



Dr. Capute

**Arnold J. Capute, M.D., M.P.H., FAAP**, of Baltimore, died of congestive heart failure Nov. 30 at age 80. The



Dr. Drinkaus



Dr. Katsampes

Arnold J. Capute Award from the AAP Section on Children with Disabilities recognizes a physician who makes a



Dr. Law



Dr. Luhby

notable contribution to the health and well-being of children with disabilities. **Harold J. Drinkaus, M.D. FAAP**,



Dr. Rapkin



Dr. Reyes

of Salt Lake City, died Nov. 15 at age 67.

**William E. Hart Jr., M.D., FAAP**, of West Hartford, Conn., died Nov. 10 at age 78.

**Chris P. Katsampes, M.D., FAAP**, of Richmond, Va., died from hypertensive cardiovascular disease Nov. 11 at age 93.

**Nancy E. Law, M.D., FAAP**, of Bloomfield, Conn., died Nov. 9 at age 40.

**A. Leonard Luhby, M.D., FAAP**, of Bronx, N.Y., died from complications suffered in a fall Nov. 14 at age 86.

**Lawrence K. Pickett, M.D., FAAP**, of Ithaca, N.Y., died Nov. 15 at age 84.

**Richard H. Rapkin, M.D., FAAP**, of Somerville, N.J., died from brain cancer Nov. 9 at age 68.

**Amelia Reyes, M.D., FAAP**, of Port Washington, N.Y., died Nov. 15 at age 66.

**Revenue** *Continued from page 27*

Address business issues, including recognition of the entire CPT coding system (especially important for special needs children), prompt pay/billing relationships and utilization management issues. Be aggressive! Look for win/win relationships with payers. Know your negotiating position and whenever possible have data to support your position and value.

Create, utilize and maximize relationships with the Academy, AAP state chapters, state medical association and the American Medical Association, insurance brokers, businesses (human resource coordinators), state department of human services and politicians. Look for alignment of issues and incentives with health care and advocacy organizations. Promote the medical home as a win/win, providing value with decreased emergency department utilization, decreased length of hospital stay and improved pharmacy management.

Most importantly, focus on improving coding. It is the easiest and most effective way to increase your bottom line without working harder. It also has the bonus of decreasing liability and resulting in accurate encounter-based information flow critical to tracking and demonstrating provider value. Let's improve our bottom line by working smarter, we can't work harder!

*Dr. Tuck is a member of the AAP Section on Administration and Practice Management and serves on the AAP Committee on Coding and Nomenclature and is the AAP liaison to the Relative Value Update Committee.*

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**OMNICEF®**  
(cefdinir)

**BRIEF SUMMARY**  
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

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

**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  $\beta$ -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.

**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.

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  $\beta$ -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<sub>4</sub>) 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 Clinistix®, 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<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/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  $\geq 100$  mg/kg/day, and in rat offspring at  $\geq 32$  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.

**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 in adult and adolescent patients (N = 3841 cefdinir-treated patients [1733 males and 2108 females]): 1) Incidence  $\geq 1\%$ : diarrhea (15%), vaginal moniliasis (4% of women), nausea (3%), headache (2%), abdominal pain (1%), vaginitis (1% of women); 2) 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%).

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 in 3841 adult and adolescent patients: 1) Incidence  $\geq 1\%$ : Urine leukocytes (2%), Turine protein (2%),  $\uparrow$ gamma-glutamyltransferase<sup>†</sup> (1%),  $\downarrow$ lymphocytes (1%),  $\uparrow$ microhematuria (1%); 2) Incidence <1% but  $>0.1\%$ :  $\uparrow$ glucose (0.9%), Turine glucose (0.9%),  $\uparrow$ white blood cells (0.9%),  $\downarrow$ white blood cells (0.7%), Talanine aminotransferase (ALT) (0.7%), Teosinophils (0.7%), Turine specific gravity (0.6%), Urine specific gravity<sup>‡</sup> (0.2%),  $\downarrow$ bicarbonate<sup>§</sup> (0.6%),  $\uparrow$ phosphorus (0.6%),  $\downarrow$ phosphorus<sup>§</sup> (0.3%),  $\uparrow$ aspartate aminotransferase (AST) (0.4%), Talikaline phosphatase (0.3%),  $\uparrow$ blood urea nitrogen (BUN) (0.3%),  $\downarrow$ hemoglobin (0.3%),  $\uparrow$ polymorphonuclear neutrophils (PMNs) (0.3%),  $\downarrow$ PMNs (0.2%),  $\uparrow$ bilirubin (0.2%),  $\uparrow$ lactate dehydrogenase<sup>¶</sup> (0.2%),  $\uparrow$ lymphocytes (0.2%),  $\uparrow$ platelets (0.2%),  $\uparrow$ potassium<sup>\*\*</sup> (0.2%), Turine pH<sup>††</sup> (0.2%). (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 [977 males and 806 females]): 1) Incidence  $\geq 1\%$ : diarrhea (8%), rash (3%), vomiting (1%); 2) Incidence <1% but  $>0.1\%$ : cutaneous moniliasis (0.9%), abdominal pain (0.8%), leukopenia<sup>‡</sup> (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<sup>¶</sup> (0.2%), maculopapular rash (0.2%), nausea (0.2%). († 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  $\leq 2$  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  $\leq 2$  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 in 1783 pediatric patients: 1) Incidence  $\geq 1\%$ :  $\uparrow$ lymphocytes (2%), Talikaline phosphatase (1%),  $\downarrow$ bicarbonate<sup>§</sup> (1%), Teosinophils (1%),  $\uparrow$ lactate dehydrogenase (1%),  $\uparrow$ platelets (1%),  $\uparrow$ PMNs (1%),  $\downarrow$ PMNs (1%), Turine protein (1%); 2) Incidence <1% but  $>0.1\%$ :  $\uparrow$ phosphorus (0.9%), Turine pH (0.8%),  $\downarrow$ lymphocytes (0.8%),  $\downarrow$ white blood cells (0.7%),  $\downarrow$ calcium<sup>\*\*</sup> (0.5%),  $\downarrow$ hemoglobin (0.5%), Turine leukocytes (0.5%),  $\uparrow$ monocytes (0.4%),  $\downarrow$ phosphorus (0.4%),  $\uparrow$ AST (0.3%),  $\uparrow$ potassium<sup>\*\*</sup> (0.3%), Turine specific gravity (0.3%),  $\uparrow$ white blood cells (0.3%),  $\downarrow$ hematocrit<sup>††</sup> (0.2%), Urine specific gravity (0.1%). († 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, 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  $\beta$ -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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(cefdinir)