# Axoral CAPSULE / SUSPENSION

( C e f i x i m e )

# ایگزورل کیپسول/سسپینشن

(سیفگزائم)

**COMPOSITION:**

**Axoral Suspension 100mg/5ml**
Each 5ml after reconstitution contains:
Cefixime (as trihydrate).....100mg
**(USP Specifications)**

**Axoral DS Suspension 200mg/5ml**
Each 5ml after reconstitution contains:
Cefixime (as trihydrate).....200mg
**(USP Specifications)**

**Axoral Capsule 200mg**
Each Capsule contains:
Cefixime Trihydrate eq. to Cefixime .....200mg
**(Manufacturer's specifications)**

**Axoral Capsule 400mg**
Each Capsule contains:
Cefixime (as trihydrate) .....400mg
**(Manufacturer's specifications)**

**DESCRIPTION:**
Cefixime is a semi synthetic, cephalosporin antibiotic for oral administration.

**MECHANISM OF ACTION:**
The bactericidal action of Cefixime is due to the inhibition of cell wall synthesis. It binds to one of the penicillin binding proteins (PBPs) which inhibits the final transpeptidation step of the peptidoglycan synthesis in the bacterial cell wall, thus inhibiting biosynthesis and arresting cell wall assembly resulting in bacterial cell death.

**INDICATIONS:**
AXORAL (Cefixime) is a cephalosporin antibacterial indicated in the treatment of adults and pediatric patients six months of age or older with the following infections when caused by susceptible isolates of the designated bacteria:

**Uncomplicated Urinary Tract Infections:**
Uncomplicated Urinary Tract Infections caused by Escherichia coli and Proteus mirabilis.

**Otitis Media:**
Otitis Media caused by Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes. (Efficacy for Streptococcus pyogenes in this organ system was studied in fewer than 10 infections).
Note: For patients with otitis media caused by Streptococcus pneumoniae, overall response was approximately 10% lower for cefixime than for the comparator.

**Pharyngitis and Tonsillitis**:
Caused by Streptococcus pyogenes. (Note: Penicillin is the usual drug of choice in the treatment of Streptococcus pyogenes infections. AXORAL is generally effective in the eradication of Streptococcus pyogenes from the nasopharynx; however, data establishing the efficacy of AXORAL in the subsequent prevention of rheumatic fever is not available).

**Acute Exacerbations of Chronic Bronchitis:**
Caused by Streptococcus pneumoniae and Haemophilus influenzae.

**Uncomplicated Gonorrhea (cervical/urethral):**
Uncomplicated Gonorrhea (cervical/urethral) caused by Neisseria gonorrhoeae (penicillinase-and non-penicillinase-producing isolates).

**DOSAGE & ADMINISTRATION:**

**Adults:**
The recommended dose of cefixime is 400 mg daily. This may be given as a 400 mg capsule daily. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. The capsule may be administered without regard to food. In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

**Pediatric Patients (6 months or older):**
The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours.

**PEDIATRIC DOSAGE CHART**

| | | 100 mg/5 mL | 200 mg/5 mL |
|---|---|---|---|
| **Patient Weight (kg)** | **Dose/Day (mg)** | **Dose/Day (mL)** | **Dose/Day (mL)** |
| 5 to 6.2 | 50 | 2.5 | 1.25 |
| 6.3 to 12.5 | 100 | 5 | 2.5 |
| 12.6 to 18.8 | 150 | 7.5 | 3.75 |
| 18.9 to 25 | 200 | 10 | 5 |
| 25.1 to 31.3 | 250 | 12.5 | 6.25 |
| 31.4 to 37.5 | 300 | 15 | 7.5 |
| 37.6 to 43.8 | 350 | 17.5 | 8.75 |
| 43.9 to 50 | 400 | 20 | 10 |

Children weighing more than 50 kg or older than 12 years should be treated with the recommended adult dose. Otitis media should be treated with the suspension. Clinical trials of otitis media were conducted with the suspension, and the suspension results in higher peak blood levels than the tablet when administered at the same dose. Therefore, the tablet or capsule should not be substituted for the suspension in the treatment of otitis media.
In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

**PHARMACOKINETICS:**

***Absorption:***
AXORAL capsule and suspension, given orally, are about 40% to 50% absorbed whether administered with or without food; however, time to maximal absorption is increased approximately 0.8 hours when administered with food.

***Distribution:***
Serum protein binding is concentration independent with a bound fraction of approximately 65%. In a multiple dose study conducted with a research formulation which is less bioavailable than the tablet or suspension, there was little accumulation of drug in serum or urine after dosing for 14 days. Adequate data on CSF levels of cefixime are not available.

***Metabolism and Excretion:***
There is no evidence of metabolism of cefixime in vivo. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. In animal studies, it was noted that cefixime is also excreted in the bile in excess of 10% of the administered dose. The serum half-life of cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours but may range up to 9 hours in some normal volunteers.

**WARNINGS AND PRECAUTIONS:**

**Hypersensitivity Reactions**
Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime. Before therapy with AXORAL is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross hypersensitivity among beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to AXORAL occurs, discontinue the drug.

**Clostridium difficile-Associated Diarrhea**
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including AXORAL, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing isolates of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

**Dose Adjustment in Renal Impairment**
The dose of AXORAL should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD). Patients on dialysis should be monitored carefully.

**Coagulation Effects**
Cephalosporins, including AXORAL, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

**Development of Drug-Resistant Bacteria**
Prescribing AXORAL (cefixime) in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

**Pregnancy**
**Pregnancy Category B**.
There are 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.

**Labor and Delivery**
Cefixime has not been studied for use during labor and delivery. Treatment should only be given if clearly needed.

**Nursing Mothers**
It is not known whether cefixime is excreted in human milk. Consideration should be given to discontinuing nursing temporarily during treatment with this drug.

**SIDE EFFECTS:**

**Gastrointestinal**
Several cases of documented pseudomembranous colitis were identified in clinical trials. The onset of pseudomembranous colitis symptoms may occur during or after therapy.

**Hypersensitivity Reactions**
Anaphylactic/anaphylactoid reactions (including shock and fatalities), skin rashes, urticaria, drug fever, pruritus, angioedema, and facial edema. Erythema multiforme, Stevens-Johnson syndrome, and serum sickness-like reactions have been reported.

**Hepatic**
Transient elevations in SGPT, SGOT, alkaline phosphatase, hepatitis, jaundice.

**Renal**
Transient elevations in BUN or creatinine, acute renal failure.

**Central Nervous System**
Headaches, dizziness, seizures.

**Hemic and Lymphatic System**
Transient thrombocytopenia, leukopenia, neutropenia, prolongation in prothrombin time, elevated LDH, pancytopenia, agranulocytosis, and eosinophilia.

**Abnormal Laboratory Tests**
Hyperbilirubinemia.

**Other Adverse Reactions**
Genital pruritus, vaginitis, candidiasis, toxic epidermal necrolysis.

**Adverse Reactions Reported for Cephalosporin-class Drugs**
Allergic reactions, superinfection, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage, and colitis.
Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

**DRUG INTERACTIONS:**

**Carbamazepine**
Elevated carbamazepine levels have been reported in postmarketing experience when cefixime is administered concomitantly. Drug monitoring may be of assistance in detecting alterations in carbamazepine plasma concentrations.

**Warfarin and Anticoagulants**
Increased prothrombin time, with or without clinical bleeding, has been reported when cefixime is administered concomitantly.

**Drug/Laboratory Test Interactions**
A false-positive reaction for ketones in the urine may occur with tests using nitroprusside but not with those using nitroferricyanide. The administration of cefixime may result in a false-positive reaction for glucose in the urine using Benedict's solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose oxidase reactions be used. A false positive direct Coombs test has been reported during treatment with other cephalosporins, therefore, it should be recognized that a positive Coombs test may be due to the drug.

**CONTRAINDICATIONS**
Cefixime is contraindicated in patients with known allergy to cefixime or other cephalosporins.

**DIRECTIONS FOR RECONSTITUTION:**
To make 30ml suspension, first shake the bottle well to loosen the powder. Add previously boiled and cooled water into the bottle upto the mark.
Close the cap of bottle tightly and shake well to form uniform suspension.

**STORAGE & INSTRUCTIONS:**
Store between 15-25°C. Protect from heat, sunlight & moisture. Keep away from the reach of children.
**To be sold on prescription of registered medical practitioner only.**

**HOW SUPPLIED:**
**Axoral Suspension 100mg/5ml** :30ml
**Axoral-DS Suspension 200mg/5ml:** 30ml
**Axoral Capsule 200mg:** 5's
**Axoral Capsule 400mg:** 5's

**دوا بنانے کا طریقہ:**

۳۰ ملی لیٹر سسپینشن بنانے کے لیے بوتل کو اچھی طرح ہلائیں تا کہ پاؤڈر بوتل کی سطح سے علیحدہ ہو جائے۔ پہلے سے اُبلا ہوا اور ٹھنڈا پانی بوتل پر دیے گئے نشان تک ڈال کر ڈھکن بند کر کے اچھی طرح ہلائیں۔

**خوراک و ہدایات:**

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔ دوا کو ۱۵-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔ دھوپ، گرمی، نمی، اور بچوں کی پہنچ سے دور رکھیں۔ تیار شدہ دوا کو کمرے کے درجہ حرارت پر رکھیں اور ۷ دن میں استعمال کریں۔ ۷ دن کے بعد بچ جانے والی دوا کو ضائع کر دیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549, Sundar Industrial Estate,
Lahore, Pakistan.