

Nominations from FDA's Center for Drug Evaluation and Research

1. Genotoxicity and Carcinogenicity testing of Cefuroxime (CDER)

Cefuroxime is a semi-synthetic, broad-spectrum cephalosporin antibiotic for oral administration. Chemically, cefuroxime is formulated as the axetil with a molecular formula of $C_{20}H_{22}N_4O_{10}S$, and it has a molecular weight of 510.48. Cefuroxime antibiotics are indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in: 1) Pharyngitis and Tonsillitis caused by *Streptococcus pyogenes*, 2) Acute Bacterial Otitis Media caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, or *Streptococcus pyogenes*, 3) Acute Bacterial Maxillary Sinusitis caused by *Streptococcus pneumoniae* or *Haemophilus influenzae*, 4) Acute Bacterial Exacerbation of Chronic Bronchitis caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Haemophilus parainfluenzae*, 5) Uncomplicated Skin and Skin-Suture Infections caused by *Staphylococcus aureus* or *Streptococcus pyogenes*, 6) Uncomplicated Urinary Tract Infections caused by *Escherichia coli* or *Klebsiella pneumoniae*, 7) Uncomplicated Gonorrhoea caused by strains of *Neisseria gonorrhoeae*, and 8) Early Lyme Disease caused by *Borrelia burgdorferi*.

Cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolyzed by non-specific esterases in the intestinal mucosa and blood to Cefuroxime, which is distributed throughout the extracellular fluids. The axetil moiety is metabolized to acetaldehyde and acetic acid. Cefuroxime is excreted unchanged in the urine (about 50% after 12 hours is in the urine).

There have been no animal carcinogenicity testing for this cefuroxime, if fact, no cephalosporin class antibiotic has undergone carcinogenicity testing.

CDER believes that because of use patterns, its excellent absorption and distribution throughout the extracellular fluids, the fact that this class of antibiotic has not been tested for carcinogenicity, and potential prolonged exposures to this drug, that chronic carcinogenicity studies are warranted.