SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

TIENAM® 500 Sterile Powder for Injection

TIENAM® MONO 500 Sterile Powder for Injection **(Dose Not Marketed)**

COMPOSITION

TIENAM 500: Each vial (20 ml) contains Imipenem equivalent to 500 mg of anhydrous Imipenem and Cilastatin Sodium equivalent to 500 mg of the free acid.

Excipient: sodium bicarbonate (sterile)

TIENAM MONO 500: Each vial (22 ml) contains Imipenem equivalent to 500 mg of anhydrous Imipenem and Cilastatin Sodium equivalent to 500 mg of the free acid. **(Dose Not Marketed)**

Excipient: sodium bicarbonate (sterile)

PHARMACOLOGICAL CLASSIFICATION

A 20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION

Imipenem belongs to the thienamycin class of beta-lactam antibiotics and provides a broad spectrum of bactericidal activity.

Cilastatin sodium is a specific enzyme inhibitor that blocks the metabolism of imipenem in the kidney thereby increasing the half-life of imipenem as well as maintaining imipenem concentrations in the urinary tract.

The anhydrous form of imipenem and the free form of the cilastatin are present in a 1:1 ratio by mass.

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The formulation is administered by intravenous infusion.

Microbiology

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

Imipenem is usually resistant to degradation by bacterial beta-lactamases.

Resistant strains of *Pseudomonas* species, *Proteus mirabilis* and *Staphylococcus epidermidis* have been reported to develop during treatment.

INDICATIONS

TIENAM is indicated for the treatment of the following infections caused by susceptible strains of the designated micro-organisms in the conditions listed below:

Intra-abdominal infections

Enterococcus faecalis, Staphylococcus aureus (penicillinase-producing strains)*, *Staphylococcus epidermidis, Citrobacter* species, *Enterobacter* species, *Escherichia coli, Klebsiella* species, *Morganella morganii**, *Proteus* species, *Pseudomonas aeruginosa, Bifidobacterium* species, *Clostridium* species, *Eubacterium* species, *Peptococcus* species, *Peptostreptococcus* species, *Propionibacterium* species*, *Bacteroides* species including *B. fragilis, Fusobacterium* species.

Lower respiratory tract infections

Staphylococcus aureus (penicillinase-producing strains), *Acinetobacter* species, *Enterobacter* species, *Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae**, *Klebsiella* species, *Serratia marcescens.*

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

Gynaecological infections

Enterococcus faecalis, Staphylococcus aureus (penicillinase-producing strains)*, *Staphylococcus epidermidis, Streptococcus agalactiae (*Group B streptococcus*), Enterobacter* species*, *Escherichia coli, Gardnerella vaginalis, Klebsiella* species*, *Proteus* species*, Bifidobacterium* species*, *Peptococcus* species*, *Peptostreptococcus* species*, Propionibacterium* species*, *Bacteroides* species including *B. fragilis.*

Septicaemia

Enterococcus faecalis, Staphylococcus aureus (penicillinase-producing strains)*, Enterobacter* species*, Escherichia coli, Klebsiella* species*, Pseudomonas aeruginosa, Serratia* species*, *Bacteroides* species including *B. fragilis*.*

Genito-urinary tract infections (complicated and uncomplicated)

Enterococcus faecalis, Staphylococcus aureus (penicillinase-producing strains)*, *Enterobacter* species*, *Escherichia coli, Klebsiella* species*, Morganella morganii*, *Proteus vulgaris, Providencia rettgeri*, Pseudomonas aeruginosa.*

Bone and joint infections

Enterococcus faecalis, Staphylococcus aureus (penicillinase-producing strains)*, *Staphylococcus epidermidis, Enterobacter* species*, *Pseudomonas aeruginosa.*

Skin and soft tissue infections

Enterococcus faecalis, Staphylococcus aureus (penicillinase-producing strains)*, *Staphylococcus epidermidis*, *Acinetobacter* species*, *Citrobacter* species*, *Enterobacter* species*, *Escherichia coli*, *Klebsiella* species*, *Morganella morganii, Proteus vulgaris, Providencia rettgeri*, *Pseudomonas aeruginosa, Serratia* species*, *Peptococcus* species*, *Peptostreptococcus* species*, *Bacteroides* species including *B. fragilis, Fusobacterium* species*.*

Endocarditis

Staphylococcus aureus (penicillinase-producing strains)*

TIENAM 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 faecal flora or flora originating from the vagina, skin and mouth. In these mixed infections, *Bacteroides fragilis* is usually susceptible to TIENAM.

TIENAM has demonstrated efficacy against many infections caused by aerobic and anaerobic Gram-positive and Gram-negative bacteria resistant to other antibiotics.

TIENAM is not indicated for the treatment of meningitis.

Prophylaxis1,

To reduce the risk of wound sepsis in adult patients after colorectal surgery

CONTRA-INDICATIONS

- Hypersensitivity to any component of this product.
- Meningitis
- Pregnancy and lactation

WARNINGS AND SPECIAL PRECAUTIONS

TIENAM is not recommended for the therapy of meningitis. If meningitis is suspected, an appropriate antibiotic should be used (See **CONTRA-INDICATIONS**). TIENAM may be used in children with sepsis as long as they are not suspected of having meningitis.

General

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

There is some clinical and laboratory evidence of partial cross-allergenicity between TIENAM and the other beta-lactam antibiotics, penicillins and cephalosporins. Severe reactions (including anaphylaxis) have been reported with most beta-lactam antibiotics. Before therapy with TIENAM, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. If an allergic reaction to TIENAM occurs, the drug should be discontinued and appropriate measures undertaken.
Case reports in the literature have shown that co-administration of carbapenems, including imipenem, to patients receiving valproic acid or divalproex sodium results in a reduction in valproic acid concentrations. The valproic acid concentrations may drop below the therapeutic range as a result of this interaction, therefore increasing the risk of breakthrough seizures. Increasing the dose of valproic acid or divalproex sodium may not be sufficient to overcome this interaction. The concomitant use of imipenem and valproic acid/divalproex sodium is generally not recommended. Anti-bacterials other than carbapenems should be considered to treat infections in patients whose seizures are well controlled on valproic acid or divalproex sodium. If administration of TIENAM is necessary, supplemental anti-convulsant therapy should be considered (See DRUG INTERACTIONS.)
Pseudomembranous colitis 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 diarrhoea 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.

Paediatric Use

Clinical data are insufficient to recommend the use of TIENAM in children less than 3 months of age, or paediatric patients with impaired renal function (serum creatinine greater than 0,02g/l). (See also PAEDIATRIC DOSAGE SCHEDULE).

Central Nervous System

Central nervous system side effects such as myoclonic activity, confusional states, or seizures have been reported with the formulation, especially when recommended dosages based on renal function and body mass 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 AND DIRECTIONS FOR USE**). 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 TIENAM should be decreased or discontinued.

Patients with creatinine clearances of less than or equal to 5 ml/min/1,73 m² should not receive TIENAM unless haemodialysis is instituted within 48 hours. For patients on haemodialysis, TIENAM is recommended only when the benefit outweighs the potential risk of seizures.

INTERACTIONS

In *in vitro* experiments, TIENAM has been reported to induce beta-lactamases capable of hydrolyzing other beta-lactam antibiotics. Although the clinical significance of this is unknown, caution should be exercised in combining TIENAM with other beta-lactam antibiotics. Generalized seizures have been reported in patients who received ganciclovir and TIENAM. These drugs should not be used concomitantly unless the potential benefits outweigh the risks. Also see under **STORAGE INSTRUCTIONS**.

Case reports in the literature have shown that co-administration of carbapenems, including imipenem, to patients receiving valproic acid or divalproex sodium results in a reduction of valproic acid concentrations. The valproic acid concentrations may drop below the therapeutic range as a result of this interaction, therefore increasing the risk of breakthrough seizures. Although the mechanism of this interaction is unknown, data from in vitro and animal studies suggest that carbapenems may inhibit the hydrolysis of valproic acid's glucuronide metabolite (VPA-g) back to valproic acid, thus decreasing the serum concentrations of valproic acid. (See WARNINGS AND PRECAUTIONS.)

PREGNANCY AND LACTATION

Use in pregnancy

There are no adequate and well-controlled studies in pregnant women. TIENAM should therefore not be used during pregnancy.

Nursing mothers

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

DOSAGE AND DIRECTIONS FOR USE

NB: Refer to **STORAGE INSTRUCTIONS** for stability of reconstituted TIENAM. The dosage recommendations for TIENAM represent the quantity of imipenem to be administered. An equivalent amount of cilastatin is also present in the solution.

The total daily dosage and route of administration of TIENAM 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 mass.

INTRAVENOUS INFUSION

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 greater than 70 ml/min/1,73 m^2) and a body weight of greater than or equal to 70 kg. A reduction in dose must be made for a patient with a creatinine clearance less than or equal to 70 ml/min/1,73 m^2 (See Table 2 and 3) and/or body weight less than 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 b.i.d. dosage regimen may also be used. In infections due to less susceptible organisms, the daily dosage of TIENAM may be increased to a maximum of 4 g/day or 50 mg/kg/day, whichever is lower.

Each dose of less than or equal to 500 mg of TIENAM should be given by intravenous infusion over 20 to 30 minutes. Each dose greater than 500 mg should be infused over 40 to 60 minutes. In patients who develop nausea during the infusion, the rate of infusion may be slowed.

TABLE 1 – DOSAGE SCHEDULE FOR ADULTS WITH NORMAL RENAL FUNCTION AND BODY WEIGHT GREATER THAN OR EQUAL TO 70 kg

Type or Severity of Infection	A Fully susceptible organisms including gram-positive and gram-negative aerobes and anaerobes	B Moderately susceptible organisms, primarily some strains of *P. aeruginosa*
Mild	250 mg 6 hly (TOTAL DAILY DOSE = 1,0 g)	500 mg 6 hly (TOTAL DAILY DOSE = 2,0 g)
Moderate	500 mg 8 hly (TOTAL DAILY DOSE = 1,5 g) or 500 mg 6 hly (TOTAL DAILY DOSE = 2,0 g)	500 mg 6 hly (TOTAL DAILY DOSE = 2,0 g) or 1 g 8 hly (TOTAL DAILY DOSE = 3,0 g)
Severe, life threatening only	500 mg 6 hly (TOTAL DAILY DOSE = 2,0 g)	1 g 8 hly (TOTAL DAILY DOSE = 3,0 g) or 1 g 6 hly (TOTAL DAILY DOSE = 4,0 g)
Uncomplicated urinary tract infection	250 mg 6 hly (TOTAL DAILY DOSE = 1,0 g)	250 mg 6 hly (TOTAL DAILY DOSE = 1,0 g)
Complicated urinary tract infection	500 mg 6 hly (TOTAL DAILY DOSE = 2,0 g)	500 mg 6 hly (TOTAL DAILY DOSE = 2,0 g)

It is recommended that the maximum total daily dosage does not exceed 50 mg/kg/day or 4 g/day whichever is the lower. However, cystic fibrosis patients with normal renal function have been treated with TIENAM at doses up to 90 mg/kg/day in divided doses, not exceeding 4 g/day.

TIENAM has been used successfully as monotherapy in immunocompromised cancer patients for confirmed or suspected infections such as sepsis.

TREATMENT : ADULT DOSAGE SCHEDULE FOR PATIENTS WITH IMPAIRED RENAL FUNCTION

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

1. The total daily dose is chosen from Table 1 based on infection characteristics.

2. From Table 2 and 3 the appropriate reduced dosage regimen is selected based on the daily dose from Table 1 and the patients creatinine clearance category. (For infusion times see TREATMENT: ADULT DOSAGE SCHEDULE FOR PATIENTS WITH NORMAL RENAL FUNCTION).

TABLE 2 - REDUCED DOSAGE OF TIENAM I.V. IN ADULTS WITH IMPAIRED RENAL FUNCTION AND/OR BODY WEIGHT LESS THAN 70 kg

	If TOTAL DAILY DOSE from TABLE 1 is:											
	1,0 g/day				1,5 g/day				2,0 g/day			
	and creatinine clearance (ml/min/1,73 m^2) is:				and creatinine clearance (ml/min/1,73 m^2) is:				and creatinine clearance (ml/min/1,73 m^2) is:			
And Body Weight (kg) is:	Greater than or equal to 71	41-70	21-40	6-20	Greater than or equal to 71	41-70	21-40	6-20	Greater than or equal to 71	41-70	21-40	6-20
	then the reduced dosage regimen (mg) is:				then the reduced dosage regimen (mg) is:				then the reduced dosage regimen (mg) is:			
Greater than or equal to 70	250 6 hly	250 8 hly	250 12 hly	250 12 hly	500 8 hly	250 6 hly	250 8 hly	250 12 hly	500 6 hly	500 8 hly	250 6 hly	250 12 hly
60	250 8 hly	125 6 hly	250 12 hly	125 12 hly	250 6 hly	250 8 hly	250 8 hly	250 12 hly	500 8 hly	250 6 hly	250 8 hly	250 12 hly
50	125 6 hly	125 6 hly	125 8 hly	125 12 hly	250 6 hly	250 8 hly	250 12 hly	250 12 hly	250 6 hly	250 6 hly	250 8 hly	250 12 hly
40	125 6 hly	125 8 hly	125 12 hly	125 12 hly	250 8 hly	125 6 hly	125 8 hly	125 12 hly	250 6 hly	250 8 hly	250 12 hly	250 12 hly
30	125 8 hly	125 8 hly	125 12 hly	125 12 hly	125 6 hly	125 8 hly	125 8 hly	125 12 hly	250 8 hly	125 6 hly	125 8 hly	125 12 hly

TABLE 3 - REDUCED DOSAGE OF TIENAM I.V. IN ADULTS WITH IMPAIRED RENAL FUNCTION AND/OR BODY WEIGHT LESS THAN 70 kg

	If TOTAL DAILY DOSE from TABLE 1 is:							
	3,0 g/day				4,0 g/day			
	and creatinine clearance (ml/min/1,73 m^2) is:				and creatinine clearance (ml/min/1,73 m^2) is:			
And Body Weight (kg) is:	Greater than or equal to 71	41-70	21-40	6-20	Greater than or equal to 71	41-70	21-40	6-20
	then the reduced dosage regimen (mg) is:				then the reduced dosage regimen (mg) is:			
Greater than or equal to 70	1000 8 hly	500 6 hly	500 8 hly	500 12 hly	1000 6 hly	750 8 hly	500 6 hly	500 12 hly

60	750 8 hly	500 8 hly	500 8 hly	500 12 hly	1000 8 hly	750 8 hly	500 8 hly	500 12 hly
50	500 6 hly	500 8 hly	250 6 hly	250 12 hly	750 8 hly	500 6 hly	500 8 hly	500 12 hly
40	500 8 hly	250 6 hly	250 8 hly	250 12 hly	500 6 hly	500 8 hly	250 6 hly	250 12 hly
30	250 6 hly	250 8 hly	250 8 hly	250 12 hly	500 8 hly	250 6 hly	250 8 hly	250 12 hly

When the 500 mg dose is used in patients with creatinine clearances of 6-20 ml/min/1,73 m² there may be an increased risk of seizures.

Patients with creatinine clearances of less than or equal to 5 ml/min/1,73 m² should not receive TIENAM unless haemodialysis is instituted within 48 hours.

Haemodialysis

When treating patients with creatinine clearances of less than 5 ml/min/1,73 m² who are undergoing haemodialysis use the dosage recommendations for patients with creatinine clearances of 6-20 ml/min/1,73 m² (see TREATMENT: ADULT DOSAGE SCHEDULE FOR PATIENTS WITH IMPAIRED RENAL FUNCTION).

Both imipenem and cilastatin are cleared from the circulation during haemodialysis. The patient should receive TIENAM after haemodialysis and at 12 hour intervals timed from the end of that haemodialysis session. Dialysis patients, especially those with background Central Nervous System disease, should be carefully monitored; for patients on haemodialysis, TIENAM is recommended only when the benefit outweighs the potential risk of seizures (see **SIDE EFFECTS**).

Currently there are inadequate data to recommend use of TIENAM for patients on peritoneal dialysis. Renal status of elderly patients may not be accurately portrayed by measurement of blood urea

nitrogen or creatinine alone. Determination of creatinine clearance is suggested to provide guidance for dosing in such patients.

PROPHYLAXIS: ADULT DOSAGE SCHEDULE

To reduce the risk of wound sepsis in adults after colorectal surgery: 1000 mg TIENAM intravenously on induction of anaesthesia and 1000 mg three hours later; with two additional 500 mg doses at eight and sixteen hours after induction.

TABLE 4- RECONSTITUTION OF TIENAM 500

Dose of TIENAM (mg of imipenem)	Volume of Diluent to be Added (ml)	Approximate Average Concentration of TIENAM (mg/ml of imipenem)
500	100	5

There are insufficient data on which to base a dosage recommendation for prophylaxis in patients with a creatinine clearance of less than or equal to 70 ml/min/1,73 m^2.

TREATMENT: PAEDIATRIC DOSAGE SCHEDULE (3 months or older)

Experience with TIENAM in children is limited.

For children and infants the following dosage schedule is recommended:

a. CHILDREN greater than or equal to 40 kg body weight should receive adult doses.

b. CHILDREN AND INFANTS less than 40 kg body weight should receive 15 mg/kg every six hours. The total daily dose should not exceed 2 gm.

Clinical data are insufficient to recommend dosing for children less than 3 months of age, or paediatric patients with impaired renal function (serum creatinine greater than 0,02 g/l).

RECONSTITUTION OF INTRAVENOUS SOLUTION

TIENAM 500 for intravenous infusion is supplied as a sterile powder in vials containing 500 mg imipenem equivalent and 500 mg cilastatin equivalent.

TIENAM is buffered with sodium bicarbonate to provide solutions in the pH range of 6,5 to 8,5. There is no significant change in pH when solutions are prepared and used as directed. TIENAM 500 contains 37,5 mg of sodium (1,6 mEq).

TIENAM 500 should be reconstituted as shown in Table 4. It should be shaken until a clear solution is obtained. Variations of colour, from colourless to yellow, do not affect the potency of the product.

Reconstitution of 20 ml vial

Contents of the vial 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 **STORAGE INSTRUCTIONS**, Stability, Table 5) 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 the 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.

INTRAVENOUS INFUSION: MONOVIAL SYSTEM **(Dose not marketed)**

The MONOVIAL system is also for intravenous use and consists of a glass vial with an attached needle which is used in conjunction with an I.V. bag. The major medical significance is that it is a closed system thus offering greater assurance of aseptic delivery to the patient and provides added safety for health care providers.

PREPARATION STEPS

Step 1: EXAMINE

Examine the vial for any foreign material in the powder contents, make sure the tamper evident seal between the cap and the vial is intact.

Step 2: REMOVE CAP

Remove the cap by twisting it first and pulling it up to break the tamper evident seal.

Step 3: CONNECT

Insert the needle into the infusion-bag connector. Push the needle holder and vial together until they “click” into place.

Step 4: MIX

Hold the vial in an upright position. Squeeze the infusion bag several times to transfer the diluent into the vial. Shake the vial to reconstitute the substance.

Step 5: TRANSFER

Now reverse the connected I.V. assembly, holding the vial upside down. Squeeze the infusion bag several times. This will create an over-pressure in the vial, allowing the contents of the vial to be transferred back into the infusion bag. Repeat 4 and 5 until the vial is completely empty.

Step 6: IDENTIFY

Fill out the peel-off label on the vial and affix it to the infusion bag for proper identification.

SIDE EFFECTS

The most common adverse reactions have been local reactions following intravenous injection.

The following side effects have been reported in clinical studies or during post-marketing experience:

The frequencies of adverse events are ranked according to the following: Very Common (greater than 1/10), Common (greater than or equal to 1/100, less than 1/10), Uncommon (greater than or equal to 1/1000, less than 1/100), Rare (greater than or equal to 1/10,000, less than 1/1000), Very rare (less than 1/10,000) and isolated cases.

Infections and infestations:

Rare: candidiasis, pseudomembranous colitis

Blood and Lymphatic system disorders:

Common: eosinophilia

Uncommon: leukopaenia, thrombocytopaenia, thrombocytosis.

Rare: neutropaenia, agranulocytosis.

Very Rare: pancytopaenia

Immune system disorders:

Rare: anaphylactic reactions

Psychiatric disorders:

Uncommon: psychic disturbances including hallucinations and confusional states

Frequency unknown: agitation.

Nervous system disorders

Uncommon: myoclonic activity, seizures

Rare: taste perversion, paraesthesia

Very Rare: encephalopathy

Frequency unknown: dyskinesia.

Ear and labyrinth disorders:

Rare: hearing loss

Vascular disorders:

Common: thrombophlebitis

Gastrointestinal disorders:

Common: nausea, vomiting, diarrhoea.

Drug-related nausea and/or vomiting appear to occur more frequently in granulocytopaenic patients than in non-granulocytopaenic patients treated with TIENAM I.V.

Rare: staining of teeth and/or tongue

Hepatobiliary disorders:

Rare: hepatic failure

Very Rare: hepatitis, fulminant hepatitis

Skin and subcutaneous tissue disorders:

Common: rash

Uncommon: erythema, pruritus, urticaria

Rare: angioedema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis

Renal and urinary disorders:

Uncommon: reddish urine discoloration (harmless and should not be confused with hematuria)

Rare: oliguria/anuria, polyuria, acute renal failure

The role of TIENAM 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.

General disorders and administration site conditions:

Uncommon: local pain and induration, fever including drug fever

Investigations:

Common: increases in serum transaminases, increases in serum alkaline phosphatase

Uncommon: a positive direct Coombs' test, elevations in blood urea nitrogen, decreased hemoglobin, prolonged prothrombin time, increases in total serum bilirubin, elevations in serum creatinine

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

There are no data available on overdosage. Treatment is symptomatic and supportive. Imipenem - cilastatin sodium is haemodialysable. However, usefulness of this procedure in the overdosage setting is unknown.

IDENTIFICATION

TIENAM 500 : A white to light yellow powder

TIENAM 500 reconstituted solution : A clear, colourless pale to yellow solution

TIENAM MONO 500 : White to light yellow powder **(Dose Not Marketed)**

TIENAM MONO 500 reconstituted solution: A clear, colourless pale to yellow solution **(Dose Not Marketed)**

PRESENTATION

TIENAM 500 is supplied in 20 ml glass vials, packed in 1's.

TIENAM MONO 500 is supplied in 22 ml glass vials with attached needle transfer sets. **(Dose Not Marketed)**

STORAGE INSTRUCTIONS

STABILITY:

Dry Powder

Store the dry powder below 25°C and protect from light. Protect from freezing.

Reconstituted Solution

Table 5 shows the stability period for TIENAM when reconstituted with selected infusion solutions, and stored at room temperature or under refrigeration.

Caution

TIENAM is chemically incompatible with lactate and 5% sodium bicarbonate and should not be reconstituted in diluents containing lactate and bicarbonate anions. TIENAM can be administered, however, into an I.V. system through which a lactate solution is being infused.

TIENAM should not be mixed with or physically added to other antibiotics.

TABLE 5 - STABILITY OF RECONSTITUTED TIENAM

Diluent	Stability Period	
	Room Temperature (25°C)	Refrigeration (4°C)
Isotonic Sodium Chloride	4 hours	24 hours
5 % Dextrose in Water	4 hours	24 hours

10 % Dextrose in Water	4 hours	24 hours
5 % Dextrose & 0,9 % NaCl	4 hours	24 hours
5 % Dextrose & 0,45 % NaCl	4 hours	24 hours
5 % Dextrose & 0,225 % NaCl	4 hours	24 hours
5 % Dextrose & 0,15 % KCl	4 hours	24 hours
Mannitol 5 % and 10 %	4 hours	24 hours

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

TIENAM 500 : S/20.1.1/175

TIENAM MONO 500 : 31/20.1.1/0693 **(Dose Not Marketed)**

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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DATE OF PUBLICATION OF THIS PACKAGE INSERT

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