For the Use Only of a Registered Medical Practitioner

BACQURE INJECTION
(Imipenem and Cilastatin for Injection USP)

COMPOSITION

Imipenem Ph. Eur. (Sterile)	
equivalent to anhydrous Imipenem	500 mg
Cilastatin Sodium Ph. Eur. (Sterile)	
equivalent to Cilastatin	500 mg
Sodium Bicarbonate USP (Sterile)	added as buffer

PRODUCT DESCRIPTION
White to pale yellow powder giving colourless to yellow solution on reconstitution.

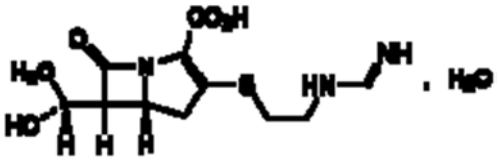
DESCRIPTION

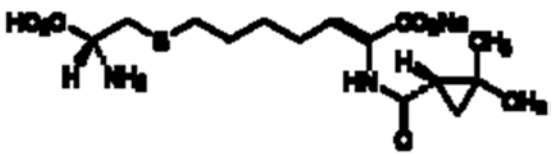
BACQURE is a sterile formulation of imipenem (a thienamycin antibiotic) and cilastatin sodium (the inhibitor of the renal dipeptidase, dehydropeptidase I) with sodium bicarbonate added as buffer, for intravenous use. **BACQURE** (imipenem and cilastatin) is a potent broad-spectrum antibacterial agent for intravenous administration only.

Imipenem (N-formimidoylthienamycin monohydrate) is a crystalline derivative of thienamycin, which is produced by *Streptomyces cattleya*. It is chemically designated as (5R,6S)-6-[(*R*)-1-hydroxyethyl]-3-[[2- [(iminomethyl)amino]ethyl]sulphanyl]-7-oxo- 1- azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid. The empirical formula for imipenem is $C_{12}H_{17}N_3O_4S \bullet H_2O$, and its molecular weight is 317.4.

Cilastatin sodium is the sodium salt of a derivatized heptenoic acid. It is chemically designated as sodium (*Z*)-7-[[(*R*)-2-amino-2-carboxyethyl] sulphanyl]-2-[[[(1*S*)-2,2 dimethylcyclopropyl] carbonyl] amino] hept-2-enoate. The empirical formula for cilastatin sodium is $C_{16}H_{25}N_2NaO_5S$, and its molecular weight is 380.4.

Imipenem, when administered alone, is metabolized in the kidneys by dehydropeptidase I resulting in relatively low levels in urine. Cilastatin sodium, an inhibitor of this enzyme, effectively prevents renal metabolism of imipenem so that when imipenem and cilastatin sodium are given concomitantly, fully adequate antibacterial levels of imipenem are achieved in the urine.





IMIPENEM **CILASTATIN SODIUM**

STRUCTURAL FORMULAE

PHARMACOLOGY

- **Mechanism of action:** Imipenem and cilastatin sodium is a broad-spectrum β-lactam antibiotic supplied as IV infusion only. Imipenem and cilastatin consists of 2 components: (1) Imipenem, the 1st of a new class of β-lactam antibiotics, the thienamycins; and (2) cilastatin sodium, a specific enzyme inhibitor that blocks the metabolism of imipenem in the kidney, and substantially increases the concentration of intact imipenem in the urinary tract. Imipenem and cilastatin sodium are present in a 1:1 ratio by weight.

The thienamycin class of antibiotics, to which imipenem belongs, is characterized by a spectrum of potent bactericidal activity broader than that provided by any other antibiotic studied.

Microbiology: Imipenem and cilastatin is a potent inhibitor of bacterial cell wall synthesis and is bactericidal against a broad spectrum of pathogens: Gram-positive and gram-negative, aerobic and anaerobic.

Imipenem and cilastatin shares with the newer cephalosporins and penicillins a broad spectrum of activity against gram-negative species, but is unique in retaining the high potency against gram-positive species, previously associated only with earlier narrow-spectrum β-lactam antibiotics. The spectrum of activity of Imipenem and cilastatin includes *Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis* and *Bacteroides fragilis*, a diverse group of problem pathogens commonly resistant to other antibiotics.

Imipenem and cilastatin is resistant to degradation by bacterial β-lactamases, which makes it active against a high percentage of organisms e.g., *Pseudomonas aeruginosa*, *Serratia* sp, and *Enterobacter* sp which are inherently resistant to most β-lactam antibiotics.

The antibacterial spectrum of imipenem and cilastatin is broader than that of any other antibiotic studied, and includes virtually all clinically significant pathogens. Organisms against which imipenem and cilastatin are usually active *in vitro* include:

Gram-Negative Aerobes: *Achromobacter* sp; *Acinetobacter* sp (formerly *Mima-*

Herellea); *Aeromonas hydrophila; Alcaligenes* sp; *Bordetella bronchicanis; Bordetella bronchiseptica; Bordetella pertussis; Brucella melitensis; Campylobacter* sp; *Capnocytophaga* sp; *Citrobacter* sp; *Citrobacter diversus; Citrobacter freundii; Eikenella corrodens; Enterobacter* sp; *Enterobacter aerogenes; Enterobacter agglomerans; Enterobacter cloacae; Escherichia coli; Haemophilus ducreyi; Gardnerella vaginalis; Haemophilus influenzae* (including β- lactamase-producing strains); *Haemophilus parainfluenzae; Hafnia alvei; Klebsiella* sp; *Klebsiella oxytoca; Klebsiella ozaenae; Klebsiella pneumoniae; Moraxella* sp; *Morganella morganii* (formerly *Proteus morganii*); *Neisseria gonorrhoeae* (including penicillinase-producing strains); *Neisseria meningitidis; Pasteurella* sp; *Pasteurella multocida; Plesiomonas shigelloides; Proteus* sp; *Proteus mirabilis; Proteus vulgaris; Providencia* sp; *Providencia alcalifaciens; Providencia rettgeri* (formerly *Proteus rettgeri*); *Providencia stuartii; Pseudomonas* sp**; *Pseudomonas aeruginosa; Pseudomonas fluorescens; Pseudomonas pseudomallei; Pseudomonas putida; Pseudomonas stutzeri; Salmonella* sp; *Salmonella typhi; Serratia* sp; *Serratia proteamaculans* (formerly *Serratia liquefaciens*); *Serratia marcescens; Shigella* sp; *Yersinia* sp (formerly *Pasteurella*); *Yersinia enterocolitica; Yersinia pseudotuberculosis*.

***Xanthomonas maltophilia* (formerly *Pseudomonas maltophilia*) and some strains of *Pseudomonas cepacia* are generally not susceptible to imipenem and cilastatin.

Gram-Positive Aerobes: *Bacillus* sp; *Enterococcus faecalis; Erysipelothrix rhusiopathiae; Listeria monocytogenes; Nocardia* sp; *Pediococcus* sp; *Staphylococcus aureus* (including penicillinase-producing strains); *Staphylococcus epidermidis* (including penicillinase-producing strains); *Staphylococcus saprophyticus; Streptococcus agalactiae*; Streptococcus Group C; Streptococcus Group G; *Streptococcus pneumoniae; Streptococcus pyogenes;* Viridans group streptococci (including α- and γ-hemolytic strains).

Enterococcus faecium and methicillin-resistant are not susceptible to imipenem and cilastatin.

Gram-Negative Anaerobes: *Bacteroides* sp; *Bacteroides distasonis; Bacteroides fragilis; Bacteroides ovatus; Bacteroides thetaiotaomicron; Bacteroides vulgatus; Bacteroides uniformis; Bilophila wadsworthia; Fusobacterium* sp; *Fusobacterium necrophorum; Fusobacterium nucleatum; Porphyromonas asaccharolyticus* (formerly *Bacteroides asaccharolyticus*); *Prevotella bivia* (formerly *Bacteroides bivius*); *Prevotella disiens* (formerly *Bacteroides disiens*); *Prevotella intermedia* (formerly *Bacteroides intermedius*); *Prevotella melaninogenica* (formerly *Bacteroides melaninogenicus*); *Veillonella* sp.

Gram-Positive Anaerobes: *Actinomyces* sp; *Bifidobacterium* sp; *Clostridium* sp; *Clostridium perfringens*; *Eubacterium* sp; *Lactobacillus* sp; *Microaerophilic streptococcus; Mobiluncus sp; Peptococcus* sp; *Peptostreptococcus* sp; *Propionibacterium* sp (including *P. acnes*).

Others: *Mycobacterium fortuitum; Mycobacterium smegmatis*.

In vitro tests show imipenem act synergistically with aminoglycoside antibiotics

against some isolates of *Pseudomonas aeruginosa*.

- **Pharmacokinetics**

The product is administered intravenously; therefore bioavailability data are not relevant.

Imipenem: Peak plasma levels of 36.4 mcg/ml after 500 mg, half-life 62.0 (±3.9) mins; plasma clearance 225.5 (±15.9) ml/min.

Co-administration of cilastatin sodium increases plasma concentrations of imipenem and increases the AUC by about 20%. There is also a decrease in plasma clearance (194.9 ml/min) and an increase in renal clearance, urinary recovery and urinary concentration.

INDICATIONS

Treatment: The activity of **BACQURE** (imipenem and cilastatin) against an unusually broad spectrum of pathogens makes it particularly useful in the treatment of polymicrobic and mixed aerobic/anaerobic infections, as well as initial therapy prior to the identification of the causative organisms. **BACQURE** (imipenem and cilastatin) is indicated for the treatment of the following infections due to susceptible organisms: Intra-abdominal infections; lower respiratory tract infections; gynecological infections; septicemia; genitourinary tract infections; bone and joint infections; skin and soft tissue infections; endocarditis.

BACQURE (imipenem and cilastatin) is indicated for the treatment of mixed infections caused by susceptible strains of aerobic and anaerobic bacteria. The majority of these mixed infections are associated with contamination by fecal flora or flora originating from the vagina, skin and mouth. In these mixed infections, Bacteroides fragilis is the most commonly encountered anaerobic pathogen and is usually resistant to aminoglycosides, cephalosporins and penicillins. However, Bacteroides fragilis is usually susceptible to **BACQURE**.

BACQURE (imipenem and cilastatin) has demonstrated efficacy against many infections caused by aerobic and anaerobic gram-positive and gram-negative bacteria resistant to the cephalosporins, including cefazolin, cefoperazone, cephalothin, cefoxitin, cefotaxime, moxalactam, cefamandole, ceftazidime and ceftriaxone. Similarly, many infections caused by organisms resistant to aminoglycosides (gentamicin, amikacin, tobramycin) and/or penicillins (ampicillin, carbenicillin, penicillin-G, ticarcillin, piperacillin, azlocillin, mezlocillin) responded to treatment with **BACQURE**.

BACQURE (imipenem and cilastatin) is not indicated for the treatment of meningitis.

Prophylaxis: **BACQURE** (imipenem and cilastatin) is also indicated for the prevention of certain postoperative infections in patients undergoing contaminated or potentially contaminated surgical procedures or where the occurrence of postoperative infection could be especially serious.

DOSAGE AND ADMINISTRATION

BACQURE (imipenem and cilastatin) is available as IV infusion only.

The dosage recommendations for **BACQURE** (imipenem and cilastatin) represent the quantity of imipenem to be administered. An equivalent amount of cilastatin is also present.

The total daily dosage of **BACQURE** (imipenem and cilastatin) should be based on the type or severity of infection and given in equally divided doses based on consideration of degree of susceptibility of the pathogen(s), renal function and body weight.

Treatment:

Adult Dosage Schedule for Patients with Normal Renal Function:

Doses cited in Table 1 are based on a patient with normal renal function (creatinine clearance of >70 mL/min/1.73 m^2) and a body weight of ≥70 kg. A reduction in dose must be made for a patient with a creatinine clearance ≤70 mL/min/1.73 m^2 (see Table 2) and/or a body weight <70 kg. The reduction for body weight is especially important for patients with much lower body weights and/or moderate/severe renal insufficiency.

Most infections respond to a daily dose of 1-2 g administered in 3-4 divided doses. For the treatment of moderate infection, a 1-g twice daily dosage regimen may also be used. In infections due to less susceptible organisms, the daily dosage of **BACQURE** (imipenem and cilastatin) may be increased to a maximum of 4 g/day or 50 mg/kg/day, whichever is lower.

Each dose of ≤500 mg of **BACQURE** (imipenem and cilastatin) should be given by IV infusion over 20-30 min. Each dose >500 mg should be infused over 40-60 min. In patients who develop nausea during the infusion, the rate of infusion may be slowed. See Table 1.

Due to high antimicrobial activity of **BACQURE** (imipenem and cilastatin), it is recommended that the maximum total daily dosage not exceed 50 mg/kg/day or 4 g/day, whichever is lower. However, cystic fibrosis patients with normal renal function have been treated with **BACQURE** (imipenem and cilastatin) at doses up to 90 mg/kg/day in divided doses, not exceeding 4 g/day.

BACQURE (imipenem and cilastatin) has been used successfully as monotherapy in immunocompromised cancer patients for confirmed or suspected infections e.g., sepsis.

Treatment: Adult Dosage Schedule for Patients with Impaired Renal Function:

To determine the reduced dose for adults with impaired renal function: The total daily

dose is chosen from Table 1 based on infection characteristics. From Table 2, the appropriate reduced dosage regimen is selected based on the daily dose from Table 1 and the patient's creatinine clearance category (**For infusion times, see Treatment: Adult Dosage Schedule for Patients with Normal Renal Function**). See Table 2.

When the 500-mg dose is used in patients with creatinine clearances of 6-20 mL/min/1.73 m^2 there may be an increased risk of seizures.

Patients with creatinine clearances of ≤5 mL/min/1.73 m^2 should not receive **BACQURE** (imipenem and cilastatin) unless hemodialysis is instituted within 48 hrs.

Hemodialysis: When treating patients with creatinine clearances of ≤5 mL/min/1.73 m^2 who are undergoing hemodialysis, use the dosage recommendations for patients with creatinine clearances of 6-20 mL/min/1.73 m^2 (see Treatment: Adult Dosage Schedule for Patients with Impaired Renal Function).

Both imipenem and cilastatin are cleared from the circulation during hemodialysis. The patient should receive **BACQURE** (imipenem and cilastatin) after hemodialysis and at 12-hr intervals timed from the end of that hemodialysis session. Dialysis patients, especially those with background CNS disease, should be carefully monitored; for patients on hemodialysis, **BACQURE** (imipenem and cilastatin) is recommended only when the benefit outweighs the potential risk of seizures (see Precautions).

Currently there are inadequate data to recommend use of **BACQURE** (imipenem and cilastatin) for patients on peritoneal dialysis.

Renal status of elderly patients may not be accurately portrayed by measurement of BUN or creatinine alone. Determination of creatinine clearance is suggested to provide guidance for dosing in such patients.

Prophylaxis:

Adult Dosage Schedule: For prophylaxis against post-surgical infections in adults, 1000 mg imipenem and cilastatin should be given IV on induction of anesthesia and 1000 mg 3 hrs later. For high-risk (e.g., colorectal) surgery, 2 additional 500-mg doses can be given at 8 and 16 hrs after induction.

There are insufficient data on which to base a dosage recommendation for prophylaxis in patients with a creatinine clearance of ≤70 mL/min/1.73m^2.

Treatment:

Pediatric Dosage Schedule (≥3 months): For children and infants, the following dosage schedule is recommended:

Children ≥40 kg body weight should receive adult doses.

Children and infants <40 kg body weight should receive 15 mg/kg at 6-hr intervals. The total daily dose should not exceed 2 g.

Insufficient information is available to recommend dosing in children under 3 months of age, or pediatric patients with impaired renal function (serum creatinine >2 mg/dL).

BACQURE (imipenem and cilastatin) is not recommended for the therapy of meningitis. If meningitis is suspected, an appropriate antibiotic should be used.

BACQURE (imipenem and cilastatin) may be used in children with sepsis as long as they are not suspected of having meningitis.

Table 1. IV Dosage Schedule for Adults with Normal Renal Function and Body Weight ≥70

Severity of Infection	**Dose (mg of imipenem)**	**Dosage Interval (hrs)**	**Total Daily Dosage (g)**
Mild	250	6	1
Moderate	500 1000	8 12	1.5 2
Severe - Fully Susceptible	500	6	2
Severe and/or Life-Threatening Due to less susceptible organisms (primarily some strains of *P. aeruginosa*)	1000 1000	8 6	3 4

*A further proportionate reduction in dose administered must be made for patients with a body weight <70 kg.

Table 2. Reduced Dosage of BACQURE (imipenem and cilastatin) in Adults with Impaired Renal

Total Daily Dose from Table 1	**Creatinine Clearance (mL/min/1 73 m^2)**		
	41-70	**21-40**	**6-20**
1 g/day	250 every 8 hrs	250 every 12 hrs	250 every 12 hrs
1.5 g/day	250 every 6 hrs	250 every 8 hrs	250 every 12 hrs
2 g/day	500 every 8 hrs	250 every 6 hrs	250 every 12 hrs
3 g/day	500 every 6 hrs	500 every 8 hrs	500 every 12 hrs
4 g/day	750 every 8 hrs	500 every 6 hrs	500 every 12 hrs

*A further proportionate reduction in dose administered must be made for patients with a body weight <70 kg.

DIRECTIONS FOR USE

Contents of the vials must be suspended and transferred to 100 mL of an appropriate infusion solution.

A suggested procedure is to add approximately 10 mL from the appropriate infusion solution (see list of diluents under **STABILITY AND COMPATIBILITY**) to the vial. Shake well and transfer the resulting suspension to the infusion solution container.

Caution: ***THE SUSPENSION IS NOT FOR DIRECT INFUSION.***

Repeat with an additional 10 mL of infusion solution to ensure complete transfer of vial contents to the infusion solution. The resulting mixture should be agitated until clear.

Benzyl alcohol as a preservative has been associated with toxicity in neonates. While toxicity has not been demonstrated in pediatric patients greater than three months of age, small pediatric patients in this age range may also be at risk for benzyl alcohol toxicity. Therefore, diluents containing benzyl alcohol should not be used when **BACQURE** (imipenem and cilastatin) is constituted for administration to pediatric patients in this age range.

STABILITY AND COMPATIBILITY

Before reconstitution the dry powder should be stored at a temperature below 25°C (77°F).
Solutions of **BACQURE** (imipenem and cilastatin) range from colorless to yellow. Variations of color within this range do not affect the potency of the product.
BACQURE (imipenem and cilastatin) reconstituted with the following diluents (See **DIRECTIONS FOR USE**), maintains satisfactory potency for 4 hours at room temperature (25°C) or for 24 hours under refrigeration (4°C).
Solutions of **BACQURE** (imipenem and cilastatin) should not be frozen.
0.9% Sodium Chloride Injection
5% or 10% Dextrose Injection
5% Dextrose and 0.9% Sodium Chloride Injection
5% Dextrose Injection with 0.225% or 0.45% saline solution
5% Dextrose Injection with 0.15% potassium chloride solution
Mannitol 5% and 10%
BACQURE (imipenem and cilastatin) should not be mixed with or physically added to other antibiotics. However, **BACQURE** (imipenem and cilastatin) may be administered concomitantly with other antibiotics, such as aminoglycosides.

Incompatibility

Do not mix **BACQURE** with, or physically add to, other antibacterial drugs
BACQURE may be administered concomitantly with other antibacterial drugs, such as aminoglycosides.

PRECAUTIONS

- **General**

Central Nervous System: As with other β-lactam antibiotics, CNS side effects e.g., myoclonic activity, confusional states, or seizures have been reported with the IV formulation, especially when recommended dosages based on renal function and body weight were exceeded. These experiences have been reported most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) and/or compromised renal function in whom accumulation of the administered entities could occur. Hence, close adherence to recommended dosage schedules is urged, especially in these patients (see **Dosage & Administration**). Anticonvulsant therapy should be continued in patients with a known seizure disorder.

If focal tremors, myoclonus or seizures occur, patients should be evaluated neurologically and placed on anticonvulsant therapy if not already instituted. If CNS symptoms continue, the dosage of imipenem and cilastatin should be decreased or discontinued.

Patients with creatinine clearances of ≤5 mL/min/1.73 m^2 should not receive imipenem and cilastatin unless hemodialysis is instituted within 48 hrs. For patients on hemodialysis, imipenem and cilastatin is recommended only when the benefit outweighs the potential risk of seizures.

- **Warnings**

General: There is some clinical and laboratory evidence of partial cross-allergenicity between imipenem and cilastatin and the other β-lactam antibiotics, penicillins and cephalosporins. Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with β-lactams. Before initiating therapy with **BACQURE** (imipenem and cilastatin), careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other β-lactam agents. If an allergic reaction occurs **BACQURE** (imipenem and cilastatin) must be discontinued immediately and appropriate alternative therapy instituted.

Pseudomembranous colitis has been reported with virtually all antibiotics and can range from mild to life- threatening in severity. Antibiotics should, therefore, be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. It is important to consider a diagnosis of pseudomembranous colitis in patients who develop diarrhea in association with antibiotic use. While studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of antibiotic-associated colitis, other causes should also be considered.

BACQURE (imipenem and cilastatin) also contains Sodium Bicarbonate as an inactive ingredient. This is to be used with caution in patients who have/had been advised to be on low sodium diet (a compound found in common salt).

- **Contraindications**

BACQURE (imipenem and cilastatin) is contraindicated in patients who have shown hypersensitivity to any component of this product.

- **Pregnancy**

There are no adequate and well-controlled studies in pregnant women. Imipenem and cilastatin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

- **Lactation**

Imipenem has been detected in human milk. If the use of imipenem and cilastatin is deemed essential, the patient should stop nursing.

- **Pediatrics**

Insufficient information is available to recommend the use of imipenem and cilastatin for children under 3 months of age, or pediatric patients with impaired renal function (serum creatinine >2 mg/dL) (See also **Pediatric Dosage Schedule under Dosage & Administration**).

- **Geriatrics**

No overall differences in safety or effectiveness between elderly subjects (≥ 65 years) and younger subjects have been reported. However, a greater sensitivity of some older individuals cannot be ruled out.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

No dosage adjustment is required based on age. Dosage adjustment in the case of renal impairment is necessary.

- **Carcinogenicity/Mutagenicity/Impairment of fertility**

Long term studies in animals have not been performed to evaluate carcinogenic potential of imipenem- cilastatin.

Genetic toxicity studies were performed in a variety of bacterial and mammalian tests *in vivo* and *in vitro*. The tests used were: V79 mammalian cell mutagenesis assay (imipenem-cilastatin sodium and imipenem alone), Ames test (cilastatin sodium alone and imipenem alone), unscheduled DNA synthesis assay (imipenem- cilastatin sodium) and *in vivo* mouse cytogenetics test (imipenem-cilastatin sodium). None of these tests showed any evidence of genetic alterations.

Reproductive tests in male and female rats were performed with imipenem-cilastatin sodium at dosage levels up to 11 times the maximum daily recommended human dose of the intramuscular formulation (on a mg/kg basis). Slight decreases in live fetal body weight were restricted to the highest dosage level. No other adverse effects were observed on fertility, reproductive performance, fetal viability, growth or postnatal development of pups. Similarly, no adverse effects on the fetus or on lactation were observed when imipenem-cilastatin sodium was administered to rats late in gestation.

- **Drug Interactions**

Generalized seizures have been reported in patients who received ganciclovir and imipenem and cilastatin. These drugs should not be used concomitantly unless the potential benefits outweigh the risks.

- **Adverse reactions**

Imipenem and cilastatin is generally well tolerated as cefazolin, cephalothin and cefotaxime. Side effects rarely require cessation of therapy and are generally mild and transient; serious side effects are rare. The most common adverse reactions have been local reactions.

Local Reactions: Erythema, local pain and induration, thrombophlebitis.

Allergic Reactions/Skin: Rash, pruritus, urticaria, erythema multiforme, Stevens-Johnson syndrome, angioedema, toxic epidermal necrolysis (rarely), exfoliative dermatitis (rarely), candidiasis, fever including drug fever, anaphylactic reactions.

Gastrointestinal Reactions: Nausea, vomiting, diarrhea, staining of teeth and/or tongue. In common with virtually all other broad-spectrum antibiotics, pseudomembranous colitis has been reported.

Blood: Eosinophilia, leukopenia, neutropenia, including agranulocytosis, thrombocytopenia, thrombocytosis, and decreased hemoglobin and prolonged prothrombin time have been reported. A positive direct Coombs' test may develop in some individuals.

Liver Function: Increases in serum transaminases, bilirubin and/or serum alkaline phosphatase; hepatitis (rarely).

Renal Function: Oliguria/anuria, polyuria, acute renal failure (rarely). The role of imipenem and cilastatin in changes in renal function is difficult to assess, since factors predisposing to pre-renal azotemia or to impaired renal function usually have been present.

Elevations in serum creatinine and blood urea nitrogen have been observed. Urine discoloration is harmless and should not be confused with hematuria.

Nervous System/Psychiatric: As with other β-lactam antibiotics, CNS side effects e.g., myoclonic activity, psychic disturbances including hallucinations, confusional states, or seizures have been reported with the IV formulation. Paresthesia.

Special Senses: Hearing loss, taste perversion.

Granulocytopenic Patients: Drug-related nausea and/or vomiting appear to occur more frequently in granulocytopenic patients than in non-granulocytopenic patients treated with imipenem and cilastatin.

OVERDOSAGE

No specific information is available on the treatment of overdosage with imipenem and cilastatin. Imipenem- cilastatin sodium is hemodialyzable. However, usefulness of this procedure in the overdosage setting is unknown.

STORAGE

The dry powder should be stored below 30°C, protected from light.
After suspension vial contents must be transferred to 100 ml infusion solution. After reconstitution keep at room temperature (25°C) for up to 4 hours or under refrigeration (4°C) for up to 24 hours.

Solutions of **BACQURE** should not be frozen.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN

SUPPLY

Single clear glass type I USP tubular vial of 500mg per box.

Date of Revision: February 2020

Manufactured in India by:
SUN PHARMACEUTICAL IND. LTD.
INDUSTRIAL AREA - 3
DEWAS- 455 001

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