1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

- Attached

National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Generic Name or International Non-Proprietary Name (INN)
CEFIXIME TABLETS USP 200MG

Brand Name
CEFEXITAB 200

Strength
200MG

Pharmaceutical Dosage Form
Solid oral dosage form, Film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Film coated tablet contains:
Cefixime (As Trihydrate) USP
Eq. to Anhydrous Cefixime....200 mg
Excipients.....q.s.
Colors: Approved colors used.

Qty of Cefixime trihydrate is approx. 223.840mg equivalent to Cefixime Tablets USP 200mg.
Batch Size: 91,463 Tablets

Sr. No	Ingredients	Grade	Rationale	Label Claim	Quantity Tablet (mg)	Quantity / Batch (Kg)
DRY MIXING						
1.	Cefixime Trihydrate (Compacted)*	USP	Active	200 mg	223.840	20.473
2.	Microcrystalline Cellulose-102 (Spray dried) $	USP-NF	Diluent	-----	60.660	5.548
3.	Lactose Monohydrate	USP-NF	Disintegrant	-----	11.000	1.006
4.	Colloidal Silicon Dioxide (Aerosil)	USP-NF	Lubricant	-----	2.000	0.183
5.	Talc	USP-NF	Lubricant	-----	5.000	0.457
6.	Croscarmellose Sodium	USP-NF	Binder	-----	5.500	0.503
Total Pre-Lubricated Weight					**308.000**	**28.170**
LUBRICATION						
7.	Magnesium Stearate	USP-NF	Lubricant	-----	4.000	0.366
Compressed tablet weight					**312.00**	**28.536**
	COATING					
8.	Colorcoat FC4S-I (Yellow)	IHS	Coloring Agent	-----	9.000	0.823
9.	Isopropyl Alcohol	USP-NF	Solvent	-----	48.800	4.463
10.	Methylene Chloride	USP-NF	Solvent	-----	73.200	6.695
Coated Tablet weight					**321.000**	**29.359**

Note:

1. ***** Mentioned quantity is considering Assay (on anhydrous basis) as 100%, Potency correction to be done while dispensing considering the actual assay on anhydrous basis.

2. $ Microcrystalline cellulose (Spray dried) to be compensate after potency correction of Cefixime trihydrate (Compacted).
3. ** Isopropyl alcohol and Methylene chloride will evaporate while coating.

EQUIVALENCY:
Molecular weight of Cefixime Trihydrate = 507.5g/mol
Molecular weight of Cefixime = 453.452 g/mol
Dose for Cefixime = 200mg

453.45 g/mol Cefixime = 200mg
507.5 g/mol Cefixime Trihydrate = $\frac{200 \times 507.5}{453.452}$ = 223.840 mg of Cefixime Trihydrate required

USP- United States of pharmacopoeia, Current version
USP-**NF**-United states of pharmacopoeia National Formulary, Current version
IHS - In-house specification

3. PHARMACEUTICAL FORM

Yellow coloured, Circular shaped biconvex plain on both side film coated tablets.

4. Clinical particulars

4.1 Therapeutic indications

Cefixime is an orally active cephalosporin antibiotic which has marked in vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms.

It is indicated for the treatment of the following acute infections when caused by susceptible micro-organisms:

Upper Respiratory Tract Infections (URTI): e.g. otitis media; and other URTI where the causative organism is known or suspected to be resistant to other commonly used antibiotics, or where treatment failure may carry significant risk.

Lower Respiratory Tract Infection: e.g. bronchitis.

Urinary Tract Infections: e.g. cystitis, cystourethritis, uncomplicated pyelonephritis.

Clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Kliebsiella species, Haemophilus influenzae (beta-lactamase positive and negative), Branhamella catarrhalis (beta-lactamase positive and negative) and Enterobacter species. Cefixime is highly stable in the presence of beta-lactamase enzymes.

Most strains of enterococci (Streptococcus faecalis, group D Streptococci) and Staphylococci (including coagulase positive and negative strains and methicillin-resistant strains) are resistant to Cefixime. In addition, most strains of Pseudomonas, Bacteriodes fragalis, Listeria monocytogenes and Clostridia are resistant to Cefixime.

4.2 Posology and method of administration

The usual course of treatment is 7 days. This may be continued for up to 14 days if required.

Posology

Adults and Children over 10 years or weighing more than 50 kg:

The recommended dose is 200 – 400 mg daily according to the severity of infection, given either as a single dose or in two divided doses.

Children under 10 years:

Cefixime Tablets 200 mg are not recommended for use in children under 10 years old. The safety and efficacy of cefixime has not been established in children less than 6 months.

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.

Renal impairment:

Cefixime may be administered in the presence of impaired renal function. Normal dose and schedule may be given in patients with creatinine clearances of 20 ml/min or greater. In patients whose creatinine clearance is less than 20 ml/min, it is recommended that a dose of 200 mg once daily should not be exceeded. The dose and regimen for patients who are maintained on chronic ambulatory peritoneal dialysis or haemodialysis should follow the same recommendation as that for patients with creatinine clearances of less than 20 ml/min.

Method for administration

For oral administration. Absorption of Cefixime is not significantly modified by the presence of food.

4.3 Contraindications

Hypersensitivity to the cephalosporin group of antibiotics or to any of the excipients.

4.4 Special warnings and precautions for use

Encephalopathy

Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARS) including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS) drug rash with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in association with cefixime. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. Treatment should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of skin hypersensitivity.

Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs.

Hypersensitivity to penicillins

As with other cephalosporins, cefixime should be given with caution to patients with a history of hypersensitivity to penicillin, as there is some evidence of partial cross-allergenicity between the penicillins and cephalosporins**.**

Patients have had severe reactions (including anaphylaxis) to both classes of drugs. If an allergic effect occurs with Cefixime, the drug should be discontinued and the patient treated with appropriate agents if necessary.

Haemolytic-anaemia

Drug-induced haemolytic anaemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of haemolytic anaemia after re-administration of cephalosporins in a patient with a history of cephalosporin (including cefixime) –associate haemolytic anaemia has also been reported.

Acute renal failure

As with other cephalosporins, cefixime may cause acute renal failure including tubulointerstitial nephritis as an underlying pathological condition. When acute renal failure occurs, cefixime should be discontinued and appropriate therapy and/or measures should be taken.

Renal impairment

Cefixime should be administered with caution in patients with markedly impaired renal function.

Pediatric use

Safety of cefixime in premature or newborn infant has not been established.

Antibiotic-associated colitis

Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by Clostridium difficile is a primary cause of antibiotic-associated diarrhoea. Pseudomembranous colitis is associated with the use of broad-spectrum antibiotics (including macrolides, semi-synthetic penicillins, lincosamides and cephalosporins); it is therefore important to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Symptoms of pseudomembranous colitis may occur during or after antibiotic treatment. Management of pseudomembranous colitis should include sigmoidoscopy, appropriate bacteriologic studies, fluids, electrolytes and protein supplementation. If the colitis does not improve after the drug has been discontinued, or if the symptoms are severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by C. difficile. Other causes of colitis should be excluded.

4.5 Interaction with other medicinal products and other forms of interaction

Anticoagulants

In common with other cephalosporins, increases in prothrombin times have been noted in a few patients. Care should therefore be taken in patients receiving anticoagulation therapy.

Cefixime should be administered with caution to patients receiving coumarin-type anticoagulants, e.g. warfarin potassium. Since cefixime may enhance effects of the anticoagulants, prolonged

prothrombin time with or without bleeding may occur.

Other forms of interaction

A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions.

A false positive direct Coombs test has been reported during treatment with cephalosporin antibiotics, therefore it should be recognised that a positive Coombs test may be due to the drug.

4.6 Pregnancy and Lactation

Reproduction studies have been performed in mice and rats at doses up to 400 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefixime. In the rabbit, at doses up to 4 times the human dose, there was no evidence of a teratogenic effect; there was a high incidence of abortion and maternal death which is an expected consequence of the known sensitivity of rabbits to antibiotic-induced changes in the population of the microflora of the intestine. There are no adequate and well-controlled studies in pregnant women. Cefixime should therefore not be used in pregnancy or in nursing mothers unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

In the case of side effects such as encephalopathy (which may include convulsion, confusion, impairment of consciousness, movement disorders), the patient should not operate machines or drive a vehicle.

4.8 Undesirable effects

Cefixime is generally well tolerated. The majority of adverse reactions observed in clinical trials were mild and self-limiting in nature.

The following adverse reaction (Preferred term# or equivalent) will be considered listed:

Blood and lymphatic system disorders:	Eosinophilia Hypereosinophilia Agranulocytosis Leucopenia Neutropenia Granulocytopenia Haemolytic anaemia Thrombocytopenia Thrombocytosis
Gastrointestinal disorders:	Abdominal pain Diarrhoea* Dyspepsia

	Nausea Vomiting Flatulence
Hepatobiliary disorders:	Jaundice
Infections and infestations:	Pseudomembranous colitis Vaginitis
Investigations:	Aspartate aminotransferase increased Alanine aminotransferase increased Blood bilirubin increased Blood urea increased Blood creatinine increased
Nervous system disorders:	Dizziness Headache Cases of convulsions have been reported with cephalosporins including cefixime (frequency not known)[**] Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment (frequency not known)[**]
Respiratory, thoracic and mediastinal disorders:	Dyspnoea
Renal and urinary disorders:	Acute renal failure with tubulointerstitial nephritis.
Immune system disorders:	Anaphylactic reaction Angio-oedema Serum sickness-like reaction
Skin and subcutaneous tissue disorders:	Drug rash with eosinophilia and systemic symptoms (DRESS) Erythema multiforme Stevens-Johnson syndrome Toxic epidermal necrolysis Urticaria Rash Pruritus Acute generalised exanthematous pustulosis (AGEP)
General disorders and administrative site conditions:	Drug Fever

	Arthralgia Pyrexia Face oedema Genital pruritus

The above mentioned listed adverse reactions have been observed during clinical studies and/or during marketed use.

*Diarrhoea has been more commonly associated with higher doses. Some cases of moderate to severe diarrhoea have been reported; this has occasionally warranted cessation of therapy. Cefixime should be discontinued if marked diarrhoea occurs.

**Cannot be estimated from available data

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

There is a risk of encephalopathy in cases of administration of beta-lactam antibiotics, including cefixime, particularly in case of overdose or renal impairment.

Adverse reactions seen at dose levels up to 2 g Cefixime in normal subjects did not differ from the profile seen in patients treated at the recommended doses. Cefixime is not removed from the circulation in significant quantities by dialysis.

No specific antidote exists. General supportive measures are recommended.

5. PHARMACOLOGICAL PROPERTIES

Pharmacodynamics properties

Pharmacotherapeutic group: third generation cephalosporin, ATC code: J01DD08

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.

Clinical efficacy has been demonstrated in infections caused by commonly occurring pathogens including Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Klebsiella species, Haemophilus influenzae (beta-lactamase positive and negative), Branhamella catarrhalis (beta-lactamase positive and negative) and Enterobacter species. It is highly stable in the presence of beta-lactamase enzymes.

Most strains of enterococci (Streptococcus faecalis, group D Streptococci) and Staphylococci (including coagulase positive and negative strains and methicillin-resistant strains) are resistant to cefixime. In addition, most strains of Pseudomonas, Bacteroides fragilis, Listeria monocytogenes and Clostridia are resistant to cefixime.

5.1 Pharmacokinetic properties

The absolute oral bioavailability of cefixime is in the range of 22 – 54%. Absorption is not significantly modified by the presence of food. Cefixime may therefore be given without regard to meals. From in vitro studies, serum or urine concentrations of 1 mcg/mL or greater were considered to be adequate for most common pathogens against which cefixime is active. Typically, the peak serum levels following the recommended adult or paediatric doses are between 1.5 – 3 mcg/ml. little or no accumulation of cefixime occurs following multiple dosing.

The pharmacokinetics of cefixime in healthy elderly (age > 64 years) and young volunteers (11 – 35) compared the administration of 400 mg doses once daily for 5 days. Mean Cmax and AUC values were slightly greater in the elderly. Elderly patients may be given the same dose as the general population. Cefixime is predominantly eliminated as unchanged drug in the urine. Glomerular filtration is considered the predominant mechanism. Metabolites of cefixime have not been isolated from human serum or urine. Serum protein binding is well characterised for human and animal sera; cefixime is almost exclusively bound to the albumin fraction, the mean free fraction being approximately 30%. Protein binding of cefixime is only concentration dependent in human serum at very high concentrations which are not seen following clinical dosing. Transfer of 14C-labelled cefixime from lactating rats to their nursing offspring through breast milk was quantitatively small (approximately 1.5% of the mothers' body content of cefixime in the pup). No data are available on secretion of cefixime in human breast milk. Placental transfer of cefixime was small in pregnant rats dosed with labelled cefixime.

5.2 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose – 102 (Spray dried)
Lactose Monohydrate
Colloidal Silicon Dioxide (Aerosil)
Talc
Croscarmellose Sodium
Magnesium Stearate
Solvent
Colorcoat FC4S-I (Yellow)
Isopropyl Alcohol
Methylene Chloride

6.2 Incompatibilities

No compatibilities

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Store at temperature not exceeding 30^0C. Protect from light.

6.5 Nature and contents of container

Pack 1 ALU-ALU blister of 10 tablets with 1 inner Carton along with a leaflet.

Inner Carton must have 2D Barcode overprinted

Pack 10 inner cartons with outer carton.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

MANUFACTURER:

NAME	:	**GLOBELA LABORATORIES PVT. LTD**
ADDRESS	:	PLOT NO. 5536, ROAD NUMBER 55, SACHIN G.I.D.C, SURAT- 394230 GUJARAT, INDIA.
COUNTRY	:	INDIA
TELEPHONE	:	+91–0261–6158000
E-MAIL	:	glpra@globelapharma.com

APPLICANT:

NAME	:	**SJS LIFE SCEINCE LTD**
ADDRESS	:	H.NO.11, OLU-AKERELE STREET, IKEJA, LAGOS STATE, NIGERIA.
COUNTRY	:	NIGERIA
TELEPHONE	:	+234–8114441430
E-MAIL	:	jkpandey3s@gmail.com

Marketing authorization numbers

Not applicable

Date of first authorization/renewal of the authorization

Not applicable

Date of revision of the text

To be given after approval of the product