LINZ

A Specialized Cephalosporin Manufacturing Unit

Cefresh™ 0.25G, 0.5G & 1G IM/IV Injection

(Cephradine U.S.P)

Sterile Powder for Injection

Inject Slowly For I.V. Injection

سیفریش

۲۵۰ ملی گرام، ۵۰۰ ملی گرام، ۱ گرام انجکشن

پٹھوں/وریدی استعمال کے لئے۔

(سیفراڈین یو۔ ایس۔ پی)

وسیع العمل فرسٹ جنریشن سیفلوسپورن

Broad Spectrum 1st Generation Cephalosporin

Composition:

Each Vial of **Cefresh** 250 mg , 500 mg & 1000 mg contains: Sterile Cephradine for Injection eq. to Cephradine USP 250 mg, 500 mg & 1000mg respectively.

Description:

Cefresh (Sterile Cephradine for Injection) is a semi synthetic cephalosporin antibiotic,

Cefresh (Sterile Cephradine for Injection) is a sterile powder blend of Cephradine monohydrate and L-arginine intended for intramuscular or intravenous administration.

Clinical Pharmacology:

Following intramuscular administration of a single 1 gram dose of cephradine to normal volunteers, the average peak serum concentration was 15.1µg/ml at approximately 1 hour, and declined to 6.2µg/ml at 3 hours and 1.5µg/ml at 6 hours. A single 1 gram intravenous dose resulted in serum concentration of 86µg/ml at 5 minutes and declined to 12µg/ml at 1 hour and 1µg/ml at 4 hours. Continuous infusion of 500mg per hour in a 70kg man maintained a concentration of about 21.4µg/ml Cephradine activity. A serum concentration of approximately 3µg/ml can be obtained for each milligram of cephradine administered per kg of body weight per hour of infusion. Cephradine is minimally bound to serum proteins at (8 to 17%). Assays of bone and cardiac tissue (atrial appendage) obtained at surgery have shown that Cephradine penetrate these tissues. Cephradine does not pass across the blood brain barrier to any appreciable extent.

Cephradine is excreted unchanged in the urine. The kidneys excrete 57% to 80% of an intramuscular dose in the first 6 hours; this results in a high urine concentration. Probenecid slows tubular excretion and increases serum concentration.

MICROBIOLOGY:

Cefresh (Cephradine) is a broad-spectrum, bactericidal antibiotic active against both gram-positive and gram-negative bacteria.

Cephradine is active against the following organisms in vitro:

- Group A beta-hemolytic streptococci
- Staphylococci, including coagulase-positive, coagulase-negative, and penicillinase-producing strains
- Escherichia coli
- Streptococcus pneumoniae (formerly Diplococcus pneumoniae)
- Proteus mirabilis
- Klebsiella species
- Hemophilus influenzae

Cephradine is not active against most strains of Enterobacter species, Morganella morganii (formerly Proteus morganii), and Proteus vulgaris. Most strains of enterococci (Enterococcus faecalis) are resistant to cephradine. It has no activity against Pseudomonas or Herellea species. When tested by in vitro methods, staphylococci exhibit cross-resistance between cephradine and methicillin-type antibiotics.

Cephalosporin-class discs are used in disc susceptibility testing.

INDICATIONS:

Cefresh (Cephradine monohydrate) is indicated in the treatment of the following infections due to susceptible organisms:

- Respiratory tract infections
- Urinary tract infections,
- Skin and skin structure infections
- Bone infections
- Septicemia
- Otitis media

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.

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

Cefresh (Cephradine for injection) is effective in the prevention of postsurgical infections in patients about to undergo surgical procedures which are classified as contaminated or potentially contaminated., or in which infection at the operative site would present a serious risk, e.g., vaginal hysterectomy, cesarean section, and prosthetic arthroplasty. (See DOSAGE AND ADMINISTRATION).

CONTRAINDICATIONS:

Cefresh (Cephradine) is contraindicated in patients with known hypersensitivity to the cephalosporin group of antibiotics.

PRECAUTIONS:

General

Patients should be followed carefully so that any side effects or unusual manifestations of drug idiosyncrasy may be detected. If a hypersensitivity reaction occurs, the drug should be discontinued and the patient treated with the usual agents, e.g., pressor amines, antihistamines, or corticosteroids. Administer Cephradine with caution in the presence of markedly impaired renal function. In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be made prior to and during therapy as Cephradine accumulates in the serum and tissues. See **(DOSAGE AND ADMINISTRATION)** section for information on treatment of patients with impaired renal function.

Pregnancy Category B

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

Nursing Mothers

Since Cephradine is excreted in breast milk during lactation, caution should be exercised when Cephradine is administered to a nursing woman.

Pediatric Use

See **(DOSAGE AND ADMINISTRATION).** Adequate information is unavailable on the efficacy of b.i.d. regimens in children under nine months of age.

SIDE EFFECTS:

As with other cephalosporins, untoward reactions are limited essentially to gastrointestinal disturbances and, on occassion, to hypersensitivity phenomena. The later are more likely to occur in individuals who have previously demonstrated hypersensivity and those with a history of allergy, asthma, hay fever, or urticaria.

The following adverse reactions have been reported following the use of cephradine:

Gastrointestinal: Glossitis, nausea, vomiting, diarrhea or loose stools, tenesmus, abdominal pain, colitis, and pseudomembranous colitis.
Hypersensitivity: Mild urticaria or skin rash, edema, erythema, pruritus, joint pains, and drug fever. As with other cephalosporins, there have been rare reports of anaphylaxis, erythema multiforme, Stevens-Johnson Syndrome, and toxic epidermal necrolysis.
Hematologic: Mild, transient eosinophilla, leukopenia, and neutropenia.
Liver: Instances of elevated SGOT, SGPT, total bilirubin, alkaline phosphatase, and LDH have been observed; in most patients, the values were only midly elevated and tended to return to normal at the end of therapy. No consistent pattern was observed that would suggest hepatocellular damage.
Renal: Mild elevations in BUN have been observed in some patients treated with cephalosporins; their frequency increases in patients over 50 years old and in children under three. In adults for whom serum creatinine determinations were performed, the rise in BUN was not accompanied by a rise in serum

creatinine. (See also **PRECAUTIONS**).
Other adverse reactions have included headache, dizziness, dyspnea, paresthesia, candidal overgrowth and vaginitis, isolated instances of hepatomegaly, and thrombophlebitis at the site of injection. Pain on intramuscular injection has been experienced by some patients. Since sterile abscesses have been reported following accidental subcutaneous injection, the preparation should be administered by deep intramuscular injection.

DOSAGE AND ADMINISTRATION:

Adults : The usual daily dosage of **Cefresh** (Cephradine for Injection) is 2 to 4g daily in four equally divided doses intramuscularly or intravenously (e.g., 500 mg to 1g qid). A dosage of **Cefresh** 500 mg qid is adequate in uncomplicated pneumonia, skin and skin structure infections and most urinary tract Infections. In bone infections the usual dosage of **Cefresh** is 1g qid administered intravenously. In severe infections such as endocarditis, 2g qid given intravenously is recommended. Alternatively, in severe infections, the dose may be increased by giving injection every four hours. The maximum dose should not exceed 8g per day

Prophylaxis: To prevent postoperative infection in contaminated or potentially contaminated surgery recommended dose are as follows
a. Cefresh 1g IV or IM administered 30 to 90 minutes prior to start of surgery
b. Cefresh 1g every 4 to 6 hour after the first dose for one to two doses, or upto 24 hours postoperatively.
Prophylaxis in Cesarean section: The first dose of **Cefresh** 1g is administered intravenously as soon as the umbilical cord is clamped. The second and third doses should be given as 1g intravenously or intramuscularly at 6 and 12 hours after the first dose.
Infants and Children: The usual dose range is 50 to 100 mg/kg/day (approximately 23 - 45 mg/lb/day) in equally divided doses four times a day and should be regulated by age, weight of the patient, and severity of the infection being treated. The maximum pediatric daily dose should not exceed the dose recommended for adults.
All patients, Regardless of Age and Weight: Therapy should be continued for a minimum of 48 to 72 hours after the patient become asymptomatic or evidence of bacterial eradication has been obtained. Persistent infection may require treatment for several weeks. Doses smaller than those indicated above should not be used. Parenteral therapy may be followed by oral **Cefresh** either as capsules or oral suspension.
Cefresh (Cephradine for Injection) 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 thigh.
Patients with Impaired Renal Function (Not On Dialysis): The following dosage schedule is suggested as a guideline based on dosage of 500mg Q6H and on creatinine clearance. Further modification in the dosage schedule may be required because of the dosage selected and individual variation.

Creatinine Clearance	Dose	Time Interval
> 20 mL/min	500 mg	6 hours
5-20 mL/min	250 mg	6 hours
< 5 mL/min	250 mg	12 hours

On Chronic, Intermittent Hemodialysis,
250 mg start
250mg at 12 hours
250mg 36-48 hours (after start)

Children may require dosage modification proportional to their weight and severity of infection.
Reconstitution and Storage:
For Intramuscular Use: Aseptically add Sterile Water for Injection or Bacteriostatic Water for Injection,* according to the following table.

Single Dose	Water for Injection	Approximate Concentration
250 mg	1.2 ml	208 mg/ml
500 mg	2.0 ml	250 mg/ml
1G	4.0 ml	250 mg/ml

*Not for use in neonates if benzyl alcohol is present in the bacteriostatic water for injection.
Shake the effect solution and withdraw the required amount **Cefresh** contains no bacteriostat and is not intended for multiple dose use. Solutions should be used within 2 hours if held at room temperature, if stored in the refrigerator (5°C), solutions retain full potency for 24 hours. Reconstitution solution may vary in color from light to straw yellow, however this does not affect the potency.

For Direct Intravenous Injection: Suitable Intravenous injection diluents are Sterile Water for injection, 5% Dextrose injection, or Sodium Chloride Injection. Do not use Lactated Ringer's Injection. Aseptically add 5ml of diluent to the 250 mg or 500 mg vials, 10ml to the 1gram vial. Shake to effect solution and withdraw the entire content. 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 solution should be used within 2 hours when held at room temperature; if stored at 5°C, solutions retain full potency for 24 hours.

PRESENTATION:

Cefresh 0.25G Injection
(250mg / vial)
Sterile powder blend of Cephradine monohydrate & L-Arginine in a vial eq. to Cephradine 250mg USP, with sterile water for injection USP, pyrogen free as diluent for quick dissolution.

Cefresh 0.5G Injection
(500mg / vial)
Sterile powder blend of Cephradine monohydrate & L-Arginine in a vial eq. to Cephradine 500mg USP, with sterile water for injection USP, pyrogen free as diluent for quick dissolution.

Cefresh 1G Injection
(1000mg / vial)
Sterile powder blend of Cephradine monohydrate & L-Arginine in a vial eq. to Cephradine 1000mg USP, with sterile water for injection USP, pyrogen free as diluent for quick dissolution.

Shelf Life: 2 years

Instructions:
Protect from heat, sunlight & moisture, store below 25°C.
Keep out of the reach of children.
The expiration date refer to the product correctly stored at the required condition.
To be sold on prescription of a registered medical practitioner only.

پٹھوں/وریدی استعمال کے لئے۔

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:-

دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف معتمد ڈاکٹر کے نسخے پر فروخت کے لئے۔

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