Summary of Product Characteristics (SPC)

1. Name of the Finished Pharmaceutical product
Cefixime Capsules 400mg

2. Qualitative and quantitative composition
Each hard gelatin capsule contains:
Cefixime USP (As Trihydrate)
Eq. to Cefixime anhydrous 400 mg

3. Pharmaceutical form
Solid oral dosage form, Hard Gelatin Capsules
Purple / White coloured “0” size telescopic cap and body hard gelatin capsule containing white to off white powder.

4. Clinical particulars
4.1 Therapeutic indications
Cefixime is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms:

Upper Respiratory Tract:
Pharyngitis and tonsillitis caused by S. pyogenes.

Middle Ear:
Otitis media caused by S. pneumoniae, H. influenzae (beta-lactamase positive and negative strains), M. catarrhalis(former B. catarrhalis) (beta-lactamase positive andnegative strains) and S. pyogenes.

Paranasal sinuses:
Sinusitis caused by S. pneumoniae, H. Influenza (beta-lactamase positive and negative strains), and M. Catarrhalis (former B. catarrhalis) (beta-lactamase positive and negativestrains).

Lower Respiratory Tract:
Acute bronchitis caused by S. pneumoniae, M. Catarrhalis (former B. catarrhalis)(beta lactamase positive and negative strains) and H. influenzae (beta-lactamase positive and negative strains).

Urinary Tract:
Acute uncomplicated cystitis and urethritis caused by E. coli, P. mirabilis, and Klebsiellaspecies.

Uncomplicated Gonorrhea:
Uncomplicated gonorrhea (cervical/urethral and rectal) caused by Neisseria gonorrhoeae, including penicillinase (beta-lactamase-positive) and non penicillinase (beta- lactamasenegative) producing strains.
Appropriate cultures should be taken for susceptibility testing before initiating treatment with Cefixime. If warranted, therapy may be instituted before susceptibility results are known; however, once these are obtained, therapy may need to be adjusted.

4.2 Posology and method of administration
Adults: the recommended dose of INNOFIX is 400 mg daily. This may be given as a400 mg capsule daily or as 200 mg capsule every 12 hours.
For the treatment of uncomplicated (cervical/urethral) gonococcal infections, a single oral dose of 400 mg is recommended.

Children: 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/kgevery 12 hours.
In the treatment of infections due to S. pyogenes a therapeutic dosage of INNOFIXshould be administered for at least 10 days.

Dosage for impaired renal function:
Patients with creatinine clearance between 21 and 60ml/ min, the dosage should bereduced to (300 mg daily).
Patients with creatinine clearance < 20 ml/min, the dosage should be reduced to (200 mgdaily).

Method of administration
For oral administration only.

4.3 Contraindications
Cefixime is contraindicated in patients with known allergies to the cephalosporin or penicillin antibiotics or to any ingredients in the formulation or component of the container.

4.4 Special warnings and precautions for use

Cefixime should be given with caution to patients who have shown hypersensitivity to other drugs. Cephalosporins should be given with caution to penicillin-sensitive patients, 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. Special care is indicated in patients who have experienced any allergic reaction to penicillins or any other beta-lactam antibiotics as cross-reactions may occur.

If severe hypersensitivity reactions or anaphylactic reactions occur after administration of cefixime, the use of cefixime should be discontinued immediately and appropriate emergency measures should be initiated.

Renal insufficiency

Cefixime should be administered with caution in patients with creatinine clearance < 20ml / min. There are insufficient data regarding use of cefixime in the pediatric and adolescent age group in the presence of renal insufficiency. Therefore, the use of cefixime in these patient-groups is not recommended.

Renal function is to be monitored under a combination therapy with Cefixime preparations and aminoglycoside antibiotics, polymyxin B, colistin or high-dose loop diuretics (e.g. furosemide) because of the probability of additional renal impairment. This applies particularly for patients with already restricted renal function.

Treatment with cefixime at the recommended (400mg) dose can significantly alter the normal flora of the colon and lead to overgrowth of clostridia.

Studies indicate that a toxin produced by Clostridium difficile is a primary cause of antibiotic-associated diarrhoea.

In patients who develop severe persistent diarrhoea during or after use of cefixime, the risk of life threatening pseudomembranous colitis should be taken into account. The use of cefixime should be discontinued and appropriate treatment measures should be established. 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. The use of medicinal products inhibiting the

intestinal peristalsis is contraindicated. Influence on laboratory diagnostic tests
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 recognized that a positive Coombs' test may be due to the drug.

4.5 Interaction with other medicinal products and other forms of interaction Concomitant intake with potentially nephrotoxic substances (such as aminoglycoside antibiotics, colistin, polymyxin and viomycin) and strong-acting diuretics (e.g. ethacrynic acid or furosemide) induce an increased risk of impairment of renal function.
Nifedipine, a calcium channel blocker, may increase bioavailability of cefixime up to70%.
In common with other cephalosporins, increases in prothrombin time have been noted in a few patients. Care should therefore be taken in patients receiving anticoagulation therapy.
Administration of cefixime may reduce the efficacy of oral contraceptives. It is therefore recommended to take supplemental non-hormonal contraceptive measures.

4.6 Fertility, pregnancy and lactation
Pregnancy
There are no adequate data from the use of Cefixime in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/ foetal development, parturition or postnatal development (see section 5.3). Cefixime should not be used in pregnant mothers unless considered essential by the physician.

Lactation
It is unknown whether cefixime is excreted in human breast milk. Animal studies have shown excretion of cefixime in breast milk. A decision on whether to continue /discontinue breast-feeding or to continue/discontinue therapy with cefixime should be made taking into account the benefit of breast-feeding to the child and the benefit of cefixime therapy to the woman.
However, until further clinical experience is available, cefixime should not be prescribed to breast-feeding mothers.

4.7 Effects on ability to drive and use machines

Cefixime has no known influence on the ability to drive and use machines. However, side effects may occur, which may influence the ability to drive and use machines.

4.8 Undesirable effects

Most of the adverse reactions observed in clinical trials were of a mild and transientnature.

The most commonly seen adverse reactions were:

Gastrointestinal events: Individual event rates included diarrhea 16%, loose or frequent stools 6%, abdominal pain 3%, nausea 7% dyspepsia 3%, and flatulence 4%.

These symptoms usually responded to symptomatic therapy or ceased when CEFIXIMEwas discontinued.

Hypersensitivity reactions: skin rashes, urticaria, drug fever, and pruritus. Erythemamultiform.

Stevens-Johnson syndrom, and serum sickness-like reactions have been reported.

Hepatic: transient elevations in SGPT, SGOT, and alkaline phosphatase.
Renal: transient elevations in BUN or creatinine.
Central nervous system: Headaches or dizziness.
Hemic and lymphatic system: transient thrombocytopenia, leukopenia, and eosinophilia, prolongation in prothrombin time was seen rarely.

Other: genital pruritus, vaginitis, candidiasis.
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.

4.9 Overdose

Gastric lavage may be indicated; otherwise, no specific antidote exists.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: third generation cephalosporin**,** ATC code:

J01DD08 Mode of Action

Cefixime is an antibacterial agent of the cephalosporin class. Like other cephalosporins, cefixime exerts antibacterial activity by binding to and

inhibiting the action of penicillinbindin proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.

PK/PD relationship

The time that the plasma concentration of cefixime exceeds the MIC of the infecting organism has been shown to best correlate with efficacy in PK/PD studies.

Mechanisms of resistance

Bacterial resistance to cefixime may be due to one or more of the following mechanisms:

- Hydrolysis by extended-spectrum beta-lactamases and / or by chromosomally- encoded (AmpC) enzymes that may be induced or de-repressed in certain aerobic gramnegative bacterial species
- Reduced affinity of penicillin-binding proteins
- Reduced permeability of the outer membrane of certain gram-negative organisms restricting access to penicillin-binding proteins

Drug efflux pumpsBreakpoints

Clinical minimum inhibitory concentration (MIC) breakpoints established byEUCAST

(May 2009) for cefixime are:

□ H. influenzae: sensitive ≤0.12 mg/L, resistant > 0.12 mg/L
□ M. catarrhalis: sensitive ≤0.5 mg/L, resistant > 1.0 mg/L
□ Neisseria gonorrhoeae: sensitive ≤0.12 mg/L, resistant > 0.12 mg/L
□ Enterobacteriaceae: sensitive ≤1.0 mg/L, resistant > 1.0 mg/L (for uncomplicated urinary tract infections only). The breakpoints for Enterobacteriaceae will detect reduced susceptibility mediated by most clinically important beta-lactamases in Enterobacteriaceae
□ Occasional ESBL-producing strains will be reported susceptible. For purposes of infection control, epidemiology and surveillance, laboratories may wish to use specifictests to screen for and confirm ESBL-production.
□ Non-species related breakpoints: insufficient data.

Susceptibility

The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species
Aerobes, Gram positive: *Streptococcus pyogenes*
Aerobes, Gram negative: *Haemophilus influenzae* *Moraxella catarrhalis* *Proteus mirabilis*
Species for which resistance may be a problem
Streptococcus pneumoniae *Citrobacter freundii* $ *Enterobacter cloacae* $ *Escherichia coli* % & *Klebsiella oxytoca* % *Klebsiella pneumoniae* % *Morganella morganii* $ *Serratia marcescens* $°
Resistant species
Chlamydia spp. *Chlamydophila spp.* *Clostridium difficile* *Bacteroides fragilis* *Enterococci* *Legionella pneumophila* *Mycoplasma spp.* *Pseudomonas* species *Staphylococcus aureus*+ *Streptococcus pneumoniae* (Penicillin-intermediate and -resistant)

Cefixime has poor activity against staphylococci (regardless of susceptibility to methicillin)

$ Natural intermediate susceptibility.

% Extended spectrum beta-laktamase (ESBL) producing strains are always resistant. & Resistance rate <10% in isolates of female patients with uncomplicated cystitis, otherwise ≥10%.

5.2Pharmacokinetic properties

Absorption

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.

Distribution

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. From in vitro studies, serum or urine concentrations of 1 mg/L 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 3 mg/L. Little or no accumulation of cefixime occurs following multiple dosing.

Metabolism and Elimination
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 notbeen isolated from human serum or urine.

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 labeled cefixime.

5.3 Preclinical safety data
There are no findings from chronic toxicity investigations suggesting that any side effects unknown to date could occur in humans. Furthermore, in vivo and in vitro studies did not yield any indication of a potential to cause mutagenicity. Long-term studies oncarcinogenicity have not been conducted.

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.

6. Pharmaceutical particulars

6.1 List of excipients

- Di calcium phosphate
- Sodium Lauryl Sulphate
- Colloidal silicon dioxide
- Talc
- Empty hard gelatin capsule shell size “0” purple/white

Qualitative and Quantitative composition of Hard Gelatin Capsule Size 0 Purple/White

Ingredients	**CAP (Purple)**		**BODY (White)**	
	% w/w	**In mg**	**% w/w**	**In mg**
Gelatin	82.8041	31.4656	82.1583	47.6518
Water	14.5000	5.5100	14.5000	8.4100
SLS	0.1500	0.0570	0.1500	0.0870
Bronopol	0.1000	0.0380	0.1000	0.0580
Poly vinyl pyrrolidine	0.1750	0.0665	0.1750	0.1015
Colorants				
Titanium dioxide	1.7500	0.6650	2.9167	1.6917
Carmoisine	0.0063	0.0024	------	------
Brilliant Blue	0.1458	0.0554	------	------
Erythrosine	0.3688	0.1401	------	------

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Do not store above 30°C. Protect from light.
Prescription Only Medicines (POM)

6.5 Nature and contents of container

1 x 10 Capsules ALU-PVC packs in a unit carton.

6.6 Special precautions for disposal and other handling
No special requirements

7. Marketing authorisation holder and Manufacturing site addresses

INNOVA CAPTAB LTD.

1281/1, Hilltop Industrial Estate, Near Epip Phase-I, Jharmajri, Baddi, Dist. Solan (H.P.) India.

8. Marketing Authorization number

TAN 22 HM 0036

9. Date of first Authorization

10/01/2022

10. Date of revision of the text.

April, 2022