5.2 Summary of Product Characteristics:

5.2.1. Name of the Medicinal Product

1.1 Product Name: BEKRACINE 200

1.2 Strength: 200 mg

1.3Pharmaceutical Dosage Form: Dispersible tablet

5.2.2. Quality and Quantitative Composition:

Qualitative Declaration: Complies to USP Specifications

Each Uncoated Dispersible Tablet Contains:

Cefixime Trihydrate USP	
Eq. to. Anhydrous Cefixime	200mg
Excipients	Q.S.

5.2.3Pharmaceutical Form: White to off white coloured, round, standard biconvex, uncoated dispersible tablet with break line on one side and plain on other side.

5.2.4Clinical Particulars:

1.1Therapeutic Indication:

Bekracine 200 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. Bekracine 200 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 Bekracine 200. In addition, most strains of *Pseudomonas, Bacteriodes fragalis, Listeria monocytogenes* and *Clostridia* are resistant to Bekracine 200

1.2 Posology and method of administration
Absorption of Bekracine -200 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.

Adults and Children over 10 Years: 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.
The 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 (See "Dosage in Renal Impairment").

Children weighing more than 50 kg or older than 10 years should be treated with the recommended adult dose (200 - 400 mg daily depending on the severity of infection).
The safety and efficacy of cefixime has not been established in children less than 6 months.

Dosage In Renal Impairment: Bekracine 200may 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.

1.3 Contraindications:
Patients with known hypersensitivity to cephalosporin antibiotics or any of the other compo-nents of the product.

1.4 Special warning and precaution for use
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.
Bekracine 200should 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 Benixim-200, 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.

Renal failure acute

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

Bekracine 200 should be administered with caution in patients with markedly impaired renal function (See section 4.2 under Dosage in Renal Impairment).

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.

1.5 Interaction with other medicinal products and other form of interactions

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.

1.6 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 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. Bekracine 200 should therefore not be used in pregnancy or in nursing mothers unless considered essential by the physician.

1.7 Effect on ability to drive and use machine:

None.

1.8 Undesirable effects

Bekracine 200 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:	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
Respiratory, thoracic and mediastinal disorders:	Dyspnoea
Renal and urinary disorders:	Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition
Immune System disorders, administrative site conditions, skin and subcutaneous tissue disorders:	Anaphylactic reaction Serum sickness-like reaction Drug rash 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. Bekracine 200 should be discontinued if marked diarrhoea occurs

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. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

1.9 Overdose

There is no experience with overdoses with Benixim-200.
Adverse reactions seen at dose levels up to 2 g Bekracine 200in 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

5.2.5 Pharmacological Properties

Pharmacodynamic properties
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.

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 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 C_{max} 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 ^{14}C-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.

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.

6.0 Pharmaceutical Particulars

6.1 List of excipients

Each dispersible tablet contains:
Microcrystalline Cellulose (granules 200)
Colloidal anhydrous silica
Magnesium Stearate
Pregelatinised Starch
Orange Dry Flavour
Aspartame
Calcium hydrogen phosphate anhydrous

6.2 Incompatibilities

None

6.3 Shelf life

2 years

6.4 Special precautions for storage

Storage below 30°C in a dry place.

6.5 Nature and contents of container

Aluminium/Aluminium Blister pack. Available in 1 X 10's carton pack.

6.6 Special precautions for disposal and other handling

None

7.0 Marketing Authorization Holder

8.0 Name and address of Manufacture

Baroque Pharmaceuticals Pvt. Ltd
192/2 & 3, Sokhada-388 620 Tal: Khambhat,
Dist. Anand Gujarat.
India.

9.0 Date of revision of the text
