

Lessons Were Learned in the Mumps Outbreak

BY PATRICE WENDLING
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KANSAS CITY, MO. — The resurgence of mumps in 2006 was unexpected but provided the medical community with some valuable lessons, two infectious disease experts reported at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

Particularly vexing was the presence of cases without the classical presentation of

parotitis and the inability to rule out cases based on negative laboratory results, said Dr. Gustavo H. Dayan of the CDC's Division of Viral Diseases, and Measles, Mumps, and Rubella team leader.

In Iowa, the hardest-hit state in the nation, 71 of 113 (63%) cases at two colleges presented without classic symptoms.

Laboratory diagnosis was very challenging because IgM response was usually absent and performance of different IgM assays was variable. Immunoglobulin

G was present in many patients at the moment of diagnosis. Viral culture and polymerase chain reaction (PCR) had a low yield, especially when the specimens weren't taken early in the course of the disease, he said.

A viral shedding study using PCR assays in 31 consecutive Kansas cases resulted in only eight positive results. Seven of the eight samples were taken during the first 3 days after the onset of parotitis, Dr. Dayan said.

Surveillance was difficult because the new case-investigation report form was not adequate and different forms were being used by different states, he said. The Council of State and Territorial Epidemiologists clinical case definition of mumps does not include cases with classic complications of mumps without the presence of parotitis for 2 days.

"We really feel that some of the cases at the beginning of the outbreak may have been discarded based on the not very clear

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Omnicef® (cefdinir) capsules
Omnicef® (cefdinir) for oral suspension

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INDICATIONS AND USAGE

To reduce the development of drug-resistant bacteria and maintain the effectiveness of OMNICEF and other antibacterial drugs, OMNICEF 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.

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).

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*.

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*.

Pediatric Patients

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*.

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

Prescribing OMNICEF 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 OMNICEF should be reduced because high and prolonged plasma concentrations of cefdinir can result following recommended doses.

Information for Patients

Patients should be counseled that antibacterial drugs including OMNICEF should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When OMNICEF 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 OMNICEF 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 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.

Diabetic patients and caregivers 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 $t_{1/2}$.

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 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 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 Clinistest®, 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/m²/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/m²/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/m²/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 B 100 mg/kg/day, and in rat offspring at B 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.

clinical symptoms and negative results," he said. "However, during the outbreak, some of the cases may have been over-counted because the surveillance system was very enhanced and cases without symptoms may have been counted."

What is known is that the outbreak primarily affected young non-Hispanic white adults, aged 18-24, as well as females and those living on college campuses.

A total of 45 states reported mumps cases in 2006, and 8 states in the Midwest were the most affected. Iowa had the highest incidence at 66/100,000, compared with Minnesota, which had the lowest incidence at 2.8/100,000. Available data from

these eight states show that about 43% of the cases had received two doses of mumps vaccine, Dr. Dayan said in an interview.

Overall, 6,330 cases were reported to the National Notifiable Diseases Surveillance System in 2006, and approximately 120 new cases have been reported in 2007, he said. Few infants were affected, and no large school or day care outbreaks were reported. The outbreak did not spread to unvaccinated populations.

The source of the outbreak is not known. But the mumps strain in Iowa and other affected states has been identified as genotype G5, which is the same one that

circulated in the United Kingdom throughout the 2004-2006 outbreaks. Virus genotyping in Virginia from a cluster in the latter part of the year isolated the G1 genotype, which suggests a different source of importation, he said.

Compliance with the mumps-isolation recommendation proved challenging. Compliance was 87% for isolation less than 4 days and just 66% for isolation 4 days or more among 133 Kansas students for whom data was available.

Because of this and available viral shedding data, the CDC is expected to recommend in a memo to all the states that the isolation period for mumps be

changed to 5 days, Dr. Dayan said.

Kansas changed its viral isolation recommendation to 4 days in early April 2006 but, later that month, reverted to 9 days, which is the period required by Kansas state law and recommended by the CDC, Ms. Jennifer Hill, an epidemiologist with the Kansas Department of Health and Environment, said in a separate presentation during the meeting.

Kansas was the second-hardest hit state in the United States, with 986 cases reported in late 2005-2006; 40% of these were among young adults (18-24 years old), 60% were among women and girls, and 30% were among college students.

Good cooperation and communication between local health and student health centers provided follow-up on almost all of the college students. But questions arose as to whether students should be isolated at home or at school, how long the isolation should last, and who was responsible for their follow-up compliance. Students were told not to go to school for 9 days, but officials received reports some

students returned to class early to avoid missing exams, Ms. Hill said.

Kansas also vacillated between one and two doses of mumps vaccine as its definition of adequate protection before ultimately deciding that patients who

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receive one dose of measles-mumps-rubella (MMR) vaccine are adequately vaccinated. Separate guidelines and algorithms were established for health care workers and day care workers that rely on self-reported vaccination history data.

Immunization history available on 85% of cases revealed that 73% had received one dose of MMR vaccine and 7% were unvaccinated, and 64% of all vaccinated patients had a history of two doses.

Laboratories were able to communicate those results to clinicians, but at times, there weren't enough qualified workers or materials to perform the necessary testing. After the testing, it wasn't clear how to interpret negative results and how to convince local authorities that it was still mumps. "Negative results do not rule out disease," Ms. Hill said.

Delayed recognition of the outbreak, enhanced transmission in colleges, and unrecognized importations all contributed to the outbreak, according to Dr. Dayan. "In addition, two doses of mumps vaccine may confer about 90%-95% vaccine effectiveness, which may result in accumulation of susceptible persons sufficient to sustain transmission and a sizeable outbreak on a periodic basis," he said. There was no evidence of genetic drift, although the role of waning immunity is unclear.

"However, high MMR vaccine coverage levels and vaccine effectiveness likely prevented thousands of additional mumps cases, the incidence was relatively low, and the disease appeared to be modified with low rates of complications," Dr. Dayan said.

ADVERSE EVENTS

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

In clinical trials, 5093 adult and adolescent patients (3841 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. No deaths or permanent disabilities were attributed to cefdinir. One hundred forty-seven of 5093 (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. Nineteen of 5093 (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 = 3841 cefdinir-treated patients):

**ADVERSE EVENTS ASSOCIATED WITH CEFDINIR CAPSULES
US TRIALS IN ADULT AND ADOLESCENT PATIENTS
(N=3841)^a**

Incidence B 1%	Diarrhea	15%
	Vaginal moniliasis	4% of women
	Nausea	3%
	Headache	2%
	Abdominal pain	1%
	Vaginitis	1% of women
Incidence <1% but >0.1%	Rash	0.9%
	Dyspepsia	0.7%
	Flatulence	0.7%
	Vomiting	0.7%
	Abnormal stools	0.3%
	Anorexia	0.3%
	Constipation	0.3%
	Dizziness	0.3%
	Dry mouth	0.3%
	Asthenia	0.2%
	Insomnia	0.2%
	Leukorrhea	0.2% of women
	Moniliasis	0.2%
	Pruritus	0.2%
	Somnolence	0.2%

^a 1733 males, 2108 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=3841)**

Incidence B 1%	↑ Urine leukocytes	2%
	↑ Urine protein	2%
	↑ Gamma-glutamyltransferase ^a	1%
	↓ Lymphocytes, ↑ Lymphocytes	1%, 0.2%
	↑ Microhematuria	1%
Incidence <1% but >0.1%	↑ Glucose ^a	0.9%
	↑ Urine glucose	0.9%
	↑ White blood cells, ↓ White blood cells	0.9%, 0.7%
	↑ Alanine aminotransferase (ALT)	0.7%
	↑ Eosinophils	0.7%
	↑ Urine specific gravity, ↓ Urine specific gravity ^a	0.6%, 0.2%
	↓ Bicarbonate ^a	0.6%
	↑ Phosphorus, ↓ Phosphorus ^a	0.6%, 0.3%
	↑ Aspartate aminotransferase (AST)	0.4%
	↑ Alkaline phosphatase	0.3%
	↑ Blood urea nitrogen (BUN)	0.3%
	↓ Hemoglobin	0.3%
	↑ Polymorphonuclear neutrophils (PMNs), ↓ PMNs	0.3%, 0.2%
	↑ Bilirubin	0.2%
	↑ Lactate dehydrogenase ^a	0.2%
	↑ Platelets	0.2%
	↑ Potassium ^a	0.2%
	↑ Urine pH ^a	0.2%

^a N<3841 for these parameters

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

In clinical trials, 2289 pediatric patients (1783 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. Forty of 2289 (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 2289 (0.2%) 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=1783 cefdinir-treated patients):

**ADVERSE EVENTS ASSOCIATED WITH CEFDINIR SUSPENSION
US TRIALS IN PEDIATRIC PATIENTS
(N=1783)^a**

Incidence B 1%	Diarrhea	8%
	Rash	3%
	Vomiting	1%
Incidence <1% but >0.1%	Cutaneous moniliasis	0.9%
	Abdominal pain	0.8%
	Leukopenia ^b	0.3%
	Vaginal moniliasis	0.3% of girls
	Vaginitis	0.3% of girls
	Abnormal stools	0.2%
	Dyspepsia	0.2%
	Hyperkinesia	0.2%
	Increased AST ^b	0.2%
	Maculopapular rash	0.2%
	Nausea	0.2%

^a 977 males, 806 females

^b Laboratory changes were occasionally reported as adverse events.

NOTE: In both cefdinir- and control-treated patients, rates of diarrhea and rash were higher in the youngest pediatric patients. The incidence of diarrhea in cefdinir-treated patients ≤2 years of age was 17% (95/557) compared with 4% (51/1226) in those >2 years old. The incidence of rash (primarily diaper rash in the younger patients) was 8% (43/557) in patients ≤2 years of age compared with 1% (8/1226) in those >2 years old.

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 OF POSSIBLE CLINICAL SIGNIFICANCE OBSERVED WITH
CEFDINIR SUSPENSION US TRIALS IN PEDIATRIC PATIENTS
(N=1783)**

Incidence B 1%	↑ Lymphocytes, ↓ Lymphocytes	2%, 0.8%
	↑ Alkaline phosphatase	1%
	↓ Bicarbonate ^a	1%
	↑ Eosinophils	1%
	↑ Lactate dehydrogenase	1%
	↑ Platelets	1%
	↑ PMNs, ↓ PMNs	1%, 1%
	↑ Urine protein	1%
Incidence <1% but >0.1%	↑ Phosphorus, ↓ Phosphorus	0.9%, 0.4%
	↑ Urine pH	0.8%
	↓ White blood cells, ↑ White blood cells	0.7%, 0.3%
	↓ Calcium ^a	0.5%
	↓ Hemoglobin	0.5%
	↑ Urine leukocytes	0.5%
	↑ Monocytes	0.4%
	↑ AST	0.3%
	↑ Potassium ^a	0.3%
	↑ Urine specific gravity, ↓ Urine specific gravity	0.3%, 0.1%
	↓ Hematocrit ^a	0.2%

^a N=1387 for these parameters

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, serum sickness-like reactions, 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 **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.

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