PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE
TIASEP® 500 mg/500 mg powder for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 20 ml vial contains 500 mg imipenem (as imipenem monohydrate) and 500 mg cilastatin (as cilastatin sodium salt).

Excipient with known effect:
Each vial contains sodium bicarbonate equivalent to approximately 1,6 millimole sodium (approximately 37,6 mg) per vial.
Sugar free.
For a full list of excipients, see section 6.1.

Final concentration of the reconstituted solution is 5 mg/ml (see section 6.6).
Sugar free.

3. PHARMACEUTICAL FORM
Sterile powder for solution for infusion.
White to almost white or light (pale) yellow powder.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
TIASEP 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, *Eubacteria* 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.*
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)*.
TIASEP 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 TIASEP.
TIASEP has demonstrated efficacy against many infections caused by aerobic and anaerobic Gram-positive and Gram-negative bacteria resistant to other antibiotics.
TIASEP is not indicated for the treatment of meningitis.
*Efficacy of this organism in this organ system was studied in fewer than ten infections.
****If TIASEP is used in the treatment of infections caused by *Pseudomonas aeruginosa*, an aminoglycoside should be administered concomitantly.**

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

4.2. Posology and method of administration
Important: The dosage recommendations for TIASEP 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 TIASEP 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.
Posology
Treatment: Adults
Doses cited in Table 1 are based on a patient with normal renal function (creatinine clearance of greater than 70 ml/min/1,73 m²) and a body weight of greater than or equal to 70 kg.
A reduction in dose should be made for a patient with a creatinine clearance less than or equal to 70 ml/min/1,73 m² (see Tables 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 infections, a 1 g, twice daily, dosage regimen may also be used. In infections due to less susceptible organisms, the daily dosage of TIASEP 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 TIASEP 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 hourly (TOTAL DAILY DOSE = 1,0 g)	500 mg 6 hourly (TOTAL DAILY DOSE = 2,0 g)
Moderate	500 mg 8 hourly (TOTAL DAILY DOSE = 1,5 g) or 500 mg 6 hourly (TOTAL DAILY DOSE = 2,0 g)	500 mg 6 hourly (TOTAL DAILY DOSE = 2,0 g) or 1 g 8 hourly (TOTAL DAILY DOSE = 3,0 g)
Severe, life-threatening only	500 mg 6 hourly (TOTAL DAILY DOSE = 2,0 g)	1 g 8 hourly (TOTAL DAILY DOSE = 3,0 g) or 1 g 6 hourly (TOTAL DAILY DOSE = 4,0 g)
Uncomplicated urinary tract infection	250 mg 6 hourly (TOTAL DAILY DOSE = 1,0 g)	250 mg 6 hourly (TOTAL DAILY DOSE = 1,0 g)
Complicated urinary tract infection	500 mg 6 hourly (TOTAL DAILY DOSE = 2,0 g)	500 mg 6 hourly (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 lower. However, cystic fibrosis patients with normal renal function have been treated with TIASEP at doses up to 90 mg/kg/day in divided doses, not exceeding 4 g/day.
TIASEP has been used successfully as monotherapy in immunocompromised cancer patients for confirmed or suspected infections such as sepsis.
Prophylaxis: Adults
To reduce the risk of wound sepsis in adults after colorectal surgery: 1 000 mg TIASEP intravenously on induction of anaesthesia and 1 000 mg three hours later, with two additional 500 mg doses at eight and sixteen hours after induction.
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 m².
Patients with renal impairment
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 Tables 2 and 3 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: Adults*).

Table 2 - Reduced dosage of TIASEP 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				
	and creatinine clearance (ml/min/1,73 m²) is:			
And body weight (kg) is:	Greater than or equal to 71	41-70	21-40	6-20
	then the reduced dosage regimen (mg) is:			
Greater than, or equal to 70	250 6 hourly	250 8 hourly	250 12 hourly	250 12 hourly
60	250 8 hourly	125 6 hourly	250 12 hourly	125 12 hourly
50	125 6 hourly	125 6 hourly	125 8 hourly	125 12 hourly
40	125 6 hourly	125 8 hourly	125 8 hourly	125 12 hourly
30	125 8 hourly	125 8 hourly	125 8 hourly	125 12 hourly

If TOTAL DAILY DOSE from Table 1 is 1,5 g/day				
	and creatinine clearance (ml/min/1,73 m²) is:			
And body weight (kg) is:	Greater than or equal to 71	41-70	21-40	6-20
	then the reduced dosage regimen (mg) is:			
Greater than, or equal to 70	500 8 hourly	250 6 hourly	250 8 hourly	250 12 hourly
60	250 6 hourly	250 8 hourly	250 8 hourly	250 12 hourly
50	250 6 hourly	250 8 hourly	250 12 hourly	250 12 hourly
40	250 8 hourly	125 6 hourly	125 8 hourly	125 12 hourly
30	125 6 hourly	125 8 hourly	125 8 hourly	125 12 hourly

If TOTAL DAILY DOSE from Table 1 is 2,0 g/day				
	and creatinine clearance (ml/min/1,73 m²) is:			
And body weight (kg) is:	Greater than or equal to 71	41-70	21-40	6-20
	then the reduced dosage regimen (mg) is:			
Greater than, or equal to 70	500 6 hourly	500 8 hourly	250 6 hourly	250 12 hourly
60	500 8 hourly	250 6 hourly	250 8 hourly	250 12 hourly
50	250 6 hourly	250 6 hourly	250 8 hourly	250 12 hourly
40	250 6 hourly	250 8 hourly	250 12 hourly	125 12 hourly
30	250 8 hourly	125 6 hourly	125 8 hourly	125 12 hourly

Table 3 - Reduced dosage of TIASEP 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				
	and creatinine clearance (ml/min/1,73 m²) is:			
And body weight (kg) is:	Greater than or equal to 71	41-70	21-40	6-20
	then the reduced dosage regimen (mg) is:			
Greater than, or equal to 70	1 000 8 hourly	500 6 hourly	500 8 hourly	500 12 hourly
60	750 8 hourly	500 8 hourly	500 8 hourly	500 12 hourly
50	500 6 hourly	500 8 hourly	250 6 hourly	250 12 hourly
40	500 8 hourly	250 6 hourly	250 8 hourly	250 12 hourly
30	250 6 hourly	250 8 hourly	250 8 hourly	250 12 hourly

If TOTAL DAILY DOSE from Table 1 is 4,0 g/day				
	and creatinine clearance (ml/min/1,73 m²) is:			
And body weight (kg) is:	Greater than or equal to 71	41-70	21-40	6-20
	then the reduced dosage regimen (mg) is:			
Greater than, or equal to 70	1 000 6 hourly	750 8 hourly	500 6 hourly	500 12 hourly
60	1 000 8 hourly	750 8 hourly	500 8 hourly	500 12 hourly
50	750 8 hourly	500 6 hourly	500 8 hourly	500 12 hourly
40	500 6 hourly	500 8 hourly	250 6 hourly	250 12 hourly
30	500 8 hourly	250 6 hourly	250 8 hourly	250 12 hourly

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 TIASEP unless haemodialysis is instituted within 48 hours.
Patients on 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 *Patients with renal impairment*). Both imipenem and cilastatin are cleared from the circulation during haemodialysis. The patient should receive TIASEP 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 TIASEP is recommended only when the benefit outweighs the potential risk of seizures (see sections 4.4 and 4.8).
There are inadequate data to recommend use of TIASEP for patients on peritoneal dialysis. Renal status of elderly patients may not be accurately portrayed by measurement of blood urea or creatinine alone. Determination of creatinine clearance is suggested to provide guidance for dosing in such patients.
Paediatric patients (3 months or older)
Experience with TIASEP in children is limited.
For children and infants, the following dosage schedule is recommended:
a. CHILDREN weighing 40 kg or more should receive adult doses.
b. CHILDREN AND INFANTS weighing less than 40 kg should receive 15 mg/kg every six hours. The total daily dose should not exceed 2 g.
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).
Method of administration
TIASEP is to be reconstituted and further diluted (see sections 6.2, 6.3 and 6.6) prior to administration. Each dose of ≤ 500 mg 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.

4.3. Contraindications
- Hypersensitivity to imipenem, cilastatin or any component of TIASEP (see section 6.1).
- Hypersensitivity to any other carbapenem antibacterial medicine.
- Hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to any other type of beta-lactam antibacterial medicine (e.g. penicillins or cephalosporins).
- Meningitis.
- Pregnancy and lactation.

4.4. Special warnings and precautions for use
General
The selection of TIASEP to treat an individual patient should consider the appropriateness of using a carbapenem antibacterial medicine based on factors such as severity of the infection, the prevalence of resistance to other suitable antibacterial medicines and the risk of selecting for carbapenem-resistant bacteria.
TIASEP is **not recommended** for the treatment of meningitis (see section 4.3). If meningitis is suspected, an appropriate antibiotic should be used. TIASEP may be used in children with sepsis as long as they are not suspected of having meningitis.
Hypersensitivity/cross-sensitivity
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with beta-lactams. These reactions are more likely to occur in individuals with a history of sensitivity to multiple allergens.
Before initiating therapy with TIASEP, careful inquiry should be made concerning previous hypersensitivity reactions to carbapenems, penicillins, cephalosporins, other beta-lactams and other allergens (see section 4.3).
If an allergic reaction to TIASEP occurs, discontinue the therapy immediately. Serious anaphylactic reactions require immediate emergency treatment.
Hepatic effects
Hepatic function should be closely monitored during treatment with TIASEP due to the risk of hepatic toxicity (such as increase in transaminases, hepatic failure and fulminant hepatitis).
Use in patients with liver disease: patients with pre-existing liver disorders should have liver function monitored during treatment with TIASEP. There is no dose adjustment necessary (see section 4.2).
Haematology
A positive direct or indirect Coombs test may develop during treatment with TIASEP.
Antibacterial spectrum
The antibacterial spectrum of TIASEP should be considered, especially in life-threatening conditions before embarking on any empiric treatment. Furthermore, due to the limited susceptibility of specific pathogens associated with e.g. bacterial skin and soft tissue infections, to TIASEP, caution should be exercised.
The use of TIASEP is not suitable for treatment of these types of infections unless the pathogen is already documented and known to be susceptible or there is a very high suspicion that the most likely pathogen(s) would be suitable for treatment. Concomitant use of an appropriate anti-methicillin-resistant *Staphylococcus aureus* (MRSA) medicine may be indicated when MRSA infections are suspected or proven to be involved in the approved indications. Concomitant use of an aminoglycoside may be indicated when *Pseudomonas aeruginosa* infections are suspected or proven to be involved in the approved indications (see section 4.1).
Interaction with valproic acid
The concomitant use of TIASEP and valproic acid/ sodium valproate is not recommended (see section 4.5).
Clostridium difficile associated colitis and diarrhoea
Antibiotic-associated colitis and pseudomembranous colitis have been reported with TIASEP and may range from mild to life-threatening in severity. It is important to consider this diagnosis in patients who develop diarrhoea during or after the use of TIASEP (see section 4.8). Discontinuation of therapy with TIASEP and the administration of specific treatment for *Clostridium difficile* should be considered. Medicines that inhibit peristalsis should not be given.
Renal impairment
TIASEP should be given with caution to patients with renal impairment. Imipenem and cilastatin accumulate in patients with reduced kidney function. Central nervous system (CNS) adverse reactions may occur if the dose is not adjusted to the renal function, see section 4.2 and "Central nervous system" below.
Central nervous system (CNS)
CNS adverse reactions such as myoclonic activity, confusional states, or seizures have been reported, especially when recommended doses based on renal function and body weight were exceeded. These experiences have been reported more frequently 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 dose schedules is urged especially in these patients (see section 4.2). Anticonvulsant therapy should be continued in patients with a known seizure disorder.
Neurological symptoms or convulsions may occur in children with known risk factors for seizures, or on concomitant treatment with medicines lowering the seizures threshold. These patients should be carefully monitored.
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 dose of TIASEP should be decreased or discontinued.
Patients with creatinine clearances of less than 15 ml/min should not receive TIASEP unless haemodialysis is instituted within 48 hours. For patients on haemodialysis, TIASEP is recommended only when the benefit outweighs the potential risk of seizures (see section 4.2).
Paediatric population
Adequate data are not available to recommend the use of TIASEP in children under 3 months of age or paediatric patients with impaired renal function (serum creatinine > 0,02 g/l). See also section *4.2 Paediatric patients (3 months or older).*
Sodium content
TIASEP contains 1,6 mmol (37,6 mg) sodium per 500 mg dose (one vial). This should be taken into consideration for patients on a controlled sodium diet.

4.5. Interactions with other medicines and other forms of interaction
TIASEP can induce beta-lactamases capable of hydrolysing other beta-lactam antibiotics. Caution should be exercised if such a combination is used.
Ganciclovir
Generalised seizures have been reported in patients who received ganciclovir and TIASEP. These medicines should not be used concomitantly.
Valproic acid or divalproex sodium
Decreases in valproic acid levels that may fall below the therapeutic range have been reported when valproic acid or divalproex sodium was co-administered with carbapenem medicines. The lowered valproic acid levels may lead to inadequate seizure control; therefore, concomitant use of TIASEP and valproic acid/divalproex sodium is not recommended and alternative antibacterial or anti-convulsant therapies should be considered (see section 4.4).
Oral anti-coagulants
There have been reports of increases in the anti-coagulant effects of orally administered anti-coagulants, including warfarin, in patients who are concomitantly receiving antibacterial medicines, including TIASEP. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of the antibiotic to the increase in INR (international normalised ratio) is difficult to assess. It is recommended that the INR should be monitored frequently during and shortly after co-administration of TIASEP with an oral anti-coagulant medicine.
Probenecid
Concomitant administration of TIASEP and probenecid results in minimal increases in the plasma levels and plasma half-life of imipenem. The urinary recovery of active (non-metabolised) imipenem decreases to approximately 60 % of the dose when TIASEP is administered with probenecid. Concomitant administration of TIASEP and probenecid doubles the plasma level and half-life of cilastatin but has no effect on urinary recovery of cilastatin.

4.6. Fertility, pregnancy and lactation
Pregnancy
There are no adequate and well-controlled studies for the use of TIASEP in pregnant women.
Studies in pregnant monkeys have shown reproductive toxicity; the potential risk for humans is unknown.
TIASEP should therefore not be used during pregnancy.
Breastfeeding
Imipenem is excreted into human milk. If the use of TIASEP is deemed essential, the patient should stop nursing her baby.
Fertility
There are no data available regarding potential effects of imipenem/cilastatin treatment on male or female fertility.

4.7. Effects on ability to drive and use machines
Some side effects (such as hallucinations, dizziness, somnolence, and vertigo) have been reported that may affect some patients' ability to drive or operate machinery (see section 4.8). Patients suffering from such side effects should be advised not to drive or handle machinery.

4.8. Undesirable effects
a. Summary of the safety profile
The most frequently reported systemic adverse reactions that were reported which were at least possibly related to therapy were nausea, diarrhoea, vomiting, rash, fever, hypotension, seizures (see section 4.4), dizziness, pruritus, urticaria, somnolence. Similarly, the most frequently reported local adverse reactions were phlebitis/thrombophlebitis, pain at the injection site, erythema at the injection site and vein induration. Increases in serum transaminases and in alkaline phosphatase are also frequently reported.

b. Tabulated list of adverse reactions

System organ class/ Frequency	Adverse reactions
Infections and infestations:	
Less frequent:	Candidiasis, *C. difficile* associated pseudomembranous colitis (see section 4.4), gastro-enteritis
Blood and lymphatic system disorders:	
Frequent:	Eosinophilia
Less frequent:	Pancytopenia, neutropenia, leucopenia, thrombocytopenia, thrombocytosis, agranulocytosis, haemolytic anaemia, bone marrow depression
Immune system disorders:	
Less frequent:	Anaphylactic reactions, angioedema
Psychiatric disorders:	
Less frequent:	Psychic disturbances including hallucinations, confusional states, somnolence
Frequency unknown:	Agitation
Nervous system disorders:	
Less frequent:	Seizures, myoclonic activity, dizziness, encephalopathy, paraesthesia, focal tremor, taste perversion, aggravation of myasthenia gravis, headache
Frequency unknown:	Dyskinesia
Ear and labyrinth disorders:	
Less frequent:	Hearing loss, vertigo, tinnitus
Cardiac disorders:	
Less frequent:	Tachycardia, palpitations, cyanosis
Vascular disorders:	
Frequent:	Thrombophlebitis
Less frequent:	Hypotension, flushing
Respiratory, thoracic and mediastinal disorders:	
Less frequent:	Hyperventilation, dyspnoea, pharyngeal pain
Gastrointestinal disorders:	
Frequent:	Nausea, vomiting, diarrhoea
Less frequent:	Staining of teeth and/or tongue, haemorrhagic colitis, abdominal pain, heartburn, glossitis, tongue papilla hypertrophy, increased salivation
Hepatobiliary disorders:	
Less frequent:	Hepatic failure, hepatitis, fulminant hepatitis
Skin and subcutaneous tissue disorders:	
Frequent:	Rash (e.g. exanthematous)
Less frequent:	Urticaria, pruritus, erythema, toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, exfoliative dermatitis, hyperhidrosis, skin texture changes
Musculoskeletal and connective tissue disorders:	
Less frequent:	Polyarthralgia, thoracic spine pain
Renal and urinary disorders:	
Less frequent:	Acute renal failure, oliguria/anuria, polyuria, reddish urine discolouration (harmless; not to be confused with haematuria)
Reproductive system disorders:	
Less frequent:	Pruritus vulvae
General disorders and administration site conditions:	
Less frequent:	Fever including drug fever, erythema at injection site, local pain and induration at injection site, chest discomfort, asthenia/weakness
Investigations:	
Frequent:	Increases in serum transaminases, increases in serum alkaline phosphatase
Less frequent:	A positive direct antiglobulin (Coombs) test, prolonged prothrombin time (INR), decreased haemoglobin, increases in serum bilirubin, elevations in serum creatinine, elevations in blood urea.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9. Overdose
Symptoms
There are no data available on overdosage; refer to section 4.8.
Management
Treatment is symptomatic and supportive. Imipenem/cilastatin in TIASEP is haemodialysable. However, usefulness of this treatment is unknown.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Antibacterials for systemic use, carbapenems, ATC code: J01D H51
A 20.1.1 Broad and medium spectrum antibiotics

Imipenem belongs to the thienamycin class of beta-lactam antibiotics and provides a broad spectrum of bactericidal activity.
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.
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.
Resistance
Resistant strains of *Pseudomonas* species, *Proteus mirabilis* and *Staphylococcus epidermidis* have been reported to develop during treatment.
All methicillin-resistant staphylococci are resistant to imipenem/cilastatin.

5.2. Pharmacokinetic properties
The formulation is administered as a solution via intravenous infusion.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Sodium bicarbonate

6.2. Incompatibilities
TIASEP is chemically incompatible with lactate and 5 % sodium bicarbonate and should not be reconstituted with diluents containing lactate and bicarbonate anions. However, it can be administered into an I.V. system through which a lactate solution is being infused. TIASEP should not be mixed or physically added to other antibiotics in the same infusion.
TIASEP should not be mixed with other medicines except those mentioned in section 6.6.

6.3. Shelf-life
Vial with dry powder: 3 years.
Reconstituted solution:
Reconstituted/diluted solutions should be used immediately.
The product does not contain a preservative and should, from a microbiological point of view be used immediately once prepared. The time interval between the beginning of reconstitution and the end of intravenous infusion should not exceed four hours at or below 25 °C and no longer than 24 hours when refrigerated at 2 – 8 °C.

6.4. Special precautions for storage
Store the dry powder at or below 25 °C and keep the vial in the outer carton to protect from light.
Do not freeze the reconstituted solution.
For storage conditions after reconstitution of TIASEP, see section 6.3.

6.5. Nature and contents of the container
20 ml clear colourless Type **II** glass vials, closed with bromobutyl stoppers and an aluminium flip-off cap. The vials are packed in a carton containing 1 or 10 vials.
Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling
Each vial is for single use only.
Preparation of the intravenous solution
The following table is provided for convenience in reconstituting TIASEP for intravenous infusion:

Strength (mg of imipenem)	Volume of diluent to be added (ml)	Approximate average concentration (mg/ml of imipenem)
500	100	5

Reconstitution of vial
The 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 '*Compatibility and Stability*') 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 container.
The resulting mixture should be agitated until a clear solution is obtained.
The reconstituted solution should be inspected visually for particulate matter and discolouration prior to administration. The reconstituted solution is clear and colourless. Variations of colour within this range do not affect potency.
pH after reconstitution: 6,5 - 8,5.
The solution is for single use only. Any unused solution and the vial should be adequately disposed of, in accordance with local requirements.
Compatibility and stability
In keeping with good clinical and pharmaceutical practice, TIASEP should be administered as a freshly prepared solution in any of the following diluents:
Sodium chloride 9 mg/ml (0,9 %) solution for infusion.
In exceptional circumstances where 0,9 % sodium chloride cannot be used for clinical reasons, 5 % glucose may be used instead.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Macleods Pharmaceuticals SA (Pty) Ltd.
Office Block 1, Bassonia Estate Office Park (East),
1 Cussonia Drive, Bassonia Rock, Ext 12, Alberton.
Tel: +27 11 682 116

8. REGISTRATION NUMBER
54/20.1.1/0203

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
24 May 2022

10. DATE OF REVISION OF TEXT
Not applicable.

MACLEODS

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PM0048-02

3010

500 mg/500 mg poeier vir oplossing vir infusie.
500 mg/500 mg powder for solution for infusion /

TIASEP®

TIASEP®

500 mg/500 mg powder for solution for infusion /
500 mg/500 mg poeier vir oplossing vir infusie.

3010

ACSI079F01

FRONT

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PRODUCT CODE:
F50000402375
PRODUCT NAME:
Insert Imipenem+ Cilastatin (Tiasep) Macleods Sud Africa

SEPARATIONS:
BLACK

MEASURES (mm): **420 x 420 (105 x 52,5)**
TECHNICAL SPEC. : **ACSI079F01**
Thickness: **0,049 mm**
g/sq.mt: **40 gr/ m²**
PHARMACODE: **3010**
FONT TYPE: **N.A.**
Size: **8** Spacing: **8**

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DATE	OPERATOR	DRAFT
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PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

TIASEP®
500 mg/500 mg powder for Solution for Infusion
Imipenem /Cilastatin
Sugar free

Read all of this leaflet carefully before you are given TIASEP.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.

What is in this leaflet

1. What TIASEP is and what it is used for
2. What you need to know before you use TIASEP
3. How to use TIASEP
4. Possible side effects
5. How to store TIASEP
6. Contents of the pack and other information

1. What TIASEP is and what it is used for
TIASEP is an antibiotic medicine of the carbapenem group of antibiotics. It kills a wide range of bacteria (germs) that cause infections in various parts of the body.
Your doctor has prescribed TIASEP because you may have one (or more) of the following types of infection:
- Infection in the abdomen
- Infection affecting the lungs (pneumonia)
- Infections that you can catch during or after the delivery of your baby
- Septicaemia (bacterial infection of the blood)
- Genitourinary tract infections
- Bone and joint infections
- Skin and soft tissue infections
- Bacterial infection of the lining of the heart cavity and valves (endocarditis)
- Mixed infections
- Prevention of certain post-operative infections.

2. What you need to know before you use TIASEP
TIASEP should not be administered to you:
- if you are allergic (hypersensitive) to imipenem, cilastatin or any of the other ingredients of TIASEP (listed in section 6)
- if you are allergic (hypersensitive) to other antibiotics such as penicillins, cephalosporins, or carbapenems
- if you have meningitis (infection in the membranes that cover the brain and spinal cord)
- if you are pregnant or breastfeeding your baby.

Warnings and precautions
Tell your doctor or healthcare provider before TIASEP is given to you, if you have:
- allergies to any medicines including antibiotics (sudden life-threatening allergic reactions require immediate medical treatment)
- colitis (inflammation of the bowels) or any other gastrointestinal disease
- any central nervous system disorders such as localised tremors or epileptic seizures
- kidney or urinary problems, including reduced kidney function (TIASEP blood levels increase in patients with reduced kidney function. Central nervous system adverse reactions may occur if the dose is not adjusted to the kidney function)
- liver problems.

You may develop a positive test (Coombs test) which indicates the presence of antibodies that may destroy red blood cells. Your doctor will explain this to you.
Tell your doctor if you are taking medicines called valproic acid or divalproex sodium (see "Other medicines and TIASEP").

Use in children
TIASEP is not recommended in children less than 3 months of age or children with kidney problems.

Other medicines and TIASEP
Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

Tell your doctor if you are taking:
- ganciclovir, which is used to treat some viral infections
- valproic acid or divalproex sodium (used to treat epilepsy, bipolar disorder, migraine, or schizophrenia)
- blood thinners such as warfarin
- probenecid (a medicine used for gout).

Your doctor will decide whether you should use TIASEP in combination with these medicines.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before you receive TIASEP.
TIASEP has not been studied in pregnant women. TIASEP should therefore not be used during pregnancy (see "TIASEP should not be administered to you").
TIASEP may pass into breastmilk and it may affect the baby. It is important to tell your doctor if you are breastfeeding or if you intend to breastfeed your baby.
There is no information available on the effect of TIASEP on fertility.

Driving and using machines
There are some side effects associated with TIASEP (such as seeing, hearing, or feeling something that is not there, dizziness, sleepiness, and a spinning sensation) that may affect your ability to drive or operate machinery (see section 4).

TIASEP contains sodium
TIASEP contains 1,6 millimole (approximately 37,6 mg) sodium per 500 mg dose (one vial). Tell your doctor if you are on a controlled sodium diet.

3. HOW TO USE TIASEP
Do not share medicine prescribed for you with any other person.
You will not be expected to give yourself TIASEP. It will be given to you by a person who is qualified to do so.
Your doctor will decide how much TIASEP you need. This will depend upon your condition and the severity of your infection.

Adults and adolescents
The usual daily dose is 1 - 2 g administered in 3 - 4 divided doses.
If you have kidney problems or if you weigh less than 70 kg, your doctor may lower your dose.

Children
The usual dose for children and infants (3 months or older) is 15 mg/kg every 6 hours.
TIASEP is not recommended in children under 3 months of age and children with kidney problems.

Method of administration
TIASEP is given intravenously (into a vein) over 20 to 30 minutes for a dose of 500 mg or less, or 40 to 60 minutes for a dose of 500 mg or more. The rate of infusion may be slowed if you feel sick.

If you are given more TIASEP than you should
Since a healthcare provider will administer TIASEP, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you miss a dose of TIASEP
Since a healthcare provider will administer TIASEP, it is unlikely that a dose will be missed.
However, if you are concerned that you may have missed a dose, contact your doctor or another healthcare provider immediately.

4. Possible side effects
TIASEP can have side effects.
Not all side effects reported for TIASEP are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving TIASEP, please consult your healthcare provider for advice.

If any of the following happens, tell your doctor, as TIASEP should be stopped immediately:
- Allergic reactions including rash, swelling of the face, lips, tongue and/or throat (with difficulty in breathing or swallowing), and/or low blood pressure
- Skin peeling (toxic epidermal necrolysis)
- Severe skin reactions (Stevens-Johnson syndrome and erythema multiforme)
- Severe skin rash with loss of skin and hair (exfoliative dermatitis)
- Yellowing of your skin or eyeballs, nausea, fever, stomach swelling (hepatitis, abnormal)
- Severe watery diarrhoea, fever, abdominal pain (pseudomembranous colitis) or bloody diarrhoea (haemorrhagic colitis).

These are all very serious side effects. If you have them, you may have had a serious reaction to TIASEP. You may need urgent medical attention or further hospitalisation.

Tell your doctor if you notice any of the following:
Frequent side effects:
- Increase in some white blood cells (eosinophilia)
- Swelling and redness along a vein which is extremely tender when touched
- Nausea, vomiting, diarrhoea
- Abnormal liver function detected by blood tests
- Rash

Less frequent side effects:
- Fungal infection (candidiasis)
- Changes in the amounts of various types of blood cells
- Blood disorders affecting the cell components of the blood and usually detected by blood tests (symptoms may be tiredness, paleness of skin, and prolonged bruising after injury)
- Psychic disturbances (such as mood swings and impaired judgment)
- Seeing, hearing or feeling something that is not there (hallucinations)
- Confusion
- Sleepiness
- Seizures
- Tremors and uncontrolled twitching of muscles
- Dizziness
- Disease of the brain, tingling sensation (pins and needles), localised tremor
- Worsening of a rare disease associated with muscle weakness (aggravation of myasthenia gravis)
- Headache
- Hearing loss, ringing in the ears (tinnitus)
- Sensation of spinning (vertigo)
- Irregular heartbeat, the heart beating forcefully or rapidly
- Low blood pressure
- Flushing
- Abnormally fast and superficial breathing, difficulty breathing, chest discomfort
- Staining of the teeth and/or tongue
- Red swollen tongue, overgrowth of the normal projections on the tongue giving it a hairy appearance, heartburn, sore tongue, increase in the production of saliva, disturbances in taste
- Abdominal pain, heartburn
- Inability of the liver to perform normal function
- Local skin redness
- Excessive sweating, skin texture changes
- Skin itchiness
- Hives
- Pain in several joints, pain in the upper spine
- Inability of the kidney to perform normal function, changes in the amount of urine, changes in urine colour
- Itching of the vulva in women
- Fever
- Local pain and formation of a firm lump at the injection site
- Weakness
- Abnormal kidney, liver and blood function detected by blood tests
- A positive Coombs test

Unknown frequency:
- Agitation
- Abnormal movements

If you notice any side effects not listed in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the SAHPRA website: https://www.sahpra.org.za/Publications/Index/8.
By reporting side effects, you can help provide more information on the safety of TIASEP.

5. How to store TIASEP
Store all medicines out of reach of children.
Store at or below 25 °C. Keep in carton to protect from light.

After reconstitution:
Diluted solutions should be used immediately. The time interval between the beginning of reconstitution and the end of intravenous infusion should not exceed four hours.
Do not freeze the reconstituted solution.
Do not use after the expiry date stated on the label/carton. The expiry date refers to the last day of that month.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What TIASEP contains
Each vial contains 500 mg imipenem (as imipenem monohydrate) and 500 mg cilastatin (as cilastatin sodium salt).
The other ingredient is sodium bicarbonate.

What TIASEP looks like and contents of the pack
TIASEP is a white to almost white or light yellow powder for solution for infusion, in a clear, colourless 20 ml glass vial with a bromobutyl stopper and an aluminium flip-off cap. The vials are packed in a carton containing 1 or 10 vials.
Not all pack sizes may be marketed.

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PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS: S4

TIASEP®
500 mg/500 mg poeier vir oplossing vir infusie
Imipenem /Silastatien
Suikervry

Lees die hele inligtingsblad deeglik deur voordat die medisyne aan jou gegee word.
- Hou hierdie inligtingsblad. Dit mag nodig wees dat jy dit weer wil lees.
- Indien jy enige verdere vrae het, raadpleeg jou dokter of apteker.

Wat is in hierdie inligtingsblad

1. Wat TIASEP is en waarvoor dit gebruik word
2. Wat jy moet weet voordat jy TIASEP gebruik
3. Hoe om TIASEP te gebruik
4. Moontlike newe-effekte
5. Hoe om TIASEP te bewaar
6. Inhoud van die pakkie en ander inligting

1. Wat TIASEP is en waarvoor dit gebruik word
TIASEP is 'n antibiotiese medisyne van die karbapenemgroep antibiotika. Dit kan 'n wye verskeidenheid bakterieë (kieme) wat infeksies in verskillende dele van die liggaam veroorsaak doodmaak.
Jou dokter het TIASEP voorgeskryf omdat jy moontlik een (of meer) van die volgende soorte infeksie het:
- Infeksie in die buik
- Infeksie wat die longe aantas (pneumonie)
- Infeksies wat jy tydens of na die geboorte van jou baba kan opdoen
- Septisemie (bakteriële infeksie van die bloed)
- Geslagsurienweginfeksie
- Been- en gewrigsinfeksies
- Vel- en sagteweefselinfeksie
- Bakteriële infeksie van die voering van die hartholte en kleppe (endokarditis)
- Gemengde infeksies
- Voorkoming van sekere post-operatiewe infeksies.

2. Wat jy moet weet voordat jy TIASEP gebruik
TIASEP moet nie aan jou toegedien word nie:
- as jy allergies (hipersensitief) is vir imipenem, silastatien of enige van die ander bestanddele van TIASEP (gelys in afdeling 6)
- as jy allergies (hipersensitief) is vir ander antibiotika soos penisilliene, kefalosporiene of karbapenems
- as jy meningitis het (infeksie in die vliese wat die brein en rugmurg bedek)
- as jy swanger is, of jou baba borsvoed.

Waarskuwings en voorsorgmaatreëls
Lig jou dokter of gesondheidsorgverskaffer in voordat TIASEP aan jou gegee word, indien jy die volgende het:
- allergieë vir enige medisyne insluitend antibiotika (skielike lewensgevaarlike allergiese reaksies vereis onmiddellike mediese behandeling)
- kolitis (ontsteking van die dermkanaal) of enige ander maagdermkanaalsiekte
- enige sentrale senuweestelselaandoenings, soos gelokaliseerde bewing, of epileptiese aanvalle
- nier- of urinêre probleme, waaronder 'n verminderde nierfunksie (verhoging van die bloedvlakke van TIASEP by pasiënte met 'n verminderde nierfunksie. Ongunstige reaksies van die sentrale senuweestelsel kan voorkom as die dosis nie by die nierfunksie aangepas word nie)
- lewerprobleme.

Jy kan 'n positiewe toets kry (Coombs-toets) wat dui op die aanwesigheid van antiliggame wat rooibloedselle kan vernietig. Jou dokter sal dit aan jou verduidelik.
Lig jou dokter in as jy medisyne genaamd valproïensuur of natriumdivalproeks neem (kyk "Ander medisynes en TIASEP").

Gebruik by kinders
TIASEP word nie aanbeveel by kinders jonger as 3 maande oud of kinders met nierprobleme nie.

Ander medisynes en TIASEP
Lig altyd jou gesondheidsorgkundige in as jy enige ander medisyne neem. (Dit sluit komplementêre of tradisionele medisyne in.)

Sê vir jou dokter as jy die volgende neem:
- gansiklovir, wat gebruik word om sommige virale infeksies te behandel
- valproïensuur of natriumdivalproeks (gebruik vir die behandeling van epilepsie, bipolêre versteuring, migraine of skisofrenie)
- bloedverdunners soos warfarien
- probenesied ('n medisyne gebruik vir jig).

Jou dokter sal besluit of jy TIASEP in kombinasie met hierdie medisynes kan gebruik.

Swangerskap, borsvoeding en vrugbaarheid
Indien jy swanger is of borsvoed, dink jy is dalk swanger, of beplan om 'n baba te hê, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgverskaffer voordat jy TIASEP ontvang.
TIASEP is nie ondersoek by swanger vroue nie. TIASEP moet dus nie tydens swangerskap gebruik word nie (kyk "TIASEP moet nie aan jou toegedien word nie").
TIASEP kan in borsmelk voorkom en dit kan die baba beïnvloed. Dit is belangrik om jou dokter te vertel as jy borsvoeding gee of as jy van plan is om jou baba te borsvoed.
Daar is geen inligting beskikbaar oor die effek van TIASEP op vrugbaarheid nie.

Bestuur en gebruik van masjinerie
Daar is enkele newe-effekte geassosieer met TIASEP (soos sien, hoor of voel van iets wat nie daar is nie, duiseligheid, slaperigheid en 'n draaierige gevoel) wat jou vermoë om te bestuur of masjinerie te hanteer kan beïnvloed (kyk afdeling 4).

TIASEP bevat natrium
TIASEP bevat 1,6 millimol (ongeveer 37,6 mg) natrium per 500 mg dosis (een flessie). Lig jou dokter in as natrium in jou dieet beperk word.

3. HOE OM TIASEP TE GEBRUIK
Moenie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie.
Daar sal nie van jou verwag word om TIASEP aan jouself toe te dien nie. Dit sal aan jou gegee word deur 'n persoon wat gekwalifiseer is om dit te doen.
Jou dokter sal besluit hoeveel TIASEP jy benodig. Dit sal afhang van jou toestand en die erns van jou infeksie.

Volwassenes en adolessente
Die gewone daaglikse dosis is 1 - 2 g toegedien in 3 - 4 verdeelde dosisse.
As jy nierprobleme het of as jy minder as 70 kg weeg, kan jou dokter jou dosis verlaag.

Kinders
Die gebruiklike dosis vir kinders en babas (3 maande of ouer) is 15 mg/kg elke 6 uur.
TIASEP word nie aanbeveel by kinders onder 3 maande oud of kinders met nierprobleme nie.

Metode van toediening
TIASEP word binneaars (in 'n aar) toegedien vir 20 tot 30 minute vir 'n dosis van 500 mg of minder, of 40 tot 60 minute vir 'n dosis van 500 mg of meer. Die infusiesnelheid kan vertraag word as jy naar voel.

Indien jy meer TIASEP gegee word as wat jy moes kry
Aangesien 'n gesondheidsorgverskaffer TIASEP sal toedien, sal hy/sy die dosis beheer. In geval van oordosering sal jou dokter egter die oordosering behandel.

Indien jy 'n dosis van TIASEP oorslaan
Aangesien 'n gesondheidsorgverskaffer TIASEP sal toedien, is dit onwaarskynlik dat 'n dosis oorgeslaan sal word.
As jy bekommerd is dat jy 'n dosis oorgeslaan het, kontak dadelik jou dokter of 'n ander gesondheidsorgverskaffer.

4. Moontlike newe-effekte
TIASEP kan newe-effekte hê.
Nie alle newe-effekte wat vir TIASEP aangemeld is, is by hierdie inligtingsblad ingesluit nie. Indien jou algemene gesondheid agteruitgaan, of jy enige ongunstige effekte ervaar terwyl jy TIASEP ontvang, raadpleeg asseblief jou gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, lig dadelik jou dokter in, aangesien TIASEP dadelik gestaak moet word:
- Allergiese reaksies waaronder uitslag, swelling van die gesig, die lippe, tong en/of keel (met probleme om asem te haal of te sluk), en/of lae bloeddruk
- Velafskilfering (toksiese epidermale nekrolise)
- Erge velreaksies (Stevens-Johnson-sindroom en veelvuldige eriteem)
- Erge veluitslag met vel- of haarverlies (afskilferende dermatitis)
- Geel verkleuring van jou vel of oogballe, naarheid, koors, maag swelling (hepatitis, abnormaal)
- Erge waterige diarree, koors, buikpyn (pseudomembraneuse kolitis) of bloederige diarree (hemorragiese kolitis).

Hierdie is almal baie ernstige newe-effekte. Indien jy hulle het, het jy moontlik 'n ernstige reaksie gehad op TIASEP. Jy kan dringende mediese aandag of verdere hospitalisasie benodig.

Lig jou dokter in as jy enige van die volgende waarneem:
Gereelde newe-effekte:
- Toename van sommige witbloedselle (eosinofilie)
- Swelling en rooiheid langs 'n aar wat uiters gevoelig is by aanraking
- Naarheid, braking, diarree
- Abnormale lewerfunksie, bepaal met bloedtoetse
- Uitslag

Minder gereelde newe-effekte:
- Swaminfeksie (kandidiase)
- Veranderinge in die hoeveelhede van verskillende soorte bloedselle
- Bloedaandoenings wat die selkomponente van die bloed aantas en wat gewoonlik deur bloedtoetse opgespoor word (simptome kan moegheid, bleekheid van die vel en langdurige kneusing na 'n besering wees)
- Psigiese versteurings (soos gemoedskommelings en verswakte oordeelsvermoë)
- Sien, hoor of voel iets wat nie daar is nie (hallusinasies)
- Verwarring
- Lomerigheid
- Epileptiese aanvalle
- Bewing en ongekontroleerde spiertrekkings
- Duiseligheid
- Breinsiekte, prikkelende sensasie (speld-en-naaldprikkels), gelokaliseerde bewing
- Verergering van 'n seldsame siekte wat gepaardgaan met spierswakheid (verergering van myasthenia gravis)
- Hoofpyn
- Gehoorverlies, suising in die ore (tinnitus)
- Gevoel van tolling (vertigo)
- Onreëlmatige hartklop, die hart klop kragtig of vinnig
- Lae bloeddruk
- Gloede
- Abnormaal vinnige en oppervlakkige asemhaling, moeilike asemhaling, ongemak op die bors
- Verkleuring van die tande en/of tong
- Rooi geswelde tong, oorgroeiing van die normale uitsteeksels op die tong wat dit 'n harige voorkoms gee, sooibrand, seer tong, toename in die produksie van speeksel, smaakversteurings
- Buikpyn, sooibrand
- Onvermoë van die lewer om normaal te werk
- Plaaslike velrooiheid
- Buitensporige gesweet, veltekstuur veranderinge
- Jeukerige vel
- Netelroos
- Pyn in verskeie gewrigte, pyn in die boonste ruggraat
- Onvermoë van die nier om normaal te funksioneer, veranderinge in die hoeveelheid urien, kleurveranderinge in die urien
- Jeuking van die vulva by vroue
- Koors
- Plaaslike pyn en vorming van 'n harde knop by die inspuitplek
- Swakheid
- Abnormale lewer-, nier- en bloedfunksie, met bloedtoetse opgespoor
- 'n Positiewe Coombs toets

Frekwensie onbekend:
- Opgewondenheid
- Abnormale bewegings

Indien jy enige newe-effekte opmerk wat nie in hierdie pamflet vermeld word nie, lig asseblief jou dokter of apteker in.

Aanmelding van newe-effekte
Indien jy newe-effekte ondervind, bespreek dit met jou dokter, apteker of verpleegster. Jy kan ook newe-effekte aan SAHPRA rapporteer op die SAHPRA-webwerf: https://www.sahpra.org.za/Publications/Index/8.
Deur newe-effekte aan te meld, kan jy meer inligting verskaf oor die veiligheid van TIASEP.

5. Hoe om TIASEP te bewaar
Bewaar alle medisyne buite bereik van kinders.
Bewaar by of benede 25 °C. Hou in die karton om teen lig te beskerm.
Na hersamestelling:
Verdunde oplossings moet dadelik gebruik word. Die tydsinterval tussen die begin van die hersamestelling en die einde van die binneaarse infusie moet nie langer as vier uur duur nie.
Moenie die aangemaakte oplossing vries nie.
Moenie na die vervaldatum, wat op die etiket/karton aangedui word, gebruik nie. Die vervaldatum verwys na die laaste dag van daardie maand.
Neem alle ongebruikte medisyne terug na jou apteker.
Moenie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette) gooi nie.

6. Inhoud van die pakkie en ander inligting
Wat TIASEP bevat
Elke flessie bevat 500 mg imipenem (as imipenem monohidraat) en 500 mg silastatien (as silastatien-natriumsout).
Die ander bestanddeel is natriumbikarbonaat.

Hoe TIASEP lyk en wat die inhoud van die pakkie is
TIASEP is 'n wit tot byna wit of liggeel poeier vir oplossing vir infusie, in 'n helder, kleurlose 20 ml glasflessie met 'n broombutielprop en 'n aluminium afwipdekseltjie. Die flessies word verpak in 'n kartondosie wat 1 of 10 flessies bevat.
Nie alle verpakkingsgroottes word noodwendig bemark nie.

Houer van die registrasiesertifikaat
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Kantoorblok 1, Bassonia Estate Kantoorpark (Oos)
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Hierdie pamflet was voorheen hersien op
24 Mei 2022

Registrasienommer
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BACK

ARTWORK PDF 1.5

PRODUCT CODE:
F50000402375
PRODUCT NAME:
Insert Imipenem+ Cilastatin (Tiasep) Macleods Sud Africa

SEPARATIONS:
BLACK

MEASURES (mm): **420 x 420 (105 x 52,5)**
TECHNICAL SPEC. : **ACSI079F01**
Thickness: **0,049 mm**
g/sq.mt: **40 gr/ m²**
PHARMACODE: **3010**
FONT TYPE: **N.A.**
Size: **8** Spacing: **8**

ACS DOBFAR SpA

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05/04/2024	017	02

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Date: 2024.04.08 13:45:35 +02'00'