and type of infection treated.

Use in Special Population

Patients with renal insufficiency: Dosage adjustment is recommended in patients with markedly compromised renal function (creatinine clearance < 30 mL/min) as AUC is increased approximately 6-fold.

Hemodialysis: Dialysis (4 hours duration) removed 63% of cefdinir from the body and reduced apparent elimination t½ from 16 (± 3.5) to 3.2 (± 1.2) hours. Dosage adjustment is recommended

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.

Contraindication [1]

Cefdinir capsules are contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

Precautions

- Careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefdinir, other cephalosporins, penicillins, or other drugs. Cross hypersensitivity among β-lactam antibiotics can occur in up to 10% of patients so caution should be exercised if given to penicillin-sensitive patient.
- Clostridium difficile associated diarrhea (CDAD) has been reported with nearly all antibacterial agents, including cefdinir, and may range in severity from mild- to life-threatening. Consider this diagnosis in patients who present with diarrhea after the administration of cefdinir.
- Prescribing cefdinir capsules in the absence of a proven or strongly suspected bacterial infection or indication is unlikely to benefit the patient and increases the risk of development of drug-resistant bacteria.
- Prolonged treatment may result in the possible emergence and overgrowth of resistant organisms.
- Caution should be used when prescribing in patients with 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.

Adverse Effects [3]

More Common

Gastrointestinal: Diarrhea (8% to 15%)

Genitourinary: Vulvovaginal candidiasis (≤4%), urine abnormality (increased leukocytes: ≤2%), proteinuria (1% to 2%)

Dermatologic: Skin rash (≤3%)

Gastrointestinal: Nausea (≤3%)

Central nervous system: Headache (2%)

Hematologic & oncologic: Lymphocytosis (≤2%)

Other Less Common

Decreased serum bicarbonate (≤1%), glycosuria (≤1%), hyperglycemia (≤1%), hyperphosphatemia (≤1%), increased gamma-glutamyl transferase (≤1%), increased lactate dehydrogenase (≤1%), abdominal pain (≤1%), vomiting (≤1%), occult blood in urine (≤1%), vaginitis (≤1%), eosinophilia (1%), lymphocytopenia (1%), abnormal neutrophils (functional disorder of polymorphonuclear neutrophils: ≤1%), thrombocythemia (≤1%), change in WBC count (≤1%), increased serum alkaline phosphatase (≤1%), increased serum ALT (≤1%), increased urine pH (≤1%), increased urine specific gravity (≤1%)

Cephalosporin class adverse events [1]

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.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced.

Monitoring [3]

Monitor renal function. Observe for signs and symptoms of anaphylaxis during first dose.

Interactions [1]

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 cefdinir therapy, cefdinir should be taken at least 2 hours before or after the antacid.

Iron supplements and foods fortified with iron: Concomitant administration with iron supplements containing 60 mg of elemental iron (as ferrous sulfate) or vitamins supplemented with 10 mg of elemental iron reduce the extent of absorption by 80% and 31% respectively. Cefdinir should be taken at least 2 hours before or after iron containing supplements. No significant effect with iron-fortified infant formula. Iron fortified foods have not been studied. Reddish stools may occur, particularly in those receiving iron-containing products due to a nonabsorbable complex between cefdinir

Efficacy

Community-Acquired Pneumonia (CAP)

Cefdinir 300 mg twice daily was compared to Cefaclor 500 mg three times daily (second generation cephalosporin) in adults and adolescents for the treatment of CAP [1]. Clinical cure rates were similar between the two antibiotics, 80% and 79% respectively. Overall eradiation rates were also similar between the two antibiotics, 91% and 92% respectively.

Cefdinir 300 mg twice daily was also compared to amoxicillin/clavulanate 500/125 mg three times daily in adults and adolescents for the treatment of CAP [1]. Clinical cure rates were superior for amoxicillin/clavulanate (89%) compared to cefdinir (80%). Overall eradication rates were similar between the two antibiotics, cefdinir (89%) and amoxicillin/clavulanate (93%).

Initial Treatment Strategies for Outpatients with Community-acquired Pneumonia per 2019 American Thoracic Society & IDSA Treatment Guidelines include recommendations for those with no comorbidities or risk factors for MRSA or Pseudomonas aeruginosa and those with comorbidities [4]. Risk factors include prior respiratory isolation of MRSA or P. aeruginosa or recent hospitalization and receipt of parenteral antibiotics in the last 90 days. Comorbidities include chronic heart, lung, liver or renal disease; diabetes, alcoholism; malignancy; or asplenia. Those with no comorbidities or risk factors, amoxicillin, doxycycline or a macrolide (if local pneumococcal resistance is less than 25%) such as azithromycin or clarithromycin can be considered. Those with comorbidities, combination therapy with

amoxicillin/clavulanate or cephalosporin (examples include cefpodixime- 3rd generation or cefuroxime- 2nd generation) AND macrolide or doxycycline OR monotherapy with a respiratory fluoroquinolone (examples include levofloxacin, moxifloxacin or gemifloxacin) can be considered.

Acute Exacerbations of Chronic Bronchitis

CDC antibiotic prescribing guidelines in adults note that antibiotics are not recommended for acute uncomplicated bronchitis regardless of the cough duration [5]. Treatment options generally include symptomatic management with cough suppressants, antihistamines or decongestants. For those with chronic bronchitis half of acute exacerbations may be due to a bacterial infection [6]. For moderate to severe flares antibiotics may be indicated. Cephalosporins such as cefdinir may be used for uncomplicated flares (age less than 65, FEV1 > 50 of predicted, less than 2 exacerbations per year and no cardiac disease). In addition to antibiotics, use of corticosteroids and inhaled bronchodilators are generally also important aspects of treatment.

Acute Maxillary Sinusitis

CDC antibiotic prescribing guidelines in adults note that 98% of sinusitis cases are viral and antibiotics are not guaranteed to help [5]. **Acute bacterial rhinosinusitis** based on symptoms that are: Severe (>3-4 days), such as a fever ≥39°C (102°F) and purulent nasal discharge or facial pain; persistent (>10 days) without improvement, such as nasal discharge or daytime cough; or worsening (3-4 days) such as worsening or new onset fever, daytime cough, or nasal discharge after initial improvement of a viral upper respiratory infections (URI) lasting 5-6 days. Watchful waiting is encouraged for uncomplicated cases for which reliable follow-up is available. Amoxicillin or amoxicillin/clavulanate is the recommended first-line therapy. Macrolides such as azithromycin are not recommended due to high levels of Streptococcus pneumoniae antibiotic resistance (~40%). For penicillin-allergic patients, doxycycline or a respiratory fluoroquinolone (levofloxacin or moxifloxacin) may be used as alternative agents.

Pharyngitis/Tonsillitis

Two studies (one in adults and adolescents and the other in pediatric patients) compared cefdinir 600 mg once daily or 300 g twice daily to penicillin 250 mg (or 10 mg/kg) four times daily for 10 days in the treatment of pharyngitis/tonsillitis [1]. Cefdinir once daily or twice daily was superior to penicillin 250 mg four times daily for both eradication of S. pyogenes and clinical cure rate for the adult/adolescent population as well as the pediatric population.

Two studies (one in adults and adolescents and the other in pediatric patients) compared cefdinir 300 mg twice daily for 5 days to penicillin 250 mg (or 10 mg/kg)

four times daily for 10 days [1]. Cefdinir twice daily was equivalent to penicillin 250 mg four times daily for both eradication of S. pyogenes and clinical cure rate for the adult/adolescent population as well as the pediatric population.

Uncomplicated Skin and Skin Structure Infections caused by Staphylococcus aureus

Management of skin and soft tissue infections (SSRIs) 2014 IDSA Practice Guidelines include a number of management recommendations [7]. Staphylococcus aureus (S. aureus) and Streptococcus pyogenes are common bacteria found in skin and soft tissue infections (SSTIs). Impetigo is a common type of skin infection caused by bacteria. Topical therapy such as mupirocin topical ointment applied twice a day for 5 days is a possible treatment option for milder forms of impetigo. Oral therapy is recommended for those with numerous lesions or in outbreaks affecting several people to help decrease transmission. In addition, treatment of deeper level tissue infections such as ecthyma will require oral antibiotics.

Oral therapy for skin infections typically consist of a 7-day regimen with an agent active against S. aureus unless cultures yield streptococci alone, for which a penicillin such as penicillin VK 250-500 mg four times daily or a first-generation cephalosporin such as cephalexin 500 mg four times daily could be considered according to the IDSA guidelines for diagnosis and management of skin and soft tissue infections [7].

Antibiotics that would cover for methicillin susceptible S. aureus (MSSA) skin infections would be medications such as:

- Dicloxacillin 500 mg four times a day (adult dose) OR
- Cephalexin 500 mg four times a day (adult dose)

Statewide antibiogram information indicates good susceptibility to these antibiotics. MSSA strains also have good susceptibility to ceftriaxone, another 3rd generation cephalosporin similar to cefdinir.

When methicillin resistant S. aureus (MRSA) is suspected or confirmed antibiotics to consider would include:

- Doxycycline 100 mg twice a day (not recommended for children 8 years of age or younger) OR
- Trimethoprim/sulfamethoxazole (Bactrim DS) 1-2 double strength tablets twice a day (adult dose)

Statewide antibiogram information indicate good MRSA susceptibility to these antibiotics.

Acute Bacterial Otitis Media (pediatric indication)

CDC pediatric antibiotic prescribing guidelines note that 98% of sinusitis cases are viral and antibiotics are not guaranteed to help [8]. Mild cases with unilateral symptoms in children 6-23 months of age or unilateral or bilateral symptoms in children >2 years may be appropriate for watchful waiting based on shared decision-making. Amoxicillin remains first line therapy for children who have not received amoxicillin within the past 30 days. Amoxicillin/clavulanate is recommended if amoxicillin has been taken within the past 30 days, if concurrent purulent conjunctivitis is present, or if the child has a history of recurrent acute otitis media unresponsive to amoxicillin. For children with a non-type I hypersensitivity to penicillin (not IgE-mediated reaction): cefdinir, cefuroxime, cefpodoxime, or ceftriaxone may be considered [8].

Acute Uncomplicated Cystitis (off-label)

Antimicrobial Agents for Empiric Treatment of Acute Uncomplicated Cystitis in Women per the 2010 IDSA and European Society for Microbiology and Infectious Diseases Practice Guidelines recommend β-lactams such as cefdinir (not ampicillin or amoxicillin alone) as well as fluoroquinolones (noting high resistance in some areas) as potential second-line treatment options [2]. The first-generation cephalosporin, cephalexin, is less well studied for UTI. First-line U.S. options based on availability, allergy history and tolerance include nitrofurantoin (avoid if early pyelonephritis suspected), trimethoprim-sulfamethoxazole 160/800 mg (avoid if resistance prevalence exceeds 20% or used for UTI in previous 3 months) or fosfomycin (lower efficacy than some other agents, avoid if early pyelonephritis suspected).

At some state facilities, trimethoprim-sulfamethoxazole resistance to E. coli well exceeds 20% eliminating this first line treatment option. This leaves only nitrofurantoin and fosfomycin as possible first-line empiric treatment options for those facilities. Fluoroquinolones can be used as a second-line option and ofloxacin, ciprofloxacin and levofloxacin are efficacious in a 3 day regimen; however, this class of antibiotics is often discouraged due to emerging resistance patterns and some state facilities also have a fluoroquinolone resistance rate to E. coli well exceeding 20%. Beta-lactam antibiotics (not amoxicillin or ampicillin alone) such as amoxicillin-clavulanate, cefdinir, cefaclor (second generation cephalosporin) and cefpodoxime-proxetil (third generation cephalosporin) in 3-7 day regimens may be appropriate when other first-line options cannot be used. Some state facilities have good susceptibility of E. coli to amoxicillin-clavulanate, 3rd generation cephalosporins as well as some 2nd generation cephalosporins.

Dosage Forms/Cost

Cefdinir (Omnicef) 300 mg cap BID: $1.33/day

Cefuroxime axetil (Ceftin) 250 mg tab BID dose: $0.34/day

Ceftriaxone (Rocephin) 250 mg injection: $1.19/injection
Amoxicillin/clavulanate (Augmentin) 500/125 mg tab TID dose: $1.23/day
Penicillin V Potassium (Pen-Vee K) 250 mg tab QID dose: $0.11/day

Special Considerations

Suspension is also available

Summary/Conclusion

Cefdinir is periodically prescribed as a nonformulary medication for bacterial infections. This third generation cephalosporin is available in an oral formulation and has similar clinical cure and eradication rates for community acquired pneumonia as the second generation cephalosporin cefaclor. Community acquired pneumonia eradication rates for amoxicillin/clavulanate were also similar to cefdinir; however, clinical cure rates were superior for amoxicillin/clavulanate (89%) vs cefdinir (80%). Guidelines suggests utility for uncomplicated acute flares of chronic bronchitis. Cefdinir was superior to penicillin for the treatment of pharyngitis with a 10 day course of treatment and similar to penicillin when comparing a 5 day course of cefdinir with a 10 day course of penicillin. Cefdinir is also an option for the treatment of MSSA SSTIs. It can be an alternative treatment option to amoxicillin and amoxicillin/clavulanate in pediatric bacterial otitis media. Guidelines also suggest potential use as a second-line option in the treatment of uncomplicated cystitis. Currently the only second generation cephalosporin on formulary is cefuroxime axetil which is dosed twice daily and the only third generation cephalosporin on formulary is ceftriaxone which is only available in an injectable formulation. The addition of cefdinir would provide an oral third generation cephalosporin treatment option and the ability to dose once daily would provide an advantage over the second generation oral cephalosporin currently on formulary, cefuroxime axetil. Cefdinir is also available as an oral suspension that can be stored at room temperature after reconstitution.

Recommendation

Addition of cefdinir to the formulary is recommended.

References

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Monograph Prepared by:
Reagan Webber
ASH Pharmacy Volunteer

Reviewed by:
Lisa M. Mican, Pharm.D., BCPP
Director of Pharmacy
Clinical Pharmacist
Austin State Hospital
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