Bosch

For Medical Professional only

Cebosh®

(C e f i x i m e)

Capsules / Tablets / Suspension

سیبوش

کیپسولز/ٹیبلٹس/سسپنشن

(سیفکزائم)

DESCRIPTION:

Cebosh (Cefixime) is a semisynthetic, cephalosporin antibacterial for oral administration. Chemically, it is (6R,7R)-7-[2-(2-Amino-4 -thiazolyl) glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0] oct-2-ene-2-carboxylic acid, 72 -(Z)-[O-(carboxy methyl) oxime] trihydrate. Molecular weight = 507.50 as the trihydrate. Chemical Formula is $C_{16}H_{15}N_5O_7S_2.3H_2O$.

COMPOSITION:

Cebosh 200mg Capsule:
Each Capsule contains:
Cefixime U.S.P. .... 200mg as Cefixime Trihydrate
(Product Specs.: Bosch)

Cebosh 400mg Capsule:
Each Capsule contains:
Cefixime U.S.P. .... 400mg as Cefixime Trihydrate
(Product Specs.: Bosch)

Cebosh 200mg tablet:
Each Film Coated Tablet contains:
Cefixime U.S.P. .... 200mg as Cefixime Trihydrate
(Product Specs.: U.S.P.)

Cebosh 400mg tablet:
Each Film Coated Tablet contains:
Cefixime U.S.P. .... 400mg as Cefixime Trihydrate
(Product Specs.: U.S.P.)

Cebosh 100mg/5ml Suspension:
Each 5ml contains:
Cefixime U.S.P. .... 100mg as Cefixime Trihydrate
(Product Specs.: U.S.P.)

Cebosh 200mg/5ml Suspension:
Each 5ml contains:
Cefixime U.S.P. .... 200mg as Cefixime Trihydrate
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:

Pharmacodynamic Properties:
Pharmacotherapeutic group: third generation cephalosporin, ATC code: J01DD08

Mechanism of Action:
Cebosh (Cefixime) is an oral third generation cephalosporin which has marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms.
The bactericidal action of cefixime results from inhibition of cell wall synthesis.
Cebosh (Cefixime) is stable in the presence of certain beta-lactamase enzymes. As a result, certain organisms resistant to penicillin and some cephalosporins due to the presence of beta lactamases may be susceptible to cefixime.

Microbiology:

Gram-Positive Bacteria:
- Streptococcus pneumoniae
- Streptococcus pyogenes
- Streptococcus agalactiae

Gram-Negative Bacteria:
- Escherichia coli
- Haemophilus influenzae
- Moraxella catarrhalis
- Neisseria gonorrhoeae
- Proteus mirabilis
- Citrobacter amalonaticus
- Citrobacter diversus
- Haemophilus parainfluenzae
- Klebsiella oxytoca
- Klebsiella pneumoniae
- Pasteurella multocida
- Proteus vulgaris
- Providencia species
- Salmonella species
- Serratia marcescens
- Shigella species

Pharmacokinetic Properties

Absorption:

Cebosh (Cefixime) tablets 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 hour when administered with food. A single 200 mg tablet of cefixime produces an average peak serum concentration of approximately 2 mcg/mL (range 1 to 4 mcg/mL); a single 400 mg tablet produces an average peak concentration of approximately 3.7 mcg/mL (range 1.3 to 7.7 mcg/mL). The oral suspension produces average peak concentrations approximately 25% to 50% higher than the tablets. 200 and 400 mg doses of oral suspension produce average peak concentrations of 3 mcg/mL (range 1 to 4.5 mcg/mL) and 4.6 mcg/mL (range 1.9 to 7.7 mcg/mL), respectively. The 400 mg capsule is bioequivalent to the 400 mg tablet under fasting conditions. However, food reduces the absorption following administration of the capsule by approximately 15% based on AUC and 25% based on Cmax. Peak serum concentrations occur between 2 and 6 hours following oral administration of a single 200 mg tablet, a single 400 mg tablet or 400 mg of cefixime suspension. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200 mg of suspension. Peak serum concentrations occur between 3 and 8 hours following oral administration of a single 400 mg capsule.

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.

Metabolism & Elimination:

There is no evidence of metabolism of cefixime. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. The serum half-life of cefixime is independent of dosage form and averages 3 to 4 hours but may range up to 9 hours in some people.

SPECIFIC POPULATIONS

Renal Insufficiency

The average serum half-life of cefixime is prolonged to 6.4 hours. In severe renal impairment, the half-life increased to an average of 11.5 hours. The drug is not cleared significantly from the blood by hemodialysis or peritoneal dialysis.

Elderly:

Average AUCs at steady state in elderly patients are approximately 40% higher than average AUCs in other healthy adults. However, these increases were not clinically significant.

THERAPEUTIC INDICATIONS:

It is indicated for the following treatment;

- Upper respiratory tract infections (URTI): e.g. Otitis media, sinusitis, pharyngitis & tonsillitis
- Lower respiratory tract infections (LRTI): e.g. Bronchitis
- Urinary tract infections (UTI): e.g. Cystitis, cystourethritis, uncomplicated pyelonephritis & uncomplicated gonorrhoea (Cervical, urethral and rectal).

DOSAGE AND ADMINISTRATION:

Adults:

The recommended dose of **Cebosh** (Cefixime) is 400 mg daily. This may be given as a 400 mg tablet or capsule daily or the 400 mg tablet may be split and given as one half tablet every 12 hours. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. The capsule and tablet may be administered without regard to food.

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. Children weighing more than 45 kg or older than 12 years should be treated with the recommended adult dose. cefixime chewable tablets must be chewed or crushed before swallowing.

Safety and effectiveness of cefixime in pediatric patients younger than 6 months of age have not been established.

Otitis Media

Otitis media should be treated with the chewable tablets or suspension. The chewable tablets or 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 chewable tablets or suspension in the treatment of otitis media.

Elderly:

Elderly patients may be given the same dose as recommended for adults. Renal function should be assessed, and dosage should be adjusted in severe renal impairment.

Patients with Renal Impairment:

Cebosh (Cefixime) may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearances of 60 mL/min or greater. Refer to Table 1 below for dose adjustments for adults with renal impairment. Neither hemodialysis nor peritoneal dialysis removes significant amounts of drug from the body.

Table 1. Doses for Adults with Renal Impairment

Renal Dysfunction	Cebosh (cefixime) for oral suspension			Tablet	Chewable Tablet
Creatinine Clearance (mL/min)	100 mg/5 mL Dose/Day (mL)	200 mg/5 mL Dose/Day (mL)	500 mg/5 mL Dose/Day (mL)	400 mg Dose/Day	200 mg Dose/Day
60 or greater	Normal dose	Normal dose	Normal dose	Normal dose	Normal dose
21 to 59 * OR renal hemodialysis*	13	6.5	2.6	Not Appropriate	Not Appropriate
20 or less OR continuous peritoneal dialysis	8.6	4.4	1.8	0.5 tablet	1 tablet

* The preferred concentrations of oral suspension to use are 200 mg/5 mL or 500 mg/5 mL for patients with this renal dysfunction

RECONSTITUTION:
For reconstitution of 30ml or 60ml suspension, add half Biostatic Water as Diluent (available in the pack), close the cap and shake well. Then add remaining diluent in the bottle and shake well to make 30ml or 60ml suspension respectively.
30ml reconstituted suspension available after adding 20ml water which should be used within 7 days.
60ml reconstituted suspension available after adding 40ml water which should be used within 7 days.

CONTRAINDICATIONS:
Cebosh (Cefixime) is contraindicated in patients with known allergy to cefixime or other cephalosporins

WARNINGS AND PRECAUTIONS:
Hypersensitivity Reactions
Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime.

Before therapy with **Cebosh** (Cefixime) 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 antibacterial drugs has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to **Cebosh** (Cefixime) occurs, discontinue the drug.

Clostridium difficile-Associated Diarrhea
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including **Cebosh** (Cefixime), 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 antibacterial drug 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 antibacterial drug use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial drug treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Dose Adjustment in Renal Impairment
The dose of **Cebosh** (Cefixime) 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 **Cebosh** (Cefixime), 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 **Cebosh** (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.

Risk in Patients with Phenylketonuria
Phenylalanine can be harmful to patients with phenylketonuria (PKU). Before prescribing **Cebosh** (Cefixime) in a patient with PKU, consider the combined daily amount of phenylalanine from all sources.

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 Clinitest, Benedict's solution, or Fehling's solution. 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.

ADVERSE 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.

USE IN PREGNANCY AND LACTATION:
Pregnancy:
There are no adequate and well-controlled studies in pregnant women. **Cebosh** (Cefixime) should therefore not be used in pregnancy or in nursing mothers unless considered essential by the physician.

Lactation:
There are no available data on the presence of cefixime in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for cefixime and any potential adverse effects on the breastfed infant from cefixime or from the mother's underlying condition.

OVERDOSE:
Gastric lavage may be indicated; otherwise, no specific antidote exists. Cefixime is not removed in significant quantities from the circulation by hemodialysis or peritoneal dialysis. Adverse reactions in small numbers of healthy adult volunteers receiving single doses up to 2 g of cefixime did not differ from the profile seen in patients treated at the recommended doses.

EXPIRY DATE:
Tablets and Capsules: 3 years
Suspension: 2 years

STORAGE & INSTRUCTIONS:
Suspension: Protect from heat, sunlight and moisture, store below 30°C.
Capsules & Tablets: Store at controlled room temperature (15°C-30°C).
The expiration date refer to the product correctly stored at the required condition.
Do not take if seal is broken.
Keep out of the reach of children.
Close the bottle properly after use.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
To be sold on prescription of a registered medical practitioner only.

PRESENTATION:
Cebosh Capsule 200mg: Each pack contains 10's capsules in Cold Form & Cold Seal Alu Alu packaging.
Cebosh Capsule 400mg: Each pack contains 5's capsules in Cold Form & Cold Seal Alu Alu packaging.
Cebosh Tablet 400mg: Each pack contains 5's tablets in Cold Form & Cold Seal Alu Alu packaging.
Cebosh Tablet 200mg: Each pack contains 10's tablets in Cold Form & Cold Seal Alu Alu packaging.
Cebosh Suspension 100mg/5ml (30ml & 60ml) Strawberry flavoured suspension.
60ml bottle containing powder for preparation of 30ml suspension with 20ml biostatic water as diluent for suspension.
90ml bottle containing powder for preparation of 60ml suspension with 40ml biostatic water as diluent for suspension.
Cebosh DS Suspension 200mg/5ml (30ml) Strawberry flavoured suspension.
60ml bottle containing powder for preparation of 30ml DS suspension and each 5ml contains 200mg cefixime with 20ml biostatic water as diluent for suspension.
(for homogeneous suspension Cebosh bottle sealed and plugged with nitrogen purging.)

ہدایات:

سسپنشن: دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

کیپسولز اور ٹیبلٹس:

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

بچوں کی پہنچ سے دور رکھیں۔ کھلی سیل والی بوتل نہ لیں۔

استعمال کے بعد ڈھکن کو اچھی طرح بند رکھیں۔

صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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