DURICEF®

SB

CEFADROXIL MONOHYDRATE

ORAL

DESCRIPTION

DURICEF contains cefadroxil, a semisyntheitc cephalosporin antibiotic intended for oral administration.

DURICEF (capsules, dispersible tablets, powders for oral solution or pediatric drops) contains the following inactive ingredients:

Capsules: Magnesium Stearate.

Dispersible tablets: Avicel, Magnesium Stearate, Crospovidone, Natural & Artifical Orange Juice Flavor, Orange Flavor Terpeneless S.D., Artifical Pineapple Flavor, FD&C Yellow # 6 Dye, Sweetener, Guar Gum.

Powders for Oral solution and Pediatric Drops: Sodium Benzoate, Xanthan Gum, Polysorbate 80, Natural and Artifical Flavors, FD&C Yellow # 6 Dye, Sucrose (Medium Granulated).

CLINICAL PHARMACOLOGY

Cefadroxil is rapidly absorbed after oral administration. Following single doses of 500 mg and 1 g, average peak serum concentrations were approximately 16 and 28 mcg/ mL, respectively. Measurable serum levels were present 12 hours after administration.

Absorption characteristics are not different between fasted and nonfasted subjects. Over 90% of the drug is excreted unchanged in the urine within 24 hours. The elimination half-life is about 2 hours. Peak urine concentrations are approximately 1800 mcg/mL during the period following a single 500 mg oral dose. Increases in dosage generally produce a proportionate increase in cefadroxil urinary concentration. The urine antibiotic concentration, following a 1 gm dose, was maintained well above the MIC of susceptible urinary pathogens for 20 to 22 hours.

Microbiology

In vitro tests demonstrate that the cephalosporins are bactericidal because of their inhibition of cell-wall synthesis. **DURICEF** is active against the following organisms *in vitro*:

Beta-hemolytic streptococci.
Streptococcus pneumoniae.
Staphylococci, including coagulase-positive, coagulase-negative, and penicillinase - producing strains.
Escherichia coli.
Proteus mirabilis.
Klebsiella species.
Moraxella (Branhamella) catarrhalis.
Bacteroides species (excluding *Bacteroides fragilis*).

Other strains of sensitive gram-negative organisms include some strains of *Haemophillus influenzae, Salmonella species and Shigella species.*

Note: Most strains of Enterococci (*Enterococcus faecalis* and *E. faecium*) are resistant to **DURICEF**. **DURICEF** is not active against most strains of *Enterobacter* species, *Morganella morganii* (formerly proteus morganii), and *Proteus Vulgaris*. It has no activity against *Pseudomonas* species and *Acinetobacter calcoaceticus* (formerly *Mima* and *Herellea* species).

Disc Susceptibility Tests:

Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. One recommended laboratory procedure uses a cephalosporin class disc for testing susceptibility; interpretations correlate zone diameters of this disc test with MIC values of **DURICEF**. With this procedure, a report of "susceptible" indicates that the infecting organism is likely to respond to therapy. A report of "resistant" indicates that the infecting orgainsm is not likely to respond to therapy. A report of "intermediate susceptibility" suggests that the organism would be susceptible if the infection is confined to an area where adequate drug concentrations can be achieved, for example, the urinary tract.

INDICATIONS

DURICEF is indicated in the treatment of the following infections when due to susceptible microorganisms:

Upper and lower respiratory infections.
Skin and soft tissue infections.
Genitourinary tract infections.
Other infections: osteomyelitis and septic arthritis.

Note: Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated. Surgical procedures should be performed when indicated.

Note: Only penicillin by the intramuscular route of administration has been shown to be effective in the prophylaxis of rheumatic fever. **DURICEF** is generally effective in the eradication of streptococci from the oropharynx. However, data establishing the efficacy of **DURICEF** for the prophylaxis of subsequent rheumatic fever are not available.

CONTRAINDICATIONS

DURICEF is contraindicated in patients with known allergy to the cephalosporin group of antibiotics or to any component of the formulation.

WARNINGS

Before therapy with **DURICEF** is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to **DURICEF**, other cephalosporins, penicillins, or other drugs. If this product to be given to penicillin-sensitive patients, caution should be exercised because cross - sensitivity among beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with history of penicillin allergy. If an allergic reaction to **DURICEF** occurs, discontinue the drug. Serious acute hypersensitivity reactions may require emergency treatment measures.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, and may range 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. After the diagnosis of colitis has been established, therapeutic measures should be initiated.

PRECAUTIONS

General:

DURICEF should be used with caution in the presence of impaired renal function. (See DOSAGE AND ADMINISTRATION for dosage guidelines). In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be made prior to and during therapy.

Prolonged use of DURICEF may result in the overgrowth of non susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are peformed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

DURICEF, should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Carcinogensis, Mutagenesis and Impairment of Fertility:

No long-term studies have performed to determine carcinogenic potential. No genetic toxicity tests have been performed.

Pregnancy:

Reproduction studies have been performed in mice and rats at doses up to 11 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefadroxil. 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.

Nuring Mothers:

Cefadroxil is distributed into breast milk; therefore, this drug should be used with caution in nursing women.

ADVERSE EVENTS

The adverse events observed with cefadroxil are similar to those observed with other cephalosporins.

Gastrointestinal - Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment. Nausea, vomiting, and dyspepsia have been reported rarely. Administration with food decreases nausea. Diarrhea has also occurred.

Hypersensitivity - In common with other cephalosporins, allergic reactions, including pruritus, rash, urticaria, and angioedema have been observed. These reactions usually subsided upon discontinuation of the drug. Erythema multiforme, Stevens-Johnson syndrome, serum sickness, and anaphylaxis have been reported rarely.

Other reactions have included genital pruritus, genital candidiasis, vaginitis, moderate transient neutropenia, fever, and elevations in serum transaminase. In common with other cephalosporins, agranulocytosis, thrombocytopenia and arthralgia have been rarely reported. During postmarketing experience, hepatic dysfunction , including cholestasis has been reported, and rare reports of idiosyncratic hepatic failure have been received; because of the uncontrolled nature of these spontaneous reports, a causal relationship to **DURICEF** has not been established.

OVERDOSAGE

Data from a study of children under six years of age who had ingested a maximum of 250 mg/kg of penicillin or a cephalosporin derivative suggested that ingestion of less than 250 mg/kg of cephalosporin (i.e., 5 to 10 times recommended dose) is not associated with significant outcomes. No treatment is required other than general support and observation. During the 72-hour evaluation period, most of the children remained asymptomatic. Gastrointestinal disturbances and rash were reported in some children. For amounts greater than 250 mg/kg, induce gastric emptying (emesis induction or gastric lavage).

For information or removal of drug by hemodialysis, see Dosage and Administration.

DOSAGE AND ADMINISTRATION

DURICEF is acid stable and may be administered orally without regard to meals. Administration with food may be helpful in diminishing potential gastrointestinal complaints occasionally associated with oral cephalosporin therapy.

Adults:

Urinary Tract Infection:

For uncomplicated lower urinary tract infections (i.e., cystitis) the usual dosage is 1 or 2 g per day in a single dose or in two equally divided doses.

For all other urinary tract infections the usual dosage is 2 g per day in two equally divided doses.

Skin and Skin Structure Infections:

For skin and skin structure infections the usual dosage is 1 g per day in a single dose or two equally divided doses.

Pharyngitis and Tonsillitis:

Due to Group A beta-hemolytic streptococci.

Treatment of Group A beta-hemolytic streptococcal pharyngitis and tonsillitis - 1 g per day in a single dose or two equally divided doses for at least ten days.

Upper and Lower respiratory Tract Infections:

For mild infections the usual dosage is 1 g per day in two equally divided doses.

For moderate to severe infections the recommended dosage is 1 g to 2 g daily in two equally divided doses.

Children:

The recommended dosage for children is 25 to 50 mg/kg/day in two equally divided doses (every 12 hours) as indicated. For pharyngitis, tonsillitis, and impetigo the recommended daily dosage may be administered as a single dose or in two equally divided doses (every 12 hours).

DURICEF ORAL SUSPENSION OR PEDIATRIC DROPS (dose q 12 h)

Child's weight (Kg)	Drops 100 mg/1 mL (dropperful)	125 mg / 5 mL (25 mg / mL)	250 mg / 5 mL (50 mg / mL)	500 mg / 5 mL (100 mg / mL)
4	0.5 - 1 dropperful	--	--	--
5	--	2.5 - 5.0 mL	--	--
10	--	5.0 - 10 mL	2.50 - 5.0 mL	1.250 - 2.50 mL
15	--	7.5 - 15 mL	3.75 - 7.5 mL	1.875 - 3.75 mL
20	--	10.0 - 20 mL	5.00 - 10.0 mL	2.500 - 5.00 mL
25	--	12.5 - 25 mL	6.25 - 12.5 mL	3.125 - 6.25 mL

In the treatment of beta-hemolytic streptococcal infections, a therapeutic dosage of **DURICEF** should be administered for at least 10 days. For the treatment of beta-hemolyitc streptococcal pharyngitis or tonsillitis in both adults and children, **DURICEF** may be administered in the usual daily dose either in two divided doses or a single dose.

In patients with renal impairment, the dosage of cefadroxil should be adjusted according to creatinine clearance rates to prevent drug accumulation. The following schedule is suggested. In adults, the initial dose is 1 g of DURICEF and the maintenance dose (based on the creatinine clearance rate) is 500 mg at the time intervals listed below.

Creatinine Clearance (mL / min / 1.73 m^2)	Dosage Interval
0 - 10	36 hours
10 - 25	24 hours
25 - 50	12 hours

Patients with creatinine clearance rates over 50 mL/min/1.73 m^2 may be treated as if they were patients having normal renal function.

In five adult anuric patients, it was demonstrated that an average of 63% of a 1 g oral dose is extracted from the body during a 6 to 8 hour hemodialysis session.

Methods of Preparation:

Oral Suspension / Pediatric Drops:

Shake or tap the bottle to loosen the powder. Add appropriate amount of water (see below) in

two portions. Invert the bottle, and shake it well after each addition.
When oral suspension is constituted as specified, 5 mL of the resulting suspension contains 125 mg, 250 mg, or 500 mg of cefadroxil activity as the monohydrate, depending upon the concentration of the formulation.
When pediatric drops constituted with 7 ml of water as specified, 1 ml (dropperful) contains 100 mg of cefadroxil activity as the monohydrate.

Bottle Size	Total Amount of Water for Reconstitution
100 mL	67 mL
75 mL	51 mL
60 mL	40 mL
50 mL	34 mL
Pediatric drops 10 mL	7 mL

Constituted DURICEF for oral suspension / pediatric drops is stable for 7 days at room temperaure (store in a cool, dry place) or 14 days when stored under refrigeration. Shake bottle well before using. Keep bottle tightly closed. Discard unused portion after 7 days at room temperature or 14 days under refrigeration.

Dispersible Tablets:
After removing the foil wrapper, drop the tablet into 120 ml of water. Allow 30 to 60 seconds for the tablet to disperse. Stir contents thoroughly and swallow entirely.
Dispersible tablets should be prepared immediately prior to ingestion.

STORAGE RECOMMENDATIONS

Store at temperatures between 15°to 30°C. When stored at 15°to 30°C, in a dry place, **DURICEF** capsules, tablets, foil-wrapped dispersible tablets, and unconstituted powder will remain stable until expiration date indicated on package.

HOW SUPPLIED

DURICEF capsules:
Box of 16 capsules 250 mg or 500 mg
Each capsule contains cefadroxil monohydrate equivalent to 250 or 500 mg cefadroxil.
DURICEF for oral suspension:
Each 5 mL of reconstituted suspension contains cefadroxil monohydrate equivalent to 125 mg, 250 mg, or 500 mg cefadroxil.
DURICEF dispersible tablets:
Box off 6 dispersible tablets 1 g.
Each dispersible tablet contains cefadroxil monohydrate equivalent to 1 g cefadroxil.
DURICEF pediatric drops:
Each 1 mL (dropperful) of reconstituted pediatric drops contains cefadroxil monohydrate equivalent to 100 mg cefadroxil.

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