

AT THE HEART OF RATIONAL ANTIBIOTIC THERAPY OF INFECTIONS CAUSED BY GRAM-NEGATIVE AEROBES

Cefoperabol®

(cefoperazone)

3rd generation parenteral cephalosporin



The antibiotic for effective therapy of severe infections:

- moderate to severe lower respiratory tract infections, including nosocomial pneumonia, aspiration pneumonia, pleural empyema and lung abscesses
- severe infections of ear, nose and throat caused resistant bacteria
- intraabdominal infections
- biliary tract infections
- pelvic inflammatory disease (PID), endometritis, and other infections of female genital tract
- complicated forms of urinary tract infections
- infections of the skin and skin structures, bone and joint
- sepsis
- infections in patients with granulocytopenia, including febrile neutropenia

ABOLMED
PHARMACEUTICAL COMPANY

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DESCRIPTION

Cefoperabol® (cefoperazone) is a sterile, semisynthetic, 3rd generation parenteral cephalosporin antibiotic with a broad spectrum of bactericidal activity against many Gram-positive and Gram-negative microorganisms (including resistant to other antibiotics strains and *P.aeruginosa*) for intravenous or intramuscular administration. **Cefoperabol®** is less active against Gram-positive aerobes than ceftriaxone and cefotaxime.

CLINICAL PHARMACOLOGY

High serum and bile levels of **Cefoperabol®** are attained after a single dose of the drug. The mean serum half-life of **Cefoperabol®** is approximately 2.0 hours, independent of the route of administration. In low birth-weight neonates, the half-life of **Cefoperabol®** in serum is 6–10 hours. **Cefoperabol®** achieves therapeutic concentrations in the following body tissues and fluids: interstitial fluid, cerebrospinal fluid (in patients with inflamed meninges), ascitic fluid, bone, urine, sputum, endometrium, myometrium, sinus mucous membrane, umbilical cord blood, amniotic fluid and lung. Cefoperazone is excreted mainly in the bile (urinary recovery of cefoperazone is 20%-30% in average). Bile concentration is maximal after 1-3 h after administration and is about 100 times higher than serum levels. **Cefoperabol®** does not displace bilirubin from complex with serum proteins.

SPECTRUM OF ACTIVITY

Cefoperabol® is active against a wide range of aerobic and anaerobic, Gram-positive and Gram-negative pathogens. The bactericidal action is mediated by inhibition of bacterial cell wall synthesis. **Cefoperabol®** is highly resistant to beta-lactamases of Gram-negative bacteria (excluding extended-spectrum of beta-lactamases). **Cefoperabol®** is usually active against the following organisms:

Gram-positive aerobes

S. aureus, penicillinase and non-penicillinase producing strains, *S. epidermidis*, *Str. pneumoniae*, *Str. pyogenes* (group A beta-hemolytic streptococci), *Str. agalactiae* (group B beta-hemolytic streptococci)

Gram-negative aerobes

E.coli, *Klebsiella* species (including *K. pneumoniae*), *E.species*, *Citrobacter* spp., *H. influenzae*, *P. mirabilis*, *P. vulgaris*, *M. morgani*, *P. stuartii*, *P. rettgeri*, *S. marcescens*, *Salmonella* spp., *Shigella* spp., *P. aeruginosa*, *Pseudomonas* spp., some strains of *A. calcoaceticus*, *N. gonorrhoeae*, *N. meningitidis*, *Y. enterocolitica*

Anaerobes

Peptococcus spp., *Peptostreptococcus* spp., *Clostridium* spp. (except *C. difficile*), *B. fragilis*, *Bacteroides* spp., *Fusobacterium* spp.

Cefoperabol® is inactive against: enterococci, methicillin-resistant staphylococci, group D streptococci, *Chlamidia* spp., *L. monocytogenes*, *B. anthracis*, *B. cereus*, *C. difficile*, *Mycoplasma* spp., *Mycobacterium* spp.

INDICATIONS

Cefoperabol® is indicated for the treatment of the severe and some moderate bacterial infections, including infections in immunocompromised patients, caused by susceptible microbes: moderate to severe lower respiratory tract infections, including nosocomial pneumonia, aspiration pneumonia, pleural empyema and lung abscesses; severe infections of ear, nose and throat caused by *P. aeruginosa* and other poly-resistant bacteria (acute sinusitis, otitis media, malignant otitis externa); intraabdominal infections, including community-acquired secondary and post-operative peritonitis, intra-hepatic abscesses, cholangitis, cholecystitis and other forms of biliary tract infections; pelvic inflammatory disease (PID), endometritis, and other infections of the female genital tract; complicated forms of urinary tract infections; infections of the skin, skin structures, bones and joints caused by resistant mixed microflora, including diabetic food infection, surgical site infections, invasive burn wound infection; septicemia; infections

in patients with granulocytopenia, including febrile neutropenia. **Cefoperabol®** could be administered as monotherapy and in combination with various antibiotics (aminoglycosides, metronidazole, fluorquinolones, glycopeptides). **Cefoperabol®** and aminoglycosides demonstrate significant synergism in bactericidal action against many strains of Gram-negative bacilli.

CONTRAINDICATIONS

Cefoperabol® is contraindicated in patients who have shown hypersensitivity to cefoperazone and the cephalosporin group of antibiotics.

PRECAUTION

Pregnancy Category B. This drug should be used during pregnancy only if clearly needed. Caution should be exercised when **Cefoperabol®** is administered to a nursing woman.

Drug Interactions

Increased nephrotoxicity has been reported following concomitant administration of cephalosporins and aminoglycoside antibiotics. **A disulfiram-like reaction has been reported when alcohol was ingested within 72 hours after Cefoperabol® administration.**

ADVERSE REACTIONS

Cefoperabol® is generally well tolerated. The following reactions have been reported: thrombophlebitis at the site of IV injections, allergic reactions (rash, urticaria, flushing, pruritus, eosinophilia, fever, dyspnea, anaphylaxis, interstitial nephritis and angioedema); hypotension, diarrhea, pseudomembranous colitis, nausea and vomiting; possible exacerbation of myasthenia gravis; eosinophilia, leucopenia, anemia, thrombocytopenia and a change in Coombs' test; transient elevations in SGOT, SGPT, serum LDH, serum alkaline phosphatase and jaundice; elevations in serum creatinine and/or blood urea nitrogen.

DOSAGE AND ADMINISTRATION

The usual **adult** dosage range is 1 gram to 2 grams IM or IV every 12 hours. Dosage should be determined by susceptibility of the causative organisms, severity of infection, and the condition of the patient. In severe infections, the total daily dose and/or frequency may be increased. Patients have been successfully treated with a total daily dosage of 6–12 grams divided into 2, 3, or 4 administrations ranging from 1.5 to 4 grams per dose.

The recommended dosage in **pediatric patients** is 50 to 100 mg/kg of body weight per day divided into two to three equal doses. The higher dosages should be used for more severe or serious infections. In cases of severe infections in pediatric patients the daily dose is increased up to 200 mg/kg body weight divided into 2-3 equal doses. In **neonates** a total daily dosage of **Cefoperabol®** is 50-100 mg/kg of body weight divided into 2 equal doses. IV administration is preferred.

If *C. trachomatis* is a suspected pathogen, appropriate anti-chlamydial coverage should be added, because cefoperazone has no activity against this organism. In cases of mixed-infection (peritonitis, PID) anti-anaerobic antibiotics (metronidazole) should be added. No dosage adjustment is necessary for patients with impairment of renal or hepatic function.

The serum half-life of cefoperazone is increased 2–4 fold in patients with hepatic dysfunction. In general, total daily dosage above 4 g should not be necessary in patients with severe hepatic disease and/or biliary obstruction.

HOW SUPPLIED

Cefoperabol® is available in sterile dry powder form in vials containing sterile cefoperazone sodium equivalent to 500 mg or 1 g of cefoperazone for intramuscular and intravenous administration (package of 50 vials). Store for 2 years at or below a room temperature of 25°C (77°F).

Cefoperabol® is manufactured by ABOLMED Ltd., Russia