COMPOSITION

Vials containing Cefazolin sodium, corresponding to 1 g and 2 g Cefazolin.

Sodium content - 48.3 mg/g.

PROPERTIES AND ANTIMICROBIAL SPECTRUM

Cefazolin is a semisynthetic beta-lactam antibiotic, belonging to the first generation cephalosporins. The antibiotic exerts bactericidal effect by inhibition of the bacterial cell wall synthesis. Cefazolin is a wide-spectrum antibiotic, possessing high activity against:

- **gram-positive microorganisms** - Staphylococcus aureus (including penicillinase producing strains), Staphylococcus epidermidis, beta-hemolytic Streptococcus - gr.A and other strains of Streptococcus (many Enterococcus strains are Cefazolin-resistant), Streptococcus pneumoniae. Methicillin-resistant strains of Staphylococcus are generally Cefazolin-resistant.

- **gram-negative microorganisms** - Escherichia coli, Proteus mirabilis, Klebsiella sp., Enterobacter aerogenes, Haemophilus influenzae. Strains of indol-positive Proteus (Proteus vulgaris), Enterobacter cloacae, Morganella morganii and Providencia rettgeri are resistant to Cefazolin. Serratia sp., Pseudomonas sp., Acinetobacter sp. are always resistant to Cefazolin.

PHARMACOKINETICS
Cefazolin is hardly absorbed from the gastrointestinal tract. After intramuscular administration of 0.5 g Cefazolin, maximum serum concentration (approx. 30 µg/ml) is attained within 1-2 h. The antibiotic binds to the plasma proteins up to 90%. Provided the biliary function is normal, the concentrations attained in the bile and gallbladder are up to five times higher than the serum concentrations. The drug’s plasma half-life is 1.5 - 2 h, but becomes prolonged in patients with impaired renal function. Cefazolin penetrates in the soft tissues and bones, body fluids (including pleural, peritoneal, synovial). The antibiotic does not penetrate the blood-brain barrier. It is excreted unchanged in the urine by glomerular filtration and tubular secretion. Approximately 80% of the intramuscularly injected dose is excreted with the urine for up to 24 h. Cefazolin is also excreted with the bile. The antibiotic penetrates transplacentally from the mother into the fetus. Low concentrations of the drug are excreted in the breast-milk.

INDICATIONS

Cefazolin is indicated for the treatment of a wide range of infections, caused by Cefazolin-susceptible microorganisms:

- **respiratory tract infections** - otorhinolaryngological infections. (Cefazolin is also effective in the eradication of streptococci from nasopharynx), bronchopulmonary infections;

- **urogenital infections** - pyelonephritis, cystitis, prostatitis, epididimitis, endometritis, parametritis, Bartholinitis, pelvic peritonitis;

- **biliary infections** - cholecystitis, cholangitis, and etc;

- **infections of the skin, skin structures and soft tissues** - acute abscesses, flegmons, post-operative wound infections, lymphadenitis;
- **infections of the bones and joints** - osteomyelitis, osteitis, septic arthritis, bursitis;

- **serosites** - peritonitis, endocarditis, pleuritis and etc.

- **ophthalmological infections** - suppurative conjunctivitis, panophthalmitis;

- septic conditions of various origin;

- **for prophylaxis in surgery** - Cefazolin is used before, during and after the operation in order to reduce the incidence of post-operative infectious complications in intraabdominal operations, in patients particularly at risk (aged over 70 years, acute cholecystitis, obstructive jaundice, Caesarean section, heart operations, endoprosthetics). The prophilactic use of Cefazolin continues 24 h after the operations. In critical infectious complications during the intervention, Cephazolin use lasts for 3-5 days after the surgical intervention. If symptoms of infection occur, laboratory sensitivity test is necessary to perform in order to identify and to determine susceptibility of the causative microorganism and to administer the appropriate therapy.

**CONTRAINDICATIONS**

Known hypersensitivity to cephalosporins.

**ADVERSE EFFECTS**

Allergic reactions - rashes, eosinophilia, higher temperature, bronchospasm, anaphylaxis.

Gastrointestinal disorders and transient disturbances in the hematopoiesis have rarely been observed. Local pain after intramuscular injection may also occur.
Nephrotoxicity reaction, particularly in combined therapy with aminoglycosides and potent diuretics is also possible to appear.

**PRECAUTIONS**

Although there is no evidence of harmful effects on the fetus, Cefazolin administration during pregnancy is contraindicated. No adverse effects have been observed in the breast-fed infants, nevertheless, weaning is recommended if the treatment of the mother is imperative. Administration in newborns up to 1 month of age is contraindicated.

Approximately 10% of the patients with a history of clinically significant hypersensitivity to penicillins are allergic to cephalosporins as well, which requires great care during treatment with Cefazolin.

In elderly and renal insufficiency patients the dosage and the interval between the doses should be adjusted according to the values of the creatinine clearance.

Transitory elevation of the serum aspartate aminotransferase and alkaline phosphatase; have been observed, as well as false positive results in the urinary sugar determinations (when reduction methods are used) and in the direct Coombs’ test. Cefazolin, as the other cephalosporins, should be administered cautiously to patients with pre-existing gastrointestinal disorders, colitis in particular.

Sodium load should be borne in mind in patients on a salt restricted diet.

**DRUG INTERACTIONS**

Combined use of Cefazolin with diuretics (furanthril, ethacrynic acid) or nephrotoxic antibiotics increases the risk of renal damage. Reciprocal inactivation may be observed in case of in vitro mixing of Cefazolin with
aminoglycosides. Therefore, mixing of the two drugs in one syringe is inadvisable, when necessary they should be injected at different sites.

The antibiotic may reduce the prothrombin index, thus potentiating the effect of anticoagulants. Probenecid delays the renal tubular secretion of Cefazolin, thereby maintaining high serum concentrations for longer time.

**DOSAGE AND MODE OF ADMINISTRATION**

Cephazolin is applied intramuscularly or intravenously in daily dosage for adults - 1-3 g and for children - 20-50 mg/kg, divided in equal intervals - 2 -4 times. In severe cases the daily dosage for adults may be raised up to 6 g, and for children - up to 100 mg/kg.

Provided the renal function is impaired, the dosage and the dose intervals should be adjusted to the values of the creatinine clearance.

<table>
<thead>
<tr>
<th>Creatinine clearance dosage, ml/min</th>
<th>Usual dosage</th>
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<tbody>
<tr>
<td>≥ 55</td>
<td>Usual dosage</td>
</tr>
<tr>
<td>54 - 35</td>
<td>The usual dose every 8 hours</td>
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<tr>
<td>34 - 11</td>
<td>1/2 of the usual dose every 12 h</td>
</tr>
<tr>
<td>≤ 10</td>
<td>1/2 of the usual dose every 18 to 24 h</td>
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</table>

Cefazolin administration in nurslings up to 1 month of age is contraindicated.

In children with mild renal insufficiency and creatinine clearance of 70-40 ml/min should be applied 60% of the usual Cefazolin dose, following an interval of 12 h.

For prophylaxis in surgery, 1 g Cefazolin is applied 1/2 - 1 h before the beginning of the operation. Operations lasting more than 2 h require second dose of 500 mg - 1 g Cefazolin, applied during the operation. If risk of infectious
complications exists, Cefazolin is applied post-operatively at a dose of 500 mg - 1 g, every 6-8 hours, up to the 24th hour or for 3 - 5 days.

**RECONSTITUTION:**

For intramuscular administration - Cefazolin of 250 mg or 500 mg is dissolved in 2 ml of sterile water for injections, then agitated until entirely dissolved.

For intravenous administration - Cefazolin of 250 mg, 500 mg, 1 g and 2 g is dissolved in 5-10 ml of sterile water for injections or glucose solution (5-10%).

Intravenous drip infusion - Cefazolin of 250 mg, 500 mg, 1 g and 2 g is added to the infusion solution.

Procaine hydrochloride must not be used when Cefazolin is dissolved for intravenous administration or transfusion!

The prepared solution can be stored for up to 24 h in a refrigerator (4°C).

**PACKAGE**

Vials of 1 g and 2 g; boxes of 10.

**STORAGE**

In dry places, protected from direct sunlight, at temperature exceeding 25°C.

**SHELF LIFE**

Two years.

**MANUFACTURED BY:**

Balkanpharma - Razgrad, Bulgaria.