Lenwin™
[Cephradine]

Lenwin™ DS
[Cephradine]

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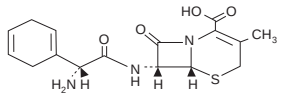
Capsules 250mg & 500mg
Powder for Oral Suspension 125mg/5mL & 250mg/5mL

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 (6*R*,7*R*)-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 oral administration as:

Lenwin Capsules 250mg
Each capsule contains:
Cephradine monohydrate equivalent to Cephradine USP… 250mg

Lenwin Capsules 500mg
Each capsule contains:
Cephradine monohydrate equivalent to Cephradine USP… 500mg

Lenwin Powder for Oral Suspension 125mg/5mL
Each reconstituted 5mL contains:
Cephradine monohydrate equivalent to Cephradine USP… 125mg

Lenwin DS Powder for Oral Suspension 250mg/5mL
Each reconstituted 5mL contains:
Cephradine monohydrate equivalent to Cephradine USP… 250mg

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
Cephradine is rapidly and almost completely absorbed from the gastrointestinal tract after oral doses. Doses of 250mg, 500mg and 1g given orally produces peak plasma concentrations of about 9µg/mL, 17µg/mL and 24µg/mL respectively at 1 hour. 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 90% of an oral dose is being recovered within 6 hours. Peak urinary concentrations of about 3µg/mL have been achieved after a 500mg oral dose.

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:

Upper respiratory tract infections:
Sinusitis, pharyngitis, tonsillitis, laryngo-tracheo bronchitis and otitis media.

Lower respiratory tract infections:
Acute and chronic bronchitis, lobar and bronchopneumonia.

Skin and soft tissue infections:
Impetigo, abscess, cellulitis and furunculosis.

Urinary tract infections:
Cystitis, urethritis and pyelonephritis.

Gastrointestinal tract infections:
Bacillary dysentery, enteritis and peritonitis.

DOSAGE & ADMINISTRATION
Lenwin (Cephradine) may be given with regards to meal.

Adults
Respiratory tract infections, skin and soft tissue infections:
The usual dose is 250mg or 500mg four times daily or 500mg or 1g twice daily depending upon the severity of infection.

Urinary tract infection:
The usual dose is 500mg four times daily or 1g twice daily. This may need to be increased for severe or chronic infections. Prolonged intensive therapy is needed for complications such as prostatitis and epididymitis.

Gastrointestinal tract infections:
500mg three or four times daily.

Pediatrics
The usual dose is 25 to 50mg/kg/day total, given in two or four equally divided doses. For otitis media daily doses from 75 to 100mg/kg in divided doses every 6 to 12 hours are recommended. The dose should not exceed 4g per day.

Duration of treatment
For severe or chronic infection larger dose of up to 1g four times daily may be given. Administration should be continued for a minimum of 48-72 hours after the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. For infections caused by hemolytic strains of streptococci, a minimum of 10 days treatment is recommended to guard against the risk of rheumatic fever or glomerulo-nephritis. For 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. Doses for children should not exceed those recommended for adults.

Special population
Renal Impairment
Patients not on dialysis:
The following dosage schedule guideline is 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.

Direction for Preparation Oral Suspension
Fill previously boiled and cooled water upto 35ml in measuring cup. Pour water from measuring cup into bottle and shake well.
After reconstitution, the suspension should be stored in a refrigerator (2°C-8°C) and can be used within 14 days. If stored at 15°C-30°C after reconstitution, the suspension can be used within 7 days. Shake well before use.

ADVERSE REACTIONS
The most common adverse effects of oral cephalosporins are generally gastrointestinal disturbances and hypersensitivity 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) Capsules 250mg are available in pack of 12's.
Lenwin (Cephradine) Capsules 500mg are available in pack of 12's.
Lenwin (Cephradine) Powder for Oral Suspension 125mg/5mL is available in 60mL.
Lenwin DS (Cephradine) Powder for Oral Suspension 250mg/5mL is available in 60mL.

STORAGE
Store at 25°C (Excursions permitted between 15°C to 30°C). Protect from sunlight and moisture.
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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