Julphacef

Broad-spectrum cephalosporin
Sterile powder for injectable solution

Julphacef is a sterile powder blend of cephradine and arginine in vials containing 500mg and 1g of cephradine activity. After reconstitution, **Julphacef** is intended for intramuscular (IM) or intravenous (IV) administration. Sterile cephradine for injection contains no sodium.

Properties

Cephradine, the active ingredient of **Julphacef**, is a broad-spectrum semisynthetic cephalosporin having bactericidal activity. It acts by inhibiting bacterial septum and cell wall synthesis in a wide spectrum of susceptible Gram-positive and Gram-negative bacteria:

Gram-positive: Staphylococci (including coagulase-positive, coagulase-negative, and penicillinase-producing strains), *Streptococcus pyogenes* (group A β-haemolytic streptococci), and *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*).

Gram-negative: *Escherichia coli*, *Proteus mirabilis*, *Klebsiella* spp., and *Haemophilus influenzae*.

Cephradine is not active against most strains of *Enterobacter* spp., *P. morganii*, *P. vulgaris*, and *Pseudomonas* spp.

In vitro, most strains of enterococci (*Enterococcus faecalis and Enterococcus faecium*) are resistant to cephradine. Nevertheless, enterococci may be susceptible to the high levels of cephradine achieved in the urine.

Following intramuscular injection, peak plasma concentrations of about 6 and 14 micrograms per mL have been obtained within 1 - 2 hours of doses of 500mg and 1 g respectively. Only about 6 - 20% is reported to be bound to plasma proteins. A plasma half-life of about 1 hour has been reported; this is prolonged in patients with renal impairment. Cephradine is widely distributed to body tissues and fluids, but does not enter the CSF in significant quantities. Therapeutic concentrations may be found in the bile. It crosses the placenta into the fetal circulation and is distributed in small amounts into breast milk. Cephradine is excreted unchanged in the urine, 60 to 80% of an intramuscular dose being recovered within 6 hours. Probenecid delays excretion. Cephradine can be removed by haemodialysis and peritoneal dialysis.

Indications

Julphacef is indicated for the treatment of the following infections when caused by susceptible bacteria: respiratory tract infections; skin and soft tissue infections; urinary tract infections; bone infections; septicaemia.

Bacteriological studies to determine the causative organisms and their sensitivity to cephradine should be performed. Therapy may be instituted prior to receiving the results of sensitivity tests.

Surgical prophylaxis: **Julphacef** injection can be used for the prevention of bacteraemia or postsurgical infections in patients undergoing surgical procedures associated with high risk of infections or in which infection at the operative site would present a serious risk, e.g., vaginal hysterectomy, caesarean section, and prosthetic arthroplasty. **Julphacef** should be administered immediately prior to surgery to help ensure adequate concentrations during the time contamination is likely to occur and should be continued during the postoperative period to reduce the incidence of postoperative infection.

Intravenous use, either by direct intravenous injection or by intravenous infusion, is recommended for the treatment of serious and life-threatening infections.

Dosage

Adults: Generally, the usual daily dosage of **Julphacef** for injection is 2 - 4g daily in 4 equally divided doses intramuscularly or intravenously (e.g., 500mg to 1g q.i.d).

Uncomplicated pneumonia, skin and soft tissue infections, and most urinary tract infections: 500mg q.i.d.

Bone infections: 1g q.i.d. given intravenously.

Severe infections such as endocarditis: 2g q.i.d. given intravenously. Alternatively, in severe infections, the dose may be increased by giving injections every four hours, not exceeding 8g per day.

Prophylaxis, to prevent postoperative infection in contaminated or potentially contaminated surgery: 1g IV or IM is to be administered 30 - 90 minutes prior to surgery, followed by 1g every 4 - 6 hours after the first dose, for one to two doses or for up to 24 hours postoperatively.

Prophylaxis in caesarean section: 1g IV is to be administered as soon as the umbilical cord is clamped, followed by 1g IV or IM at 6 and 12 hours after the first dose.

Infants and Children: 50 - 100mg/kg/day in equally divided doses 4 times a day and should be regulated by age, weight of the patient, and severity of the infection being treated. The maximum paediatric daily dose should not exceed the dose recommended for adults.

In general, as with antibiotic therapy, treatment should be continued for a minimum of 48 - 72 hours after the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. In infections caused by group A β-haemolytic streptococci, a minimum of 10 days of treatment is recommended as a prophylaxis against rheumatic fever or glomerulonephritis. In the treatment of chronic urinary tract infection, frequent bacteriologic and clinical evaluation is necessary during therapy and may be necessary for several months afterwards. Persistent infections may require treatment for several weeks. Parenteral therapy may be followed by oral **Julphacef** either as capsules or oral suspension.

Julphacef may be given intravenously or by deep intramuscular injection. To minimize pain and induration, intramuscular injections should be made into a large muscle mass, such as the gluteus or lateral aspect of the thigh.

Dosage in patients with impaired renal function

Adults with impaired renal function may require dosage reduction as follows:

Patients not on dialysis:

Creatinine clearance (mL/min)	Dose
> 20	500mg every 6 hours
5 - 20	250mg every 6 hours
< 5	250mg every 12 hours

Patients on chronic intermittent haemodialysis:

250mg at the start of dialysis, then 250mg after 12 hours, and 250mg 6 - 48 hours after the start.

Children with renal function impairment may require a reduction in dose proportional to their weight and severity of infection.

If a dose is missed

- Missed dose should be given as soon as remembered.
- If it is almost time for next dose, wait until then to give the medicine and skip the missed dose.
- Do not give two doses at one time.

Reconstitution of Solutions and Storage:

For Intramuscular Use: Aseptically add sterile Water for Injection or Bacteriostatic Water for Injection (not for use in neonates if benzyl alcohol is the bacteriostat present) according to the following table:

Single Dose Vial	Water for Injection	Approximate Concentration
500mg	2.2mL	227mg/mL
1g	4.0mL	222mg/mL

Shake to effect solution and withdraw the required amount. **Julphacef** contains no bacteriostat and is not intended for multiple-dose use. Solutions should be used within 2 hours if held at room temperature (25°C), but if stored in the refrigerator (5°C), these solutions retain full potency for 24 hours. Reconstituted solutions may vary in color from light to straw yellow, however, this does not affect the potency.

If a local anaesthetic is considered desirable, for intramuscular use only, 0.5% lidocaine hydrochloride injection is recommended as the diluent in the place of the above-mentioned volumes of Water for Injection. Other diluents also suitable for intramuscular use are lidocaine hydrochloride injection 1% or procaine hydrochloride injection 1% or 2%.

For Intravenous use: **Julphacef** may also be administered by direct intravenous injection or by intravenous infusion.

For Direct Intravenous Injection: Suitable intravenous injection diluents are Sterile Water for Injection, 5% Dextrose Injection, or Sodium Chloride Injection.

Aseptically add 5mL of diluent to the 500mg vials, 10 mL to the 1g vial. Shake to effect solution and withdraw the entire contents. The solution may be slowly injected directly into a vein over a 3- to 5-minute period or may be given as a supplementary injection through the injection site on an administration set when the infusion solution is compatible with cephradine. These solutions should be used within 2 hours when held at room temperature (25°C), but if stored at 5°C, these solutions retain full potency for 24 hours.

For continuous or intermittent IV infusion: Suitable intravenous infusion solutions for **Julphacef** are 5% or 10% Dextrose Injection, Sodium Chloride Injection, Sodium Lactate Injection (M/6 sodium lactate), Dextrose and Sodium Chloride Injection (5%:0.9%) or (5%:0.45%), 10% Invert Sugar in Water for Injection, Normosol®-R, and Ionosol® B with Dextrose 5%. Sterile Water for Injection may be used as an IV infusion solution for **Julphacef** at cephradine concentration of 30 - 50mg/mL (30mg/mL is approximately isotonic).

To prepare **Julphacef** for transfer into an IV infusion container, aseptically add 10mL of Sterile Water for Injection, or a suitable infusion solution, to the 1g vial, and shake to effect solution. Aseptically transfer the entire contents to the IV infusion container. Intravenous infusion solutions containing **Julphacef** remain potent for 10 hours at room temperature or 48 hours at 5°C at concentrations up to 50mg of cephradine per mL. For prolonged infusions, replace the infusion every 10 hours with a freshly prepared solution. Infusion solutions of **Julphacef** in Sterile Water for Injection that are frozen immediately after reconstitution in the original container are stable for as long as six weeks when stored at -20°C. Extemporaneous mixtures of cephradine with other antibiotics are not recommended.

Protect solutions of **Julphacef** from concentrated light or direct sunlight.

Contraindications

Cephradine is contraindicated in patients with a known history of hypersensitivity to cephalosporins as well as in those having porphyria.

Precautions

Like other cephalosporins, cephradine should be given cautiously to patients having a history of hypersensitivity to penicillins. If an allergic reaction occurs, the drug should be discontinued.

As with other broad-spectrum antibiotics, prolonged use of cephradine may result in overgrowth of non-susceptible organisms (e.g., vaginal candidiasis). Should superinfection occur during therapy, appropriate measures should be taken.

Use of antibiotics, including cephradine, may occasionally lead to pseudomembranous colitis; therefore, it is important to consider its diagnosis in patients who develop persisting feverish diarrhea in association with the use of antibiotic. In general, cephradine, as with other antibiotics, should be used with caution in individuals having a history of gastrointestinal disease, especially colitis.

False positive Coombs' tests have been reported during treatment with large doses of cephalosporins as well as in neonates whose mothers received a cephalosporin before delivery. In addition, like most cephalosporins, cephradine may produce a false positive reaction for glucose in urine with Benedict's solution, Fehling's solution, or reagent tablets such as Clinitest. Enzyme-based tests such as Clinistix and Tes-Tape are not affected by cephradine.

As with other cephalosporin, prothrombin time may be prolonged due to the inhibition of vitamin K synthesis by suppressing gut flora.

Paediatrics: Cephradine has been used effectively in infants, but all laboratory parameters have not been extensively studied. Use in this population needs to be assessed carefully. **Julphacef** injection contains arginine. Studies in low birth weight infants have demonstrated that arginine administration may result in increases in serum arginine, insulin, and indirect bilirubin. The consequences of exposure to this amino acid during treatment of neonates have not been fully ascertained.

Geriatrics: No specific dosage recommendations or precautions for use in elderly.

Pregnancy: The use of cephradine in pregnant women is not known to be harmful. However, as adequate and well-controlled studies in human have not been done, it should be used during pregnancy only if clearly needed.

Nursing Mothers: As with almost all other cephalosporins, cephradine is distributed into breast milk in low concentrations. However, problems in humans have not been documented to date.

Renal impairment: As cephradine is mainly excreted via the kidney, dosage reduction (according to creatinine clearance) is usually recommended in patients with moderate to severe renal impairment (See Dosage). The patient should be observed clinically and laboratory tests should be performed regularly prior to and during the course of treatment.

Side Effects

The use of cephradine is generally considered safe and well tolerated. The side effects that may occasionally be encountered include headache and gastrointestinal reactions such as nausea, vomiting, and abdominal discomfort; diarrhoea and rarely antibiotic-associated colitis are more likely to occur with higher doses.

Allergic reactions including rashes, pruritus, urticaria, and erythema multiforme have been reported occasionally. Serum sickness-like reactions with skin rash, fever, tightness in the chest, and arthralgia have been reported in some patients. Other hypersensitivity reactions such as toxic epidermal necrolysis and anaphylaxis have been experienced in rare cases. Generally, hypersensitivity reactions are more likely to occur in individuals who have a history of allergy, asthma, hay fever, or urticaria.

Rarely, reversible interstitial nephritis, hyperactivity, nervousness, sleep disturbances, confusion, hypertonia, and dizziness have been reported.

As with some other cephalosporins, slight disturbances in liver enzymes, transient hepatitis, and cholestatic jaundice were reported in rare cases.

Mild, transient eosinophilia and blood disorders including thrombocytopenia, leukopenia, agranulocytosis, aplastic anaemia, and haemolytic anaemia were rarely reported.

Transient rise in blood urea nitrogen (BUN) and serum creatinine have been reported in some patients treated with cephalosporins.

Pain and rarely thrombophlebitis at the site of injection have been experienced by some patients.

Overdosage

Since there is no specific antidote, treatment of cephradine overdose should be symptomatic and supportive. Cephradine can be removed by haemodialysis and peritoneal dialysis.

Drug Interactions

Upon concurrent use, probenecid may reduce the excretion of cephradine, increasing thereby its plasma concentration.

Loop diuretics and aminoglycosides antibiotics may increase the risk of nephrotoxicity of cephalosporins upon concurrent administration.

Presentation

Julphacef sterile powder for injectable solution is available in packs of 1 vial.

* *Store at a temperature of 15 - 25°C.*

THIS IS A MEDICAMENT

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists.

Any information ? Call Our Toll Free No. **(971) 800-4994**

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