LINZ

A Specialized Cephalosporin Manufacturing Unit

Cefresh Capsule / Suspension

(Cephradine)

(Product Specs.: U.S.P.)

سیفریش کیپسول/سسپنشن

وسیع العمل فرسٹ جنریشن سیفلوسپورن

Broad Spectrum 1st Generation Cephalosporin

Composition:

Each Capsule of **Cefresh** 250 & 500 mg contains: Cephradine monohydrate eq. to Cephradine USP 250 mg & 500 mg respectively.

Each 5ml of **Cefresh** 125 mg & 250 mg Suspension contains: (After reconstitution) Cephradine monohydrate eq. to Cephradine USP 125 mg & 250 mg respectively.

Description:

Cefresh (Cephradine) is a semi synthetic cephalosporin antibiotic, with broad spectrum bactericidal activity against susceptible gram positive and gram negative bacteria.

CLINICAL PHARMACOLOGY:

Cefresh (Cephradine) is acid stable. It is rapidly absorbed after oral administration in the fasting state. Following single doses of 250 mg and 500 mg in normal adult volunteers, average peak serum concentrations within one hour were approximately 9 µg/mL and 16.5 µg/mL respectively. In vitro studies by an ultracentrifugation technique show that at therapeutic serum antibiotic concentrations, Cephradine is minimally bound (8 to 17 percent) to normal serum protein. Cephradine does not pass across the blood-brain barrier to any appreciable extent. The presence of food in the gastrointestinal tract delays absorption but does not affect the total amount of Cephradine absorbed. Over 90 percent of the drug is excreted unchanged in the urine within six hours. Peak urine concentrations are approximately 1600 µg/mL and 3200 µg/mL following single doses of 250 mg & 500 mg respectively.

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
- Streptococcus pneumoniae (formerly Diplococcus pneumoniae)
- Escherichia coli
- Proteus mirabilis
- Klebsiella species
- Hemophilus influenzae

INDICATIONS:

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

- Respiratory tract infections, eg., tonsillitis, pharyngitis, lobar pneumonia
- Otitis media
- Skin and skin structure infections
- Urinary tract infections including prostatitis

CONTRAINDICATIONS:

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

PRECAUTIONS:

This is evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Therefore, cephradine should be used with caution in patients with known hypersensitivity to penicillins.

There have been instances of patients who have had reactions to both drug classes, including anaphylaxis **(see SIDE EFFECTS).**

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad spectrum antibiotics), including cephradine; therefore, it is important to consider this diagnosis in patients who develop diarrhea in association with antibiotic use. Mild cases of colitis may respond to drug discontinuance alone; moderate to severe cases should be managed as indicated. In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be performed since cephradine accumulates in the serum and tissues unless dosage is suitably reduced (see **DOSGE AND ADMINISTRATION**).

After treatment with cephradine, a false-positive reaction for glucose in the urine may occur with Benedict's solution, Fehling's solution, or with Clinitest® tablets, but not with enzyme-based tests such as Clinistix®, and Tes-Tape®. As with other cephalosporins, positive direct Coombs' tests have been infrequently reported. As with all antibiotics, prolonged use may result in overgrowth of nonsusceptible organisms.

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 occasion, to hypersensitivity phenomena. The later are more likely to occur in individuals who have previously demonstrated hypersensitivity and those with a history of allergy, asthma, hay fever, or utricaria.

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

Gastrointestinal

Glossitis, nausea, vomiting, heartburn, diarrhea or loose stools, abdominal pain, colitis, and pseudomembranous colitis.

Hypersensitivity

Mild urticaria or skin rash, pruritus, and joint pains. As with other cephalosporins, there have been rare reports of anaphylaxis, erythema multiforme, Stevens-Johnson Syndrome, and toxic epidermal necrolysis.

Hematologic
Mild transient eosinophilia, leukopenia, and neutropenia.
Liver
Isolated instances of elevated SGOT, SGPT, total bilirubin, and alkaline phosphatase have been observed with no evidence of hepatocellular damage.
Renal
Transitory rises in BUN have been observed in some patients treated with cephalosporins; their frequency increases in patients over 50 years old. In adults for whom serum creatinine determination were performed, the rise in BUN was not accompanied by a rise in serum creatinine.
Other adverse reactions have included dizziness, tightness in the chest and candidal viginitis.

DOSAGE AND ADMINISTRATION:

Cefresh (Cephradine) may be given without regard to meals.

Adults

For respiratory tract infections (other than lobar pneumonia) and skin and skin structure infections, the usual dose is **Cefresh** 250 mg every 6 hours or **Cefresh** 500 mg every 12 hours.
For lobar pneumonia, the usual dose is **Cefresh** 500 mg every 6 hours or 1 g every 12 hours.
For uncomplicated urinary tract infections, the usual dose is **Cefresh** 500 mg every 12 hours. In more serious urinary tract infections, including prostatitis, **Cefresh** 500 mg every 6 hours or 1 g every 12 hours may be administered.
Larger doses (up to 1 g every 6 hours) may be given for severe or chronic infections.

Children

No adequate information is available on the efficacy of b.i.d. regimens in children under nine months of age. The usual dose in children over nine months of age is 25 to 50 mg/kg/day administered in equally divided doses every 6 or 12 hours.
For otitis media due to H.influenzae, doses are from 75 to 100 mg/kg/day administered in equally divided doses every 6 or 12 hours, but should not exceed 4 g per day.
All patients, regardless of age and weight: Larger doses (up to 1g q.i.d.) may be given for severe or chronic infections. As with antibiotic therapy in general, treatment should be continued for a minimum of 48 to 72 hours after the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. In infections caused by group A beta-hemolytic streptococci, a minimum of 10 days of treatment is recommended to guard against the risk of rheumatic fever or glomerulonephritis.
In the treatment of chronic urinary tract infection, frequent bacteriologic and clinical appraisal is necessary during therapy and may be necessary for several months afterwards. Persistent infections may require treatment for several weeks. Prolonged intensive therapy is recommended for prostatitis. Doses smaller than those indicated are not recommended.

Patients With Impaired Renal Function

Not on Dialysis: The following initial dosage schedule is suggested as a guideline based on creatinine clearance. Further modification in the dosage schedule may be required because of individual variations in absorption.

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 ,250 mg at 12 hours ,250 mg 36-48 hours (after start)
Children may require dosage modification proportional to their weight and severity of infection.

PRESENTATION:

Cefresh Capsules (Cephradine Capsules USP)

Cefresh 250
(250 mg/ capsule)
Cold form Cold seal Alu Alu pack of 2 X 6's

Cefresh 500
(500 mg/ capsule)
Cold form Cold seal Alu Alu pack of 2 X 6's

Cefresh for Oral Suspension
(Cephradine for Oral Suspension USP)

Cefresh 125
(125 mg/5ml)
When reconstituted as directed on the container label, a suspension containing 125 mg per 5 mL, in Nitrogen added bottle sizes for preparation of 60 mL.

Cefresh 250
(250 mg/5ml)
When reconstituted as directed on the container label, a suspension containing 250 mg per 5 mL, in Nitrogen added bottle sizes for preparation of 60 mL.

STORAGE & INSTRUCTION:

Cefresh Capsules. Store at cool and dry place.
Cefresh for Oral Suspension - Prior to constitution, store at room temperature; avoid excessive heat. After constitution, when stored at room temperature, discard unused portion after seven days; when stored in refrigerator, discard unused portion after 14 days. Keep bottle tightly closed. Keep out of the reach of children.
To be dispensed on the prescription of a registered medical practitioner only.

خوراک اور ترکیب استعمال:

سیفریش بغیر اس خاظ کے مریض نے غذا لی ہے یا نہیں، مریض کو دی جاسکتی ہے۔
بڑوں کیلئے: سیفریش ۲۵۰ ملی گرام ۶ گھنٹے کے وقفہ سے ۴ مرتبہ روزانہ یا ۵۰۰ ملی گرام ۱۲ گھنٹے کے وقفہ سے ۲ مرتبہ روزانہ۔
بچوں کیلئے: سیفریش ۲۵ سے ۵۰ ملی گرام فی کلوگرام جسمانی وزن کے مطابق ۶ یا ۱۲ گھنٹے کے وقفہ سے برابر مقدار میں تقسیم کرکے۔ زیادہ سے زیادہ خوراک ۴ گرام یومیہ۔
یا ڈاکٹر کے مشورے کے مطابق استعمال کریں۔

ہدایات:۔

روشنی اور نمی سے محفوظ ٹھنڈی اور خشک جگہ پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔
ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

غیر استعمال شدہ سیفریش سسپنشن اگر کمرے کے درجہ حرارت پر رکھا گیا ہو تو ۷ دن کے بعد اور ریفریجریٹر میں رکھا گیا ہو تو ۱۴ دن کے بعد استعمال نہ کریں۔

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