1. NAME OF THE MEDICINAL PRODUCT

Beckracine 200 mg Dispersible Tablets.

2. Qualitative and quantitative composition

Each Uncoated Dispersible tablet contains:

Cefixime (as trihydrate) USP

Eq. to cefixime .....200 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

White to off white colored, round, standard biconvex, uncoated dispersible tablet, break line on one side and plain on other side.

4. Clinical particulars

4.1 Therapeutic indications

Bekracine 200 is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Uncomplicated Urinary Tract Infections caused by Escherichia coli and Proteus mirabilis.

Otitis Media caused by Haemophilus influenzae (beta-lactamase positive and negative strains), Moraxella (Branhamella) catarrhalis, (most of which are beta-lactamase positive) and S. pyogenes*.

Note: For information on otitis media caused by Streptococcus pneumoniae. Pharyngitis and Tonsillitis, caused by S. pyogenes.

Note: Penicillin is the usual drug of choice in the treatment of S. pyogenes infections, including the prophylaxis of rheumatic fever. Beckracine is generally effective in the eradication of S. pyogenes from the nasopharynx; however, data establishing the efficacy of Beckracine in the subsequent prevention of rheumatic fever are not available.

Acute Bronchitis and Acute Exacerbations of Chronic Bronchitis, caused by Streptococcus pneumoniae and Haemophilus influenzae (beta-lactamase positive and negative strains).

Uncomplicated gonorrhea (cervical/urethral), caused by Neisseria gonorrhoeae (penicillinase- and non-penicillinase-producing strains).

Appropriate cultures and susceptibility studies should be performed to determine the causative organism and its susceptibility to Beckracine; however, therapy may be started while awaiting the results of these studies. Therapy should be adjusted, if necessary, once these results are known.

*Efficacy for this organism in this organ system was studied in fewer than 10 infections.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Beckracine tablets and other antibacterial drugs, Beckracine should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

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*:*

Beckracine Tablets 200 mg are not recommended for use in children under 10 years old. The safety and efficacy of Beckracine 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:

Beckracine 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 Beckracine is not significantly modified by the presence of food.

4.3 Contraindications

Hypersensitivity to cephalosporin antibiotics or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Encephalopathy

Beta-lactams, including Beckracine, 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 Beckracine. 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.

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

Hypersensitivity to penicillins

As with other cephalosporins, Beckracine 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 Beckracine, 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 Beckracine) – associated haemolytic anaemia has also been reported.

Acute renal failure

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

Renal impairment

Beckracine should be administered with caution in patients with markedly impaired renal function (see section 4.2).

Paediatric use

Safety of Beckracine in premature or newborn infant has not been established (see section 4.2).

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.

Beckracine should be administered with caution to patients receiving coumarin-type anticoagulants, e.g. warfarin potassium. Since Beckracine 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 Beckracine. 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.

Beckracine 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

Beckracine 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 Beckracine (frequency not known)** Beta-lactams, including Beckracine, 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 (see section 4.4).
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) (see section 4.4)
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.

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. Beckracine 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.Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

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

Adverse reactions seen at dose levels up to 2g Beckracine in normal subjects did not differ from the profile seen in patients treated at the recommended doses. Gastric lavage may be indicated in overdosage.

No specific antidote exists. Beckracine is not removed from the circulation in significant quantities by dialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cephalosporins Antibacterial, ATC No: J01DD08

Mechanism of Action:

Beckracine is an orally active cephalosporin antibiotic, which has marked in-vitro bactericidal activity against a wide variety of Gram-positive and Gram-negative organisms. Its mechanism of action is inhibition of bacterial cell-wall synthesis. It has a high affinity for penicillin binding proteins (PBP) 1 (1a, 1b and 1c) and 3, at the site of the activity varying according to microorganisms.

Microbiology

As with other cephalosporins, bactericidal action of Beckracine results from inhibition of cell-wall synthesis. Beckracine is highly stable in the presence of beta-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins due to the presence of beta-lactamase, may be susceptible to Beckracine.

Beckracine has been shown to be active against most strains of the following organisms both in vitro and in clinical infections:

Gram-positive Organisms

Streptococcus pneumoniae,

Streptococcus pyogenes.

Gram-negative Organisms

Haemophilus influenzae (beta-lactamase positive and negative strains),

Moraxella (Branhamella) catarrhalis (most of which are beta-lactamase positive),

Escherichia coli,

Proteus mirabilis.

Neisseria gonorrhoeae (including penicillinase- and non-penicillinase-producing strains)

Beckracine has been shown to be active in vitro against most strains of the following organisms; however, clinical efficacy has not been established.

Gram-positive Organisms

Streptococcus agalactiae.

Gram-negative Organisms

Haemophilus parainfluenzae (beta-lactamase positive and negative strains),
Proteus vulgaris
Klebsiella pneumoniae,
Klebsiella oxytoca,
Pasteurella multocida,
Providencia species,
Salmonella species,
Shigella species,
Citrobacter amalonaticus,
Citrobacter diversus,
Serratia marcescens.
Note: Pseudomonas species, strains of group D streptococci (including enterococci), Listeria monocytogenes, most strains of staphylococci (including methicillin-resistant strains) and most strains of Enterobacter are resistant to Beckracine. In addition, most strains of Bacteroides fragilis and Clostridium are resistant to Beckracine.

5.2 Pharmacokinetic properties

The absolute oral bioavailability of Beckracine is in the range of 22 – 54%. Absorption is not significantly modified by the presence of food. Beckracine 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 Beckracine 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 Beckracine occurs following multiple dosing.

The pharmacokinetics of Beckracine 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.

Beckracine is predominantly eliminated as unchanged drug in the urine. Glomerular filtration is considered the predominant mechanism. Metabolites of Beckracine have not been isolated from human serum or urine.

Serum protein binding is well characterised for human and animal sera; Beckracine is almost exclusively bound to the albumin fraction, the mean free fraction being approximately 30%. Protein binding of Beckracine is only concentration dependent in human serum at very high concentrations which are not seen following clinical dosing.

Transfer of ^{14}C-labelled Beckracine from lactating rats to their nursing offspring through breast milk was quantitatively small (approximately 1.5% of the mothers' body content of Beckracine in the pup). No data are available on secretion of Beckracine in human breast milk. Placental transfer of Beckracine was small in pregnant rats dosed with labelled Beckracine.

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

Hypromellose,
Microcrystalline Cellulose,
Colloidal anhydrous silica,
Magnesium stearate,
Pregelatinised starch,
Orange Dry Flavour,
Aspartame,
Calcium hydrogen phosphate anhydrous,

6.2 Incompatibilities

None

6.3 Shelf life

24 Months

6.4 Special Precautions for storage

Storage is below 30 ^{0} C in a dry place.

6.5 Nature and Content 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. Marketing Authorisation Holder

(Company) Name: BEKRA
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8. MARKETING AUTHORIZATION NUMBER

Kenya: Registration No. CTD9949

9. DATE OF FIRST <REGISTRATION> / RENEWAL OF THE <REGISTRATION>

Date of first authorization: 08/11/2023
Date of latest renewal: Not Applicable.

10. DATE OF REVISION OF THE TEXT

O7 MAY 2025.