Lenwin™
[Cephradine]

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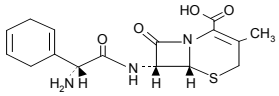
Injection 250mg, 500mg & 1g

DESCRIPTION
Lenwin (Cephradine) is a first-generation cephalosporin antibacterial given orally and by parenteral route in the treatment of susceptible infections and in the prophylaxis of infections during surgical procedures. Chemically, cephradine is (6R,7R)-7-[(R)-2-Amino-2-(1,4-cyclohexadien-1-yl)acetamido]-3- methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. The molecular formula is $C_{16}H_{19}N_3O_4S$ and the structural formula is:



Cephradine

QUALITATIVE & QUANTITATIVE COMPOSITION
Lenwin (Cephradine) is available for parenteral administration as:

Lenwin Injection 250mg
Each vial contains:
Cephradine USP... 250mg

Lenwin Injection 500mg
Each vial contains:
Cephradine USP... 500mg

Lenwin Injection 1g
Each vial contains:
Cephradine USP... 1g

CLINICAL PHARMACOLOGY
Mechanism of Action
Cephradine inhibits the final transpeptidation step of the peptidoglycan synthesis in bacterial cell wall by binding to one or more of the penicillin-binding proteins (PBPs), thus arresting cell wall synthesis leading to bacterial cell death.

Microbiology
The following organisms have shown in vitro sensitivity to cephradine:

Gram-positive:
Staphylococci (both penicillin sensitive and resistant strains), *Streptococci, Streptococcus pyogenes* (beta haemolytic) and *Streptococcus pneumonia.*

Gram-negative:
Escherichia coli, Klebsiella spp., *Proteus mirabilis, Haemophilus influenza, Shigella spp., Salmonella* spp., (including *Salmonella typhi*) and *Neisseria* spp.

Pharmacokinetics
Following intramuscular injection of cephradine, peak plasma concentrations of about 6 µg/mL and 14 µg/mL have been obtained within 1 to 2 hours of doses of 500mg and 1g respectively. Cephradine is widely distributed to body tissues and fluids, but does not enter the CSF in significant quantities. It crosses the placenta into fetal circulation and is distributed in small amounts into breast milk. Therapeutic concentrations may be found in bile. Only 8% to 12% is bound to plasma proteins. A plasma half-life of about 1 hour has been reported. Cephradine is excreted unchanged in the urine by glomerular filtration and tubular secretion. Over 60% to 80% of an intramuscular dose is being recovered within 6 hours.

Special population
Renal Impairment
Plasma concentration of cephradine is prolonged in patients with renal impairment.

THERAPEUTIC INDICATIONS
Lenwin (Cephradine) is indicated in the treatment of following infections due to susceptible organisms:
- Respiratory tract infections
- Urinary tract infections
- Skin and skin structure infections
- Bone infections
- Septicemia

Lenwin (Cephradine) 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.

DOSAGE & ADMINISTRATION
Adults
The usual daily dosage of Lenwin (Cephradine) Injection is 2 to 4g daily in four equally divided doses intramuscularly or intravenously (e.g., 500mg to 1g qid). A dosage of 500mg qid is adequate in uncomplicated pneumonia, skin and skin structure infections and most urinary tract infections. In bone infections the usual dosage 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 injections every four hours. The maximum dose should not exceed 8g per day.

Prophylaxis:
To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are as follows:
- 1g IV or IM administered 30 to 90 minutes prior to start of surgery.
- 1g every 4 to 6 hours after the first dose for one to two doses, or for up to 24 hours postoperatively.

Prophylaxis in cesarean section:
The first dose of 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.

Pediatrics
The usual dose range is 50 to 100mg/kg/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.

Duration of treatment
Therapy 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 *beta-haemolytic streptococci*, a minimum of 10 days treatment is recommended to guard against the risk of rheumatic fever or glomerulo-nephritis. In the treatment of chronic urinary tract infections, frequent bacteriological and clinical appraisal is necessary during therapy and may be necessary for several months afterwards. Persistent infections may require treatment for several weeks. Smaller doses than those indicated should not be used.

Special population
Renal Impairment
Patients not on dialysis:
The following dosage schedule guidelines are based on a dosage of 500mg 6 hourly 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

Patients on chronic, intermittent hemodialysis:

250 mg	At start of hemodialysis
250 mg	6-12 hours after start
250 mg	36-48 hours after start
250 mg	At start of next hemodialysis if >30 hours after previous dose

Children may require dosage modification proportional to their weight and severity of infection.

Directions for use
As cephradine is available in both injectable and oral forms, patients may be changed from injection to oral form (capsule and suspension) at the same dosage level.

Parenteral
Lenwin (Cephradine) may be given intravenously and by deep intramuscular injection. To minimize pain and induration, intramuscular injection should be made into a large muscle mass, such as gluteus or lateral aspect of the thigh. Intravenously, Lenwin (Cephradine) may be administered by either direct intravenous injection or by intravenous infusion. For direct intravenous injection, the solution may be slowly injected directly in to the vein over a 3 to 5 minutes 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.

For intramuscular use:
Aseptically add Sterile Water for Injection according to the following table:

Single Dose Vial	Volume of Diluent to be added	Volume After Reconstitution	Approximate Concentration
250mg	1.2 mL	1.2 mL	208 mg/mL
500mg	2.0 mL	2.2 mL	227 mg/mL
1g	4.0 mL	4.5 mL	222 mg/mL

Shake well to dissolve and withdraw the required amount. Lenwin (Cephradine) contains no bacteriostat and is not multiple-dose use. Solutions should be used within 2 hours if held at room temperature. Reconstituted solution may vary in color from light to straw yellow, however, this does not affect the potency.
If a local anesthetic is considered desirable for intramuscular use only, 0.5% lidocaine hydrochloride injection is recommended as diluent in place of abovementioned volumes of Sterile Water for Injection. Other diluents suitable for intramuscular use are lidocaine hydrochloride injection 1% or procaine hydrochloride injection 1% or 2%.

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 250mg or 500mg vials and 10mL to the 1g vial. Shake well to dissolve and withdraw the entire content. These solutions should be used within 2 hours when held at room temperature.

For continuous or intermittent IV infusion:
Suitable intravenous infusion solutions 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. Sterile Water for Injection may be used as IV infusion solution for Lenwin (Cephradine) at a cephradine concentration of 30 to 50mg/mL (30mg/mL is approximately isotonic). To prepare Lenwin (Cephradine) for transfer into an IV infusion container, aseptically add 10ml of Sterile Water for Injection or a suitable infusion solution to 1g vial and shake well to dissolve. Aseptically transfer the entire content to the IV infusion container. For prolonged infusions, replace the infusion every 10 hours with a freshly prepared solution. Infusion solutions of Lenwin (Cephradine) 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 Lenwin (Cephradine) with other antibiotics are not recommended. Protect solutions of Lenwin (Cephradine) from concentrated light or direct sunlight.

ADVERSE REACTIONS
The following adverse reactions have been reported following the use of cephradine:
Gastrointestinal: Glossitis, nausea, vomiting, diarrhea or loose stools, tenesmus, abdominal paincolitis and pseudomembranous colitis.
Hypersensitivity: Mild urticaria or skin rash, edema, erythema, pruritis, joint pain and drug fever.
Hematologic: Mild, transient eosinophilia, leukpenia and neutropenia.
Other: Headache, dizziness, dyspnea, paresthesia, candidal overgrowth and vaginitis.

CONTRAINDICATIONS
Cephradine is contraindicated in patients with known hypersensitivity to cephradine or to any excipient of the product.

PRECAUTIONS
- Cephradine should be used with caution in patients with known hypersensitivity to penicillins because of partial allergenicity between penicillins and the cephalosporins.
- Caution should be exercised in patients with renal failure and dosage should be reduced.
- False positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or with reagent tablets such as Clinitest following administration of cephradine.
- Prolonged use with antibiotics may result in overgrowth of non susceptible microorganisms.

Pregnancy
There are no adequate and well-controlled studies in pregnant women. As with all medicines, use should be avoided in pregnancy especially in the first trimester, unless considered essential by the physician.

Nursing Mothers
Cephradine is excreted in breast milk and therefore should be used with caution in nursing mothers.

Drug Interactions
- Concomitant administration with loop diuretics may increase nephrotoxicity of cephalosporins.
- Concomitant administration of probenecid raises serum concentrations of cephradine, by reducing renal clearance.

OVERDOSAGE
There is no relevant data available on overdosage. In the event of overdose, the patient be treated symptomatically and supportive measures should be instituted as required.

HOW SUPPLIED
Lenwin (Cephradine) Injection 250mg is available in pack of 1 vial with 5mL Water for Injection.
Lenwin (Cephradine) Injection 500mg is available in pack of 1 vial with 5mL Water for Injection.
Lenwin (Cephradine) Injection 1g is available in pack of 1 vial with 10mL Water for Injection.

STORAGE
Store at 25°C (Excursions permitted between 15°C to 30°C). Protect from excessive heat and light.

The expiration date refers to the product correctly stored at the required conditions.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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