1.3.1 Summary of Product Characteristics (SmPC)

The Summary of Product Characteristics is attached herewith:

===Attached===

1.5 PRODUCT INFORMATION

1.5.1 Prescribing Information (Summary of Product Characteristics)

1. Name of the medicinal product

a) Trade name : BRODCEF-400
b) Generic name : Cefixime Tablets USP 400 mg

2. Qualitative and Quantitative composition

A. <u>Qualitative Composition</u>

Composition:
Each film coated tablet contains:

Cefixime (As trihydrate)	USP	
Equivalent to Anhydrous Cefixime		400 mg.
Excipients		q.s.
Colour: Titanium Dioxide	USP	

B. <u>Quantitative composition</u>

Sr. No.	Item Code	Material Name	Spec	Clam	Quantity (mg) /Tablet	% Formula w/w	Theoretical Quantity / Batch (kg)
01	R/313	Cefixime (As Trihydrate)	USP	400	448.00	64.000	44.800
02	R/13493	Microcrystalline Cellulose (PH-112)	USP	….	87.00	12.42	8.700
03	R/9951	Dummy Granules	IHS	….	87.00	12.42	8.700
04	R/11008	Sodium starch glycolate	USP	….	56.000	8.00	5.600
05	R/22	Magnesium Sterate	USP	….	3.500	0.49	0.350
06	R/87	Talc	USP	….	3.500	0.49	0.350
07	R/3834	Colloidal silicon Dioxide	USP	….	5.000	0.69	0.500
08	R/58	Tulsion 339	IHS	….	10.000	1.32	1.000
TOTAL WEIGHT					**700**	**97.860**	**70.000**
09	R/61	Hypromellose (Hydroxy Propyl methyl cellulose	USP	….	8.800	1.02	0.880

10	R/86	Titanium Dioxide	USP	….	3.500	0.40	0.350
11	R/87	Talc	USP	….	4.200	0.48	0.420
12	R/57	Poly Ethylene Glycol 6000	USP	….	3.500	0.40	0.350
13	R/85	Isopropyl Alcohol*	USP	….	….	….	10.200
14	R/88	Methylene Chloride*	USP	….	….	…..	34.400
Total weight					**720.00**	**100**	**72.000**

3. Pharmaceutical form

Oral Solid (Film coated Tablets)

4. Clinical Particulars

4.1 Therapeutic indications

Cefixime Tablets USP 400 mg 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 occuring 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 not significantly modified by the presence of food.

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 meticillin- resistant strains) are resistant to Cefixime. In addition, most strains of *Pseudomonas, Bacteriodes fragalis, Listeria monocytogenes* and *Clostridia* are resistant to BRODCEF-400

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

***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.

***Children under 10 Years*:**

Cefixime Tablets USP 400 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.

***Renal Impairment*:**

Cefixime Tablets USP 400 mg 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 Tablets USP 400 mg is not significantly modified by the presence of food.

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

4.3 Contraindications

Hypersensitivity to cephalosporin 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 such as toxic epidermal necrolysis, Stevens- Johnson syndrome and drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in some patients on cefixime. When severe cutaneous adverse reactions occur, cefixime should be discontinued and appropriate therapy and/or measures should be taken.

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 200 mg, 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) –associated 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 Tablets USP 400 mg is not significantly modified by the presence of food.
should be administered with caution in patients with markedly impaired renal function.

Paediatric use

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

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 Fertility, 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 foetus 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. BRODCEF-400 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 Tablets USP 400 mg 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 Flatulance
Hepatobiliary disorders:	Jaundice
Infections and infestations	Pseudomembranous colitis
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	Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition
Immune system	Anaphylactic reaction, Serum sickness-like reaction, Drug rash

disorders, administrative site conditions, skin and subcutaneous tissue disorders	with eaosinophilia and systemic symptoms (DRESS), Pruritus Rash, Drug Fever, Arthralgia, Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Angio-oedema Urticaria, Pyrexia, Face oedema, Genital pruritus, Vaginitis

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

Preferred term in MedDRA (v.14.0)

*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. Suprax 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 Suprax 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

5.1 Pharmacodynamic 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 meticillin- resistant strains) are resistant to cefixime. In addition, most strains of *Pseudomonas, Bacteroides fragilis, Listeria monocytogenes* and *Clostridia* are resistant to cefixime.

5.2 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 and 3mcg/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.

Placetal transfer of cefixime was small in pregnant rats dosed with labelled cefixime.

5.3 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 (112), Dummy Granules, Magnesium Stearate, Talc, Colloidal Silicon Dioxide, Tulsion 339, Hypromellose (Hydroxy propyl methyl cellulose, Titanium Dioxide, Talc, Poly Ethylene Glycol 6000, Isopropyl Alcohol, Methylene Chloride.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months from the date of manufacturing.

6.4 Special precautions for storage

Store at a temperature below 30°C.Protect from light & moisture.

Keep medicine out of the reach and sight of Children.

6.5 Nature and contents of container

10 tablets packed in Alu/Alu blister and such 10 Alu-Alu blister packed in a printed mono carton with package insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Sam Pharmaceutical Ltd.
8/9, Oyadiran ,Estate,
Sabo,Yaba, Lagos,
Nigeria.

8. Marketing authorisation number(s)

"A4-5106

9. Date of first authorization/renewal of the authorization

NA

10. Date of revision of the text

12-10-2023, 11-10-2028