



For Medical Professional only

# CEFRINEX<sup>®</sup> Capsules/ Suspension (Cephadrine)

سیفرینیکس  
کپسولز / سسپنشن  
(سیفراڈین)

## DESCRIPTION:

CEFRINEX (Cephadrine) 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, cephadrine 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  $C_{16}H_{18}N_3O_4S$ .

## COMPOSITION:

### CEFRINEX 250mg Capsules:

Each Capsule Contains:  
Cephadrine U.S.P. ....250mg  
(Product Specs.: U.S.P.)  
"Product contains Lactose"

### CEFRINEX 500mg Capsule:

Each Capsule Contains:  
Cephadrine U.S.P. ....500mg  
(Product Specs.: U.S.P.)

### CEFRINEX 125mg/5ml Suspension:

Each 5ml Contains:  
Cephadrine U.S.P. ... 125mg  
(Product Specs.: U.S.P.)

### CEFRINEX 250mg/5ml Suspension:

Each 5ml Contains:  
Cephadrine U.S.P. ... 250mg  
(Product Specs.: U.S.P.)

## CLINICAL PHARMACOLOGY:

### Pharmacodynamic Properties:

Pharmacotherapeutic group: first generation cephalosporin. ATC code: J01DB09

### Mechanism of Action:

Cephadrine inhibits the final transpeptidation step of the peptidoglycan synthesis in bacterial cell wall by binding to one or more of the penicillinbinding proteins (PBPs), thus arresting cell wall synthesis leading to bacterial cell death.

## Microbiology:

### Gram-Positive Bacteria:

Staphylococci (both penicillin sensitive and resistant strains), Streptococci, Streptococcus pyogenes (beta haemolytic) and Streptococcus pneumoniae.

### Gram-Negative Bacteria:

Escherichia coli, Klebsiella spp., Proteus mirabilis, Haemophilus influenzae, Shigella spp., Salmonella spp., (including Salmonella typhi) and Neisseria spp.

## Pharmacokinetic Properties

### Absorption:

CEFRINEX has a high degree of stability to many beta-lactamases. It has a low degree of protein binding and a large volume of distribution. Therefore, tissue levels are generally found to be high.

Oral CEFRINEX can be given twice or four times daily and is well absorbed. Cephadrine is acid stable and is rapidly absorbed following oral administration in the fasting state.

### Distribution:

Following doses of 250mg, 500mg and 1000mg average peak serum levels of approximately 9, 16.5, and 24.2 mcg/mL, respectively, were obtained at one hour. The presence of food in the gastrointestinal tract delays the absorption but does not affect the total amount of cephadrine absorbed. Measurable serum levels are present six hours after administration.

### Elimination:

Over 90% of the drug is excreted unchanged in the urine within 6 hours. Peak urine concentrations are approximately 1600 mcg/ml following a 250mg dose, 3200 mcg/mL following a 500mg dose, and 4000 mcg/mL following a 1000mg dose. After 48 hours administration of 100mg/kg/day of CEFRINEX for the treatment of otitis media, cephadrine has been measured in the middle ear exudate at an average level of 3.6 mcg/mL.

## SPECIFIC POPULATIONS

### Renal impairment

Plasma concentration of cephadrine is prolonged in patients with renal impairment.

## THERAPEUTIC INDICATIONS:

CEFRINEX (Cephadrine) 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.

### Urinary tract infections:

Cystitis, urethritis and pyelonephritis.

### Skin and soft tissue infections:

Impetigo, abscess, cellulitis and furunculosis.

### Gastrointestinal tract infections:

Bacillary dysentery, enteritis and peritonitis

## DOSE AND ADMINISTRATION:

CEFRINEX (Cephadrine) 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.

<b><i>Creatinine Clearance</i></b>	<b><i>Dose</i></b>	<b><i>Time interval</i></b>
> 20 mL/min	500mg	6 hours
5-20 mL/min	250mg	6 hours
< 5 mL/min	250mg	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.

### Direction for Preparation Oral Suspension

Add small quantity of pre-boiled cool water in the bottle and shake, add more water upto the mark given on the label and shake vigorously to make suspension. Once reconstituted the suspension must be used within 14 days when stored in refrigerator or within 7 days at room temperature. Close the bottle properly after use.

## CONTRAINDICATIONS:

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

## WARNINGS AND PRECAUTIONS:

- Cephadrine 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 Clinistest following administration of cephradine.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose- galactose malabsorption should not take this medicine.
- Prolonged use with antibiotics may result in overgrowth of non-susceptible microorganisms.

## DRUG INTERACTIONS:

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

## ADVERSE EFFECTS:

### General:

#### 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.

**Rare:** Antibiotic-associated colitis, Headache, Vomiting, abdominal discomfort.

**Not Known:** Vaginitis, candidal overgrowth, candidiasis, Eosinophilia, blood disorders (including thrombocytopenia, leucopenia, agranulocytosis, aplastic anaemia and haemolytic anaemia), Fever, athralgia, serum sickness-like reactions, anaphylaxis, Confusion, sleep disturbances, Hypersensitivity, hyperactivity, hypertonia, dizziness, nervousness, Diarrhoea, nausea, glossitis, heartburn, Liver, enzyme disturbances, transient hepatitis, cholestatic jaundice, Rashes, toxic epidermal necrolysis, pruritis, urticaria, erythema multiforme, Stevens-Johnson syndrome, oedema, Reversible interstitial nephritis, Reversible interstitial nephritis, joint pain.

## USE IN PREGNANCY AND LACTATION:

### 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.

## Lactation:

Cephadrine is excreted in breast milk and therefore should be used with caution in nursing mothers.

## OVERDOSE:

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.

## Shelf Life: 3 Years

## INSTRUCTIONS:

Protect from heat, sunlight & moisture.

Store at room temperature (15°C-30°C).

Keep out of the reach of children.

Patients and healthcare professionals can also report suspected adverse drug reaction at [ade@bosch-pharma.com](mailto:ade@bosch-pharma.com).

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

## PRESENTATION:

CEFRINEX 250mg capsules in blister pack of 1x12's

CEFRINEX 500mg capsules in blister pack of 2x6's.

CEFRINEX 125mg / 5ml Suspension: Pack contain dry powder for 90ml suspension (after reconstitution) in Glass bottle.

CEFRINEX 250mg / 5ml Suspension: Pack contain dry powder for 90ml suspension (after reconstitution) in Glass bottle.

## ہدایات:

دھوپ، گرمی اور نمی سے محفوظ کرے کے درجہ حرارت (۱۵-۳۰ ڈگری سینٹی گریڈ) پر رکھیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔



Manufactured by:

**Bosch PHARMACEUTICALS (Pvt) Ltd.**

221-223, Sector 23, Korangi Industrial Area,

Karachi - Pakistan



ISO 9001:2015 Certified Company



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(Cephadrine) Suspension

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