INVABEX

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE
INVABEX 1 g sterile powder for solution for injection or infusion.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each vial contains ertapenem sodium equivalent to ertapenem 1 g.

Excipient with known effect:
Each 1 g dose contains approximately 6,0 millimoles of sodium (approximately 137 mg).
Sugar free.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Powder for solution for injection or infusion.
White to yellowish powder.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Adult patients
INVABEX is indicated for the treatment of adult patients with the following moderate to severe infections, caused by susceptible strains of the designated microorganisms (see section 4.2):
Complicated intra-abdominal infections due to *Escherichia coli*, *Clostridium clostridioforme*, *Eubacterium lentum*, *Peptostreptococcus* species, *Bacteroides fragilis*, *Bacteroides distasonis*, *Bacteroides ovatus*, *Bacteroides thetaiotaomicron*, or *Bacteroides uniformis*.

Complicated skin and skin structure infections including diabetic lower extremity and diabetic foot infections due to *Staphylococcus aureus* (methicillin susceptible strains only), *Streptococcus agalactiae*, *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Porphyromonas asaccharolytica* or *Peptostreptococcus* species.

Community acquired pneumonia due to *Streptococcus pneumonia* (penicillin susceptible strains only) including cases with concurrent bacteraemia, *Moraxella catarrhalis*. If community acquired pneumonia is caused by *Haemophilus influenzae*, INVABEX should be used only after confirmation of culture and sensitivity results.

Complicated urinary tract infections including pyelonephritis due to *Escherichia coli*, including cases with concurrent bacteraemia, or *Klebsiella pneumoniae*.

Acute pelvic infections including postpartum endomyometritis, septic abortion and post-surgical gynaecologic infections due to *Streptococcus agalactiae*, *Escherichia coli*, *Bacteroides fragilis*, *Porphyromonas asaccharolytica*, *Peptostreptococcus species* or *Prevotella bivia*.

Paediatric patients
INVABEX is indicated in paediatric patients 3 months - 17 years of age with the following infections (see "*Adult patients*" above for susceptible organisms):
- complicated intra-abdominal infections
- complicated skin and skin structure infections
- community acquired pneumonia
- complicated urinary tract infections
- acute pelvic infections.

Appropriate specimens for bacteriological examination should be obtained in order to isolate and identify the causative organisms and to determine their susceptibility to ertapenem. Therapy with INVABEX may be initiated empirically before results of these tests are known; once results become available, antimicrobial therapy should be adjusted accordingly.

4.2 Posology and method of administration
Posology
The usual dose of INVABEX in patients 13 years of age and older is 1 gram (g) given once a day.

The usual dose of INVABEX in patients 3 months - 12 years of age is 15 mg/kg twice daily (not to exceed 1 g/day).

Intramuscular (IM) administration of INVABEX may be used as an alternative to intravenous (IV) administration in the treatment of those infections for which intramuscular therapy is appropriate.

Dosage guidelines for adults and paediatric patients with normal renal function* and body mass

Infection	Daily dose (IV or IM) adults and paediatric patients 13 years of age and older	Daily dose (IV or IM) paediatric patients 3 months - 12 years of age	Recommended duration of total antimicrobial treatment
Complicated intra-abdominal infections	1 g	15 mg/kg twice daily§	5 - 14 days†
Complicated skin and skin structure infections including diabetic lower extremity and diabetic foot infections	1 g	15 mg/kg twice daily§	7 - 14 days‖
Community acquired pneumonia	1 g	15 mg/kg twice daily§	10 - 14 days‖
Complicated urinary tract infections including pyelonephritis	1 g	15 mg/kg twice daily§	10 - 14 days‖
Acute pelvic infections including postpartum endomyometritis, septic abortion and post-surgical gynaecologic infections	1 g	15 mg/kg twice daily§	3 - 10 days‖

* Defined as creatinine clearance greater than 90 mL/min/1,73 m^2
† Duration includes a possible switch to an appropriate oral therapy once clinical improvement has been demonstrated.
§ Not to exceed 1 g/day
‖ Patients with diabetic foot infections received up to 28 days of treatment (parenteral or parenteral plus oral switch therapy)

Special populations
Patients with renal insufficiency
INVABEX may be used for the treatment of infections in adult patients with renal insufficiency.
In adult patients whose creatinine clearance is greater than 30 mL/min/1,73 m^2, no dosage adjustment is necessary.
Adult patients with advanced renal insufficiency (creatinine clearance less than or equal to 30 mL/min/1,73 m^2), including those on haemodialysis, should receive 500 mg daily.
There are no data in paediatric patients with renal insufficiency.

Patients on haemodialysis
Following a single 1 g IV dose of ertapenem given immediately prior to a haemodialysis session, approximately 30 % of the dose may be recovered in the dialysate.
When adult patients on haemodialysis are given the recommended daily dose of 500 mg of INVABEX within 6 hours prior to haemodialysis, a supplementary dose of 150 mg is recommended after the haemodialysis session. If INVABEX is given at least 6 hours before haemodialysis, no supplementary dose is needed.
No data are available in patients undergoing peritoneal dialysis or haemofiltration.
There are also no data in paediatric patients on haemodialysis.
When only the serum creatinine is available, the following formula** may be used to calculate creatinine clearance. The serum creatinine should represent a steady state of renal function.

$$\text{Males: } \frac{(\text{weight in kg}) \times (140 - \text{age in years})}{(72) \times \text{serum creatinine (mg/100 mL)}}$$

Females: (0,85) x (value calculated for males)

** Cockcroft and Gault equation: Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976.

Patients with hepatic impairment
No dosage adjustment is recommended in patients with impaired hepatic function (see section 5.2, *Hepatic insufficiency*).
The recommended dose of INVABEX may be administered without regard to age (13 years of age and older) or gender.

Elderly
The recommended dose of INVABEX should be administered, except in cases of severe renal impairment (see Patients with renal impairment above).

Paediatric population
There is little experience with ertapenem (as in INVABEX) in children less than two years of age; thus, particular care should be taken to establish the susceptibility of the infecting organism(s) to ertapenem. INVABEX should not be used in infants under the age of 3 months, as no data are available (see section 4.3 and 4.4).

Method of administration
For instructions on the preparation of INVABEX before administration, see section 6.6.
INVABEX may be administered by intravenous (IV) infusion or intramuscular (IM) injection.
When administered intravenously, INVABEX should be infused over a period of 30 minutes.
The usual duration of therapy with INVABEX is 3 - 14 days, but it may vary according to the type of infection and causative pathogen(s). When clinically indicated, a switch to an appropriate oral antimicrobial medicine may be implemented if clinical improvement has been observed.

4.3 Contraindications
INVABEX is contraindicated in:
- hypersensitivity to ertapenem or to any of the excipients of INVABEX (see section 6.1)
- hypersensitivity to beta-lactam antibiotics
- patients with known bacterial meningitis, due to lack of sufficient cerebrospinal fluid (CSF) penetration
- INVABEX is not recommended in infants under 3 months of age, as no data are available.

Due to the use of lidocaine (lignocaine) hydrochloride as a diluent, INVABEX administered intramuscularly is contraindicated in patients with a known hypersensitivity to amide type local anaesthetics and in patients with severe shock or heart block. (Refer to the professional information for lidocaine (lignocaine) hydrochloride).

4.4 Special warnings and precautions for use
Hypersensitivity
SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTIC) REACTIONS HAVE BEEN REPORTED IN PATIENTS RECEIVING THERAPY WITH BETA-LACTAM ANTIBIOTICS, INCLUDING INVABEX.
THESE REACTIONS ARE MORE LIKELY TO OCCUR IN INDIVIDUALS WITH A HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS. THERE HAVE BEEN REPORTS OF INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY WHO HAVE EXPERIENCED SEVERE HYPERSENSITIVITY REACTIONS WHEN TREATED WITH ANOTHER BETA-LACTAM. BEFORE INITIATING THERAPY WITH INVABEX, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, OTHER BETA-LACTAMS AND OTHER ALLERGENS. IF AN ALLERGIC REACTION TO INVABEX OCCURS, DISCONTINUE INVABEX IMMEDIATELY.
SERIOUS ANAPHYLACTIC REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH ADRENALINE (EPINEPHRINE), OXYGEN, INTRAVENOUS STEROIDS, AND AIRWAY MANAGEMENT, INCLUDING INTUBATION. OTHER THERAPY MAY ALSO BE ADMINISTERED AS INDICATED.

Prescribers must adhere to the principles of antibiotic stewardship.

Hypersensitivity reactions can also progress to Kounis syndrome, (acute coronary syndrome accompanying allergic reaction) and linear IgA associated with the use of beta-lactam antibiotics, including INVABEX.

Superinfection
Prolonged use of INVABEX may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken. See Antibiotic-associated colitis below.

Antibiotic-associated colitis
Pseudomembranous colitis (antibiotic-associated colitis) has been reported with ertapenem (contained in INVABEX) and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of INVABEX.
Treatment with INVABEX alters the normal flora of the colon and may permit overgrowth of clostridia. It has been demonstrated that a toxin produced by *Clostridium difficile* is a primary cause of antibiotic-associated colitis.
After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated.
Mild cases of pseudomembranous colitis usually respond to discontinuation of INVABEX. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, parenteral nutrition and treatment with an antibacterial medicine clinically effective against *Clostridium difficile* colitis.
Medicines that inhibit peristalsis should not be given.

Seizures
Seizures and other central nervous system (CNS) adverse experiences have been reported during treatment with ertapenem (as in INVABEX); see section 4.8. Seizures occur more frequently in elderly patients and those with pre-existing CNS disorders (e.g. brain lesions or history of seizures) and/or compromised renal function.
Close adherence to the recommended dosage regimen is urged, especially in patients with known factors that predispose to convulsive activity. Anticonvulsant therapy should be continued in patients with known seizure disorder.
If focal tremors, myoclonus or seizures occur, patients should be evaluated neurologically and the dosage of INVABEX re-examined to determine whether it should be decreased or discontinued.

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Encephalopathy
Encephalopathy has been reported with the use of INVABEX (see section 4.8). If ertapenem-induced encephalopathy is suspected (e.g. myoclonus, seizures, altered mental status, depressed level of consciousness), discontinuation of INVABEX should be considered. Patients with renal impairment are at higher risk of ertapenem-induced encephalopathy and the resolution may be prolonged.

Concomitant use with valproic acid
The concomitant use of INVABEX and 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 enough to overcome this interaction. The concomitant use of INVABEX and valproic acid or divalproex sodium is not recommended (see section 4.5). Antibacterials 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 INVABEX is necessary, supplemental anticonvulsant therapy should be considered (see section 4.5).

Sub-optimal exposure
In surgical interventions exceeding 4 hours, patients could be exposed to sub-optimal ertapenem concentrations and consequently to a risk of potential treatment failure. Therefore, caution should be exercised in such unusual cases.

Considerations for use in particular populations
Experience in the use of INVABEX for severe infections is limited.
Efficacy has not been established for the use of INVABEX in the treatment of community acquired pneumonia due to penicillin-resistant *Streptococcus pneumoniae*, or for diabetic foot infections with concurrent osteomyelitis.

Caution should be taken with IM administration of INVABEX not to inject it inadvertently into a blood vessel (see section 4.2).

Lidocaine (lignocaine) hydrochloride is the diluent for intramuscular administration of INVABEX. Refer to the professional information for lidocaine hydrochloride.

Information on the inactive ingredients
INVABEX contains approximately 137 mg (approximately 6,0 millimoles) of sodium per vial, equivalent to 6,85 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Paediatric population
There is little experience with ertapenem (as in INVABEX) in children less than two years of age. In this age group, particular care should be taken to establish the susceptibility of the infecting organism(s) to ertapenem.
No data are available in children under 3 months of age, INVABEX is therefore contraindicated in this age group (see section 4.3).

4.5 Interaction with other medicines and other forms of interaction
Ertapenem does not inhibit metabolism mediated by any of the six major cytochrome P450 (CYP) isoforms: 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4.
Medicine interactions caused by inhibition of P-glycoprotein-mediated medicine clearance or CYP-mediated medicine clearance are unlikely (see section 5.2). Ertapenem does not inhibit P-glycoprotein-mediated transport of digoxin or vinblastine and is not a substrate for P-glycoprotein-mediated transport.

No specific clinical drug interaction studies have been conducted.

Valproic acid
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, including INVABEX. The lowered valproic acid levels may lead to inadequate seizure control; therefore, concomitant use of INVABEX and valproic acid/sodium valproate is not recommended and alternative antibacterial or anticonvulsant therapies should be considered.

Probenecid
Probenecid inhibits the renal excretion of ertapenem, thereby increasing its plasma concentrations and prolonging its elimination half-life.

4.6 Fertility, pregnancy and lactation
Pregnancy
Safety in pregnancy has not been established.

Breastfeeding
Ertapenem is excreted in human milk (see section 5.2). Safety in nursing mothers has not been established.

Fertility
There are no adequate and well controlled studies regarding the effect of ertapenem on fertility in men and women.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.
Dizziness and somnolence are possible undesirable effects of INVABEX (see section 4.8). If affected, patients should be warned not to drive or operate machinery.

4.8 Undesirable effects
a. Summary of the safety profile
Adults
Most adverse experiences reported in clinical studies were described as mild to moderate in severity. Medicine-related adverse experiences were reported in approximately 20 % of patients treated with ertapenem. Ertapenem was discontinued due to adverse experiences thought to be medicine-related in 1,3 % of patients.
The most frequent medicine-related adverse experiences reported during parenteral therapy in patients treated with ertapenem were diarrhoea (4,3 %), infused vein complication (3,9 %), nausea (2,9 %) and headache (2,1 %).

Paediatric population (3 months - 17 years of age):
The overall safety profile is comparable to that in adult patients. In clinical trials, most frequent medicine-related clinical adverse experiences reported during parenteral therapy were diarrhoea (5,5 %), infusion site pain (5,5 %) and infusion site erythema (2,6 %).

b. Tabulated list of adverse effects
ADULTS - 18 years of age and older

System Organ Class	Frequency	Side effects
Infections and infestations	*Less frequent*	Oral candidiasis, candidiasis, fungal infection, pseudomembranous enterocolitis, vaginitis, pneumonia, dermatomycosis, postoperative wound infection, urinary tract infection, *C. difficile*-associated diarrhoea
Blood and lymphatic system disorders	*Less frequent*	Neutropaenia, thrombocytopaenia
Immune system disorders	*Less frequent*	Allergy
	Frequency unknown	Anaphylaxis* including anaphylactoid reactions*
Metabolism and nutrition disorders	*Less frequent*	Anorexia, hypoglycaemia
Psychiatric disorders	*Less frequent*	Insomnia, somnolence, confusion, agitation, anxiety, depression
	Frequency unknown	Altered mental status* (including aggression, delirium, disorientation, mental status changes)*, hallucinations*
Nervous system disorders	*Frequent*	Headache
	Less frequent	Dizziness, taste perversion, seizure (see section 4.4), tremor, syncope
	Frequency unknown	Depressed level of consciousness*, dyskinesia*, myoclonus*, gait disturbance*, encephalopathy
Eye disorders	*Less frequent*	Scleral disorder
Cardiac disorders	*Less frequent*	Sinus bradycardia, dysrhythmia, tachycardia
	Frequency unknown	Kounis syndrome
Vascular disorders	*Frequent*	Infused vein complication, phlebitis/thrombophlebitis
	Less frequent	Hypotension, extravasation, haemorrhage, increased blood pressure
Respiratory, thoracic and mediastinal disorders	*Less frequent*	Dyspnoea, pharyngeal discomfort, nasal congestion, cough, epistaxis, rales/rhonchi, wheezing
Gastrointestinal disorders	*Frequent*	Diarrhoea, nausea, vomiting
	Less frequent	Constipation, acid regurgitation, dry mouth, dyspepsia, abdominal pain, dysphagia, faecal incontinence, pelvic peritonitis
	Frequency unknown	Stained teeth*
Hepatobiliary disorders	*Less frequent*	Cholecystitis, jaundice, liver disorder
Skin and subcutaneous tissue disorders	*Frequent*	Rash
	Less frequent	Erythema, urticaria, dermatitis, desquamation, pruritus, Linear IgA bullous dermatosis (LABD)
	Frequency unknown	Drug rash with eosinophilia and systemic symptoms (DRESS syndrome)*, toxic epidermal necrolysis*, Stevens-Johnson syndrome*, acute generalised exanthematous pustulosis (AGEP)*, hypersensitivity vasculitis*
Musculoskeletal, connective tissue and bone disorders	*Frequent*	Muscle cramp, shoulder pain
	Frequency unknown	Muscular weakness*
Renal and urinary disorders	*Less frequent*	Renal insufficiency, acute renal insufficiency
Pregnancy, puerperium and perinatal conditions	*Less frequent*	Abortion
Reproductive system and breast disorders	*Less frequent*	Genital bleeding, vaginal pruritus
General disorders and administration site conditions	*Less frequent*	Extravasation, asthenia/fatigue, fever, pain, oedema/swelling, chest pain, injection site induration, malaise

Investigations

Chemistry	*Frequent*	Elevations in alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase
	Less frequent	Increases in total serum bilirubin, direct serum bilirubin, indirect serum bilirubin, serum creatinine, serum urea, serum glucose, decreases in serum bicarbonate, serum creatinine and serum potassium; increases in serum lactate dehydrogenase (LDH), serum phosphorus, serum potassium
Haematology	*Frequent*	Elevation in platelet count
	Less frequent	Decreases in white blood cells, platelet count, segmented neutrophils, haemoglobin and haematocrit; increases in eosinophils, activated partial thromboplastin time, prothrombin time (international normalised ratio (INR)), segmented neutrophils and white blood cells, decrease in lymphocytes; increases in band neutrophils, lymphocytes, metamyelocytes, monocytes, myelocytes; atypical lymphocytes
Urinalysis	*Less frequent*	Increases in urine bacteria, urine white blood cells, urine epithelial cells and urine red blood cells; urine yeast present, increase in urobilinogen

Paediatric population
CHILDREN AND ADOLESCENTS (3 months - 17 years of age)

System Organ Class	Frequency	Side effects
Psychiatric disorders	*Frequency unknown*	Altered mental status (including aggression, hallucinations)
Nervous system disorders	*Less frequent*	Headache
Vascular disorders	*Less frequent*	Hot flush, hypertension
Gastrointestinal disorders	*Frequent*	Diarrhoea, vomiting
	Less frequent	Faeces discoloured, melaena
Skin and subcutaneous tissue disorders	*Frequent*	Diaper dermatitis, rash
	Less frequent	Erythema, rash, petechiae
General disorders and administration site conditions	*Frequent*	Infusion site pain, infusion site pruritus, infusion site erythema, infusion site swelling
	Less frequent	Infusion site burning, injection site erythema, infusion site warmth

Investigations

Chemistry	*Frequent*	Elevations in ALT and AST
Haematology	*Frequent*	Decreases in neutrophil count
	Less frequent	Increases in platelet count, activated partial thromboplastin time, prothrombin time (INR), decreases in haemoglobin, increase in eosinophils

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 medicine. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose
Signs and symptoms:
No specific information is available on the treatment of overdosage with INVABEX.

Management of overdose:
In the event of an overdose, INVABEX should be discontinued and general supportive treatment given until renal elimination takes place. INVABEX can be removed by haemodialysis; however, no information is available on the use of haemodialysis to treat overdosage.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Antibacterials for systemic use, carbapenems
ATC code: J01DH03
Pharmacological classification: A 20.1.1 Broad and medium spectrum antibiotics

Mechanism of action
Ertapenem is a long-acting 1-ß methyl-carbapenem that is structurally related to beta-lactam antibiotics, such as penicillins and cephalosporins.
Ertapenem exerts bactericidal activity by inhibiting cell wall synthesis. This activity is mediated through the binding of ertapenem to penicillin binding proteins (PBPs). In *Escherichia coli*, it has strong affinity toward PBPs 1a, 1b, 2, 3, 4 and 5 with preference for PBPs 2 and 3.
Ertapenem has *in vitro* activity against a wide range of gram-positive and gram-negative aerobic and anaerobic bacteria.
Ertapenem has significant stability to hydrolysis by most classes of beta-lactamases, including penicillinases, and cephalosporinases and extended spectrum beta-lactamases, but not metallo-beta-lactamases.

Resistant organisms
Corynebacterium spp, *Enterococcus* spp (including *Enterococcus faecalis* and *Enterococcus faecium*), methicillin resistant *Staphylococcus aureus*, methicillin resistant coagulase negative *Staphylococcus*, *Acinetobacter* spp, *Pseudomonas* spp, *Stenotrophomonas maltophilia*.

5.2 Pharmacokinetic properties
Absorption:
Ertapenem, reconstituted with 1 % lidocaine (lignocaine) hydrochloride injection, (in saline without adrenaline (epinephrine)), is well absorbed. Following IM administration of ertapenem at the recommended dose of 1 g, the mean bioavailability is approximately 92 % and the mean peak plasma concentrations (C_{max}) are reached in approximately 2 hours (T_{max}).

Distribution:
Ertapenem is highly bound to human plasma proteins. In healthy young adults, the protein binding of ertapenem decreases as plasma concentrations increase, from approximately 95 % bound at an approximate plasma concentration of less than 100 µg/mL to approximately 85 % bound at an approximate plasma concentration of 300 µg/mL.
Average plasma concentrations (µg/mL) of ertapenem following a single 30-minute IV infusion of a 1 or 2 g dose and IM administration of a single 1 g dose in healthy young adults are presented in Table 1.

Table 1
Plasma concentrations of ertapenem in adults after single dose administration

Dose/Route	Average plasma concentrations (µg/mL)								
	0,5 h	1 h	2 h	4 h	6 h	8 h	12 h	18 h	24 h
1 g IV*	155	115	83	48	31	20	9	3	1
1 g IM	33	53	67	57	40	27	13	4	2
2 g IV*	283	202	145	86	58	36	16	5	2

*IV doses were infused at a constant rate over 30 minutes

The area under the plasma concentration curve (AUC) of ertapenem in adults increases nearly dose-proportionally over the 0,5 - 2 g dose range.
Ertapenem does not accumulate in adults after multiple IV doses ranging from 0,5 - 2 g daily or IM doses of 1 g daily.
Average plasma concentrations (µg/mL) of ertapenem in paediatric patients are presented in Table 2.

Table 2
Plasma concentrations of ertapenem in paediatric patients after single IV* dose administration

Age group (Dose)	Average plasma concentrations (µg/mL)								
	0,5 h	1 h	2 h	4 h	6 h	8 h	12 h	18 h	24 h
3 - 23 months									
(15 mg/kg)†	103,8	57,3	43,6	23,7	13,5	8,2	2,5	–	103,8
(20 mg/kg)†	126,8	87,6	58,7	28,4	–	12,0	3,4	0,4	126,8
(40 mg/kg)‡	199,1	144,1	95,7	58,0	–	20,2	7,7	0,6	199,1
2 - 12 years									
(15 mg/kg)†	113,2	63,9	42,1	21,9	12,8	7,6	3,0	–	113,2
(20 mg/kg)†	147,6	97,6	63,2	34,5	–	12,3	4,9	0,5	147,6
(40 mg/kg)‡	241,7	152,7	96,3	55,6	–	18,8	7,2	0,6	241,7
13 - 17 years									
(20 mg/kg)†	170,4	98,3	67,8	40,4	–	16,0	7,0	1,1	170,4
(1 g)§	155,9	110,9	74,8	–	24,0	–	6,2	–	155,9
(40 mg/kg)‡	255,0	188,7	127,9	76,2	–	31,0	15,3	2,1	255,0

*IV doses were infused at a constant rate over 30 minutes
†Up to a maximum dose of 1 g/day
‡Up to a maximum dose of 2 g/day
§Based on three patients receiving 1 g ertapenem who volunteered for pharmacokinetic assessment in one of the two safety and efficacy studies

The apparent volume of distribution (Vdss) of ertapenem in adults is approximately 8 litres (0,11 litre/kg) and approximately 0,2 litre/kg in paediatric patients 3 months - 12 years of age and approximately 0,16 litre/kg in paediatric patients 13 - 17 years of age.
Ertapenem penetrates suction-induced skin blisters. Concentrations of ertapenem achieved in skin blister fluid at each sampling point on the third day of 1 g once daily IV doses resulted in a ratio of AUC in skin blister fluid to AUC in plasma of 0,61.
Ertapenem penetrates into breastmilk.
Ertapenem does not inhibit P-glycoprotein-mediated transport of digoxin or vinblastine and ertapenem is not a substrate for P-glycoprotein-mediated transport (see section 4.5).

Biotransformation:
After IV infusion of 1 g of radio labelled ertapenem, the plasma radioactivity consists predominantly (94 %) of ertapenem.
The major metabolite of ertapenem is the ring-opened derivative formed by hydrolysis of the beta-lactam ring.
In vitro, ertapenem does not inhibit metabolism mediated by any of the six major cytochrome P450 (CYP) isoforms: 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 (see section 4.5).

Elimination:
Ertapenem is eliminated primarily by the kidneys. The mean plasma half-life in healthy young adults and patients 13 - 17 years of age is approximately 4 hours and approximately 2,5 hours in paediatric patients 3 months - 12 years of age.
Following IV administration of a 1 g dose of ertapenem to healthy young adults, approximately 80 % is recovered in urine and 10 % in faeces. Of the 80 % recovered in urine, approximately 38 % is excreted as unchanged substance and approximately 37 % as the ring-opened metabolite.
In healthy young adults given a 1 g IV dose, average concentrations of ertapenem in urine exceed 984 µg/mL during the period 0 - 2 hours post-dose and exceed 52 µg/mL during the period 12 - 24 hours post-dose.

Pharmacokinetics in special patient groups
Elderly
Plasma concentrations are slightly higher in elderly adults (65 years or older) relative to young adults (younger than 65 years). No dose adjustment is required for elderly patients.

Hepatic insufficiency
The pharmacokinetics of ertapenem in patients with hepatic insufficiency have not been established. Due to the limited extent of hepatic metabolism of ertapenem, its pharmacokinetics are not expected to be affected by hepatic impairment. Therefore, no dosage adjustment is necessary in patients with hepatic impairment.

Renal insufficiency
Following a single 1 g IV dose of ertapenem in adults, AUC is similar in patients with mild renal insufficiency (CrCl 60 - 90 mL/min/1,73 m^2) compared with healthy persons (ages 25 - 82 years).
The AUC is increased in patients with:
- moderate renal insufficiency (CrCl 31 - 59 mL/min/1,73 m^2), approximately 1,5 fold compared with healthy persons
- advanced renal insufficiency (CrCl 5 - 30 mL/min/1,73 m^2), approximately 2,6 fold compared with healthy persons
- end-stage renal insufficiency (CrCl less than 10 mL/min/1,73 m^2), approximately 2,9 fold compared with healthy persons.

Following a single 1 g IV dose given immediately prior to a haemodialysis session, approximately 30 % of the dose is recovered in the dialysate.

There are no data in paediatric patients with renal insufficiency.
A dosage adjustment is recommended for patients with advanced or end-stage renal insufficiency (see section 4.2).

Paediatric population
Plasma concentrations of ertapenem are comparable in paediatric patients 13 - 17 years of age and adults following a 1 g once daily IV dose.
Following the 20 mg/kg dose (up to a maximum dose of 1 g), the pharmacokinetic parameter values in patients 13 - 17 years of age were generally comparable to those in healthy young adults.
To provide an estimate of the pharmacokinetic data if all patients in this age group were to receive a 1 g dose, the pharmacokinetic data were calculated adjusting for a 1 g dose, assuming linearity. A comparison of results shows that a 1 g once daily dose of ertapenem achieves a pharmacokinetic profile in patients 13 - 17 years of age comparable to that of adults. The ratios (13 - 17 years/adults) for AUC, the end of infusion concentration and the concentration at the midpoint of the dosing interval were 0,99, 1,20 and 0,84 respectively.
Plasma concentrations at the midpoint of the dosing interval following a single 15 mg/kg IV dose of ertapenem in patients 3 months - 12 years of age are comparable to plasma concentrations at the midpoint of the dosing interval following a 1 g once daily IV dose in adults (see Distribution). The plasma clearance (mL/min/kg) of ertapenem in patients 3 months - 12 years of age is approximately 2 - fold higher as compared to that in adults. At the 15 mg/kg dose, the AUC value (doubled to model a twice daily dosing regimen, i.e., 30 mg/kg/day exposure) in patients 3 months - 12 years of age was comparable to the AUC value in young healthy adults receiving a 1 g IV dose of ertapenem.

5.3 Preclinical safety data
Not applicable.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Sodium hydrogen carbonate
Sodium hydroxide (for pH adjustment)

6.2 Incompatibilities
DO NOT USE SOLVENTS OR INFUSION FLUIDS CONTAINING DEXTROSE TO RECONSTITUTE OR FOR THE ADMINISTRATION OF ERTAPENEM.
In the absence of compatibility studies, this medicine should not be mixed with other medicines except those mentioned in section 6.6.

6.3 Shelf life
Before reconstitution
Shelf-life: 24 months.

Reconstituted solutions
From a microbial point of view, the product should be used immediately.

Reconstituted intramuscular injection solution:
The reconstituted IM solution should be used within 1 hour after preparation.

Reconstituted intravenous infusion solution:
If not used immediately, the storage time and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 - 8 °C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.
Diluted solutions (approximately 20 mg/mL ertapenem) are physically and chemically stable for 6 hours at or below 25 °C and for 24 hours at 2 - 8 °C (in a refrigerator). Solutions should be used within 4 hours of their removal from the refrigerator.
Do not freeze solutions of INVABEX.
For single use only.

6.4 Special precautions for storage
Powder:
Store at or below 25 ºC. Do not freeze.
Reconstituted and diluted solution:
See section 6.3.

INVABEX 1 g sterile powder for solution for injection or infusion.

INVABEX 1 g sterile powder for solution for injection or infusion.

6.5 Nature and contents of container
INVABEX is supplied in 20 mL colourless clear Type I glass vials with chlorobutyl rubber stoppers and aluminium/ lacquered flip-off overseals.
Supplied in packs of 1 or 10 vials.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Instructions for use
For single use only.
Do not mix or co-infuse INVABEX with other medicines.
Do not use diluents containing dextrose (α-d-glucose).
- **Adults and adolescents (13 - 17 years of age)**

Preparation for intravenous administration:
1. Reconstitute the contents of a 1 g vial of INVABEX with 10 mL of water for injection, 0,9 % sodium chloride injection (154 mmol/l) or bacteriostatic water for injection to yield a reconstituted solution of approximately 100 mg/mL. Shake well to dissolve (see section 6.3).
2. Immediately transfer contents of the reconstituted vial to 50 mL of 0,9 % sodium chloride injection (154 mmol/l).
3. Diluted solutions should be used immediately (see section 6.3).
4. Complete the infusion within 6 hours of reconstitution.

Administer the infusion for a period of 30 minutes.
The reconstituted solutions should be inspected visually for particulate matter and discolouration prior to administration, whenever the container permits. Solutions of INVABEX range from colourless to pale yellow. Variations of colour within this range do not affect potency. Any unused product or waste material should be disposed of in accordance with local requirements.

Preparation for intramuscular administration:
INVABEX must be reconstituted prior to administration.
1. Reconstitute the contents of a 1 g vial of INVABEX with 3,2 mL of 1,0 % or maximum 3,2 mL of 2 % lidocaine (lignocaine) hydrochloride injection*** (without adrenaline (epinephrine)). Shake vial thoroughly to form solution. This represents the maximum recommended dose of lidocaine (lignocaine).
2. Immediately withdraw the contents of the vial and administer by deep intramuscular injection into a large muscle mass (such as the gluteal muscles or lateral part of the thigh).
3. The reconstituted IM solution should be used within 1 hour after preparation.

Note: The reconstituted solution should not be administered intravenously.
*** Refer to the professional information for lidocaine (lignocaine) hydrochloride.

- **Paediatric patients (3 months - 12 years of age)**

Preparation for intravenous administration:
INVABEX must be reconstituted and then diluted prior to administration.
Do not mix or co-infuse INVABEX with other medicines.
Do not use diluents containing dextrose (α-d-glucose).
1. Reconstitute the contents of a 1 g vial of INVABEX with 10 mL of water for injection, 0,9 % sodium chloride injection (154 mmol/l) or bacteriostatic water for injection to yield a reconstituted solution of approximately 100 mg/mL.
2. Shake well to dissolve and immediately withdraw a volume equal to 15 mg/kg of body mass (not to exceed 1 g/day) and dilute in 0,9 % sodium chloride injection (154 mmol/l) to a final concentration of 20 mg/mL or less.
3. Complete the infusion within 6 hours of reconstitution.

Administer the infusion over a period of 30 minutes.

Preparation for intramuscular administration:
INVABEX must be reconstituted prior to administration.
1. Reconstitute the contents of a 1 g vial of INVABEX with 3,2 mL of 1,0 % or maximum 3,2 mL of 2,0 % lidocaine (lignocaine) hydrochloride injection*** (without adrenaline (epinephrine)). Shake vial thoroughly to form a solution. This represents the maximum recommended dose of lidocaine (lignocaine).
2. Immediately withdraw a volume equal to 15 mg/kg of body weight (not to exceed 1 g/day) and administer by deep intramuscular injection into a large muscle mass (such as the gluteal muscles or lateral part of the thigh).
3. The reconstituted IM solution should be used within 1 hour after preparation.

Note: This reconstituted solution should not be administered intravenously.
*** Refer to the professional information for lidocaine (lignocaine) hydrochloride.

Inspect parenteral products visually for particulate matter and discolouration prior to use, whenever solution and container permit. Solutions of INVABEX range from colourless to pale yellow. Variations of colour within this range do not affect the potency of the product.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Cape Town, South Africa
Tel: +27 21 707 7000
or 0860-PHARMA (742 762)

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16 March 2021

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14 January 2025

pharma dynamics

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

INVABEX 1 g sterile powder for solution for injection or infusion
Ertapenem
Sugar free

Read all of this leaflet carefully before you are given INVABEX
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist, nurse or other healthcare provider.

What is in this leaflet

1. What INVABEX is and what it is used for
INVABEX contains ertapenem, which is an antibiotic of the beta-lactam group.
Ertapenem can kill a wide range of bacteria (germs) that cause infections in various parts of the body.
INVABEX may be given to persons 3 months of age and older.

Your doctor may have prescribed INVABEX to you or your child if you have one (or more) of the following types of infection:
- infection in the abdomen
- skin infections, including diabetic foot infections
- infection in the lungs (pneumonia)
- certain urinary infections
- acute pelvic infections.

2. What you need to know before you are administered INVABEX
INVABEX should not be administered:
- if you are hypersensitive (allergic) to the active substance (ertapenem) or any of the other ingredients of INVABEX (see section 6)
- if you are allergic to other beta-lactam antibiotics such as penicillins, cephalosporins (used to treat various infections)
- if you have bacterial meningitis (infection and inflammation of the membranes and fluid around the brain and spinal cord)
- if you are allergic to lidocaine (lignocaine) hydrochloride (a local anaesthetic). If INVABEX is injected into the muscle, it is dissolved in lidocaine (lignocaine) injection.

Warnings and precautions
Tell your doctor or healthcare professional before being given the injection:
- if you have allergies to other medicines (including other antibiotics) or other substances
- if you get an allergic reaction (such as swelling of the face, tongue or throat, trouble breathing or swallowing, skin rash) during treatment (tell your doctor straight away as you may need urgent medical treatment). Serious, sometimes fatal allergic reactions have been reported with ertapenem (contained in INVABEX). See section 4
- if you have central nervous system disorders, such as localised tremors (shaking), or seizures (fits)
- if you are taking medicines called valproic acid or divalproex sodium (see Other medicines and INVABEX below)
- if you have advanced kidney disease and if you get dialysis treatment
- if you are going to have an operation that may take longer than 4 hours.

It is important that you tell your doctor if you have diarrhoea before, during or after your treatment with INVABEX. This is because you may have a condition known as colitis (an inflammation of the bowel). Do not take any medicine to treat diarrhoea without first checking with your doctor.

INVABEX kills certain bacteria, but other bacteria and fungi may continue to grow more than normal and cause thrush or diarrhoea. This is called overgrowth. Your doctor will monitor you for overgrowth and treat you if necessary (see section 4 Possible side effects).

Children and adolescents (3 months - 17 years of age)
There is no experience in children under 3 months of age.
Experience with INVABEX is limited in children less than two years of age.

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

Tell your doctor if you take:
- valproic acid or divalproex sodium (medicines used to treat epilepsy, bipolar disorder, migraines, or schizophrenia)
- probenecid (a medicine for gout).

This is because INVABEX can affect the way some other medicines work. Your doctor will decide whether you should use INVABEX in combination with other medicines.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before receiving INVABEX.

Safety in pregnancy has not been established.
INVABEX is passed into in human breastmilk. Safety in nursing mothers has not been established. If you receive INVABEX you should not breastfeed your baby as the baby may be affected.

There is no information on the effect of INVABEX on fertility in men and women.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed.
Dizziness and sleepiness may be side effects of INVABEX. If you have these side effects, you should not drive or handle tools or machinery.
It is not always possible to predict to what extent INVABEX may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which INVABEX affects them.

INVABEX contains sodium
INVABEX contains approximately 137 mg (approximately 6,0 millimoles) of sodium (main component of cooking/table salt) in each vial. This is equivalent to 6,85 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use INVABEX
Do not share medicines prescribed for you with any other person.
You will not be expected to give yourself INVABEX. It will be given to you by a person who is qualified to do so.
Your healthcare provider will prepare INVABEX and give it to you intravenously (into a vein) or intramuscularly (into a muscle).

Adults and adolescents 13 years of age and older:
The recommended dose of INVABEX for adults and adolescents 13 years of age and older is 1 gram (g) given once a day.

Children 3 months - 12 years:
The recommended dose for children 3 months - 12 years of age is 15 mg/kg given twice daily (not to exceed 1 g/day).

Your doctor will however prescribe a dose just suitable for you, or your child. The dose will depend on the type of infection you have and the condition of your kidneys.
Your doctor will decide for how long to treat you, or your child. The duration will depend on the type of infection and your response on the treatment.
It is very important that you continue to receive INVABEX for as long as your doctor prescribes it.
If you have the impression that the effect of INVABEX is too strong or too weak, tell your doctor or pharmacist.

If you are administered more INVABEX than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Since a healthcare professional will administer INVABEX, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdose.

If you forget to use INVABEX
Since a healthcare professional will administer INVABEX, it is unlikely that the dose will be missed.

4. Possible side effects
INVABEX can have side effects.
Not all side effects reported for INVABEX are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using INVABEX, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop using INVABEX and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- fainting
- DRESS (drug rash with eosinophilia and systemic symptoms): This is a serious or life-threatening allergic reaction that may affect your skin or other parts of your body, such as your liver or blood cells. You may have fever, tender swollen glands in the neck, armpits and groin and a rash
- serious skin disorders, such as blistering or peeling of the skin, Stevens-Johnson syndrome (a complex allergic reaction, with skin and mucous membrane lesions, which may become severe and may be fatal)
- severely upset stomach (pseudomembranous colitis). You may have inflammation of the bowels, that could be life-threatening. The symptoms may include severe abdominal pain and diarrhoea, or diarrhoea tinged with blood, vomiting and fever.

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

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
Adults 18 years of age and older:
- yellowing of the eyes and skin (jaundice or a liver disorder)
- seizure, tremor
- slow heart rate, irregular heartbeat, quick heartbeat
- low or high blood pressure
- an allergic reaction called Kounis syndrome (you may experience symptoms such as chest discomfort, acute chest pain, faintness, headache, nausea and dyspnoea)
- kidney function affected. Problems to urinate or to pass adequate urine (acute renal insufficiency)
- hallucinations (hearing and seeing things that do not exist)
- altered mental state (including aggression, disturbance of mental abilities, disorientation, confusion, memory loss, personality changes)
- decreased level of consciousness.

Children and adolescents (3 months - 17 years of age):
- hallucinations
- altered mental status (including aggression)
- high blood pressure.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
Adults 18 years of age and older:
- headache
- problems with the vein into which the medicine is given (including inflammation, formation of a lump, swelling at the injection site)
- diarrhoea, nausea, vomiting
- rash, itching
- increase in various liver enzymes. Some of the signs may be yellowing of the skin, whites of the eyes, pain or swelling in the abdomen, nausea and vomiting, dark urine, pale-coloured stools
- increased blood platelet count. Some of the signs may be headache, numbness of hands or feet, weakness, bleeding in mouth or gums, bloody stool, easy bleeding or bruising, nosebleeds
- muscle cramp, shoulder pain.

Children and adolescents (3 months - 17 years of age):
- diarrhoea, vomiting
- nappy rash, rash
- pain at the infusion site
- changes in white blood cell count, changes in liver function tests.

Less frequent side effects:
Adults 18 years of age and older:
- infections, such as oral thrush, vaginal thrush, yeast and fungal infections, wound infection after an operation, urinary tract infection
- laboratory tests may show very low white cell or blood platelet counts (which may lead to more infections or bleeding)
- anorexia (eating disorder)
- low blood sugar
- sleepiness, sleeplessness
- anxiety, depression
- altered taste sensation
- changes to the white part of the eye
- bleeding
- shortness of breath, sore throat, nasal congestion, cough, abnormal breathing sounds, wheezing
- nose bleeds
- constipation
- abdominal pain, inflammation of the membrane that lines the abdomen in the pelvic area
- acid regurgitation, indigestion, dry mouth, difficulty swallowing
- faecal incontinence
- inflammation of the liver and/or the gallbladder
- skin redness, inflammation
- skin blisters in a clustered arrangement on the face and possibly perineum, that may spread to the limbs, trunk, hands, feet and scalp (linear IgA bullous disease)
- miscarriage, genital bleeding
- fatigue
- leaking of fluid into the tissue and skin around the injection site
- fever, feeling unwell, swelling, chest pain
- changes in various laboratory blood and urine tests, indicating for example effects on the liver, kidneys, sugar, blood chemistry, cholesterol.

Children and adolescents (3 months - 17 years of age):
- headache
- hot flush
- discoloured faeces, black tar-like faeces
- skin redness, skin rash, tiny purple, red, or brown spots on the skin
- burning, itching, redness and warmth at infusion site, redness at injection site
- increase in platelet count and changes in other blood clotting tests.

The following side effects have been reported but the frequency for them to occur is not known:
Adults 18 years of age and older:
- uncontrolled, involuntary movement, spasmodic, jerky contractions
- unsteady walking
- stained teeth
- weak muscles.

If you notice any side effects not mentioned 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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
By reporting side effects, you can help provide more information on the safety of INVABEX. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

5. How to store INVABEX
Store all medicines out of reach of children.

Vial with powder:
Store at or below 25 ºC. Do not freeze.
Do not use INVABEX after the expiry date which is stated on the vial and carton. The expiry date refers to the last day of that month.

After reconstitution:
For single use only.

Reconstituted solutions
From a microbial point of view, the product should be used immediately.

Reconstituted intramuscular injection solution:
The reconstituted IM solution should be used within 1 hour after preparation.

Reconstituted intravenous infusion solution:
If not used immediately, the storage time and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 - 8 °C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.
Diluted solutions (approximately 20 mg/mL ertapenem) are physically and chemically stable for 6 hours at or below 25 °C and for 24 hours at 2 - 8 °C (in a refrigerator). Solutions should be used within 4 hours of their removal from the refrigerator.
Do not freeze solutions of INVABEX.
Do not use INVABEX if you notice particulate matter and discolouration in the reconstituted solutions.
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 INVABEX contains:
The active substance is ertapenem.
Each vial of INVABEX contains ertapenem sodium equivalent to ertapenem 1 g.
The other ingredients are sodium hydrogen carbonate and sodium hydroxide (for pH adjustment).

What INVABEX looks like and contents of the pack
INVABEX is a sterile white to yellowish powder for solution for injection or infusion.
Solutions of INVABEX range from colourless to pale yellow and is free from visible particles.
INVABEX is supplied in 20 mL colourless clear Type I glass vials with chlorobutyl rubber stoppers and aluminum/ lacquered flip-off overseals.
Supplied in packs of 1 or 10 vials.
Not all pack sizes may be marketed.

Holder of Certificate of Registration
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Cape Town, South Africa
Tel: + 27 21 707 7000
or 0860-PHARMA (742 762)

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C6097

pharma dynamics

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS: S4

INVABEX 1 g steriele poeier vir oplossing vir inspuiting of infusie
Ertapenem
Suikervry

Lees die hele inligtingsblad deeglik deur voordat u INVABEX ontvang
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer.

Inhoud van hierdie inligtingsblad

1. Wat INVABEX is en waarvoor dit gebruik word
INVABEX bevat ertapenem, wat 'n antibiotikum is van die beta-laktaamgroep.
Ertapenem kan 'n wye verskeidenheid bakterieë (kieme) wat infeksies in verskillende dele van die liggaam veroorsaak, uitwis.
INVABEX mag aan persone van 3 maande oud en ouer toegedien word.

U dokter kon INVABEX aan u of u kind voorgeskryf het, indien daar een (of meer) van die volgende tipes infeksies voorgekom het:
- buikinfeksie
- velinfeksies, insluitend diabetiese voetinfeksies
- infeksie in die longe (pneumonie)
- sekere urinêre infeksies
- akute bekken infeksies.

2. Wat u moet weet voordat INVABEX aan u toegedien word
INVABEX moet nie aan u toegedien word:
- indien u hipersensitief (allergies) is vir die aktiewe bestanddeel (ertapenem) of vir enige van die ander bestanddele van INVABEX nie (sien afdeling 6)
- indien u allergies is vir ander beta-laktaam antibiotika soos penisilliene, kefalosporiene (word gebruik om verskeie infeksies te behandel) nie
- indien u bakteriële meningitis het nie (infeksie en inflammasie van die membrane en vloeistof rondom die brein en rugmurg)
- indien u allergies is vir lidokaïen (lignokaïen) hidrochloried nie ('n lokale verdowingsmiddel). Indien INVABEX in die spier ingespuit word, word dit opgelos in lidokaïen (lignokaïen) inspuiting.

Waarskuwings en voorsorgmaatreëls
Lig u dokter of gesondheidsorgverskaffer in, voordat INVABEX aan u toegedien word:
- indien u allergieë het vir ander medisyne (insluitend ander antibiotika), of ander stowwe
- indien u 'n allergiese reaksie (soos swelling in die gesig, tong of keel, asemhalings- of slukprobleme, veluitslag), tydens die behandeling ervaar (vertel u dokter dadelik, aangesien u dringende mediese behandeling mag benodig). Ernstige, soms noodlottige allergiese reaksies is met ertapenem (soos bevat in INVABEX), aangemeld. Sien afdeling 4
- indien u versteurings in die sentrale senuweestelsel, soos gelokaliseerde tremors (bewerigheid), of aanvalle (stuipe) het
- indien u medisyne, wat valproïensuur of natriumdivalproeks genoem word, neem (sien Ander medisynes en INVABEX benede)
- indien u gevorderde niersiekte het en u dialise behandeling ontvang
- indien u 'n operasie wat langer as 4 uur mag duur, moet ondergaan.

Dit is belangrik dat u vir u dokter sê as u diarree het voor, tydens of na u behandeling met INVABEX. Dit is omdat u 'n toestand mag hê wat bekend staan as kolitis ('n inflammasie van die derms). Moenie enige medisyne neem om die diarree te behandel, sonder om eers u dokter te raadpleeg nie.

INVABEX wis sekere baktterieë uit, maar ander bakterieë en swamme mag aanhou om meer as gewoonlik te groei en sproei of diarree veroorsaak. Dit staan bekend as oorgroeiing. U dokter sal u vir oorgroeiing moniteer en u behandel indien nodig (sien afdeling 4 Moontlike newe-effekte).

Kinders en adolessente (3 maande - 17 jaar oud)
Daar is geen ervaring met kinders jonger as 3 maande oud nie.
Ondervinding met INVABEX is beperk by kinders jonger as twee jaar oud.

Ander medisyne en INVABEX
Lig altyd u gesondheidsorgverskaffer in, indien enige ander medisyne neem (Dit sluit aanvullende of tradisionele medisyne in).

Vertel u dokter indien u die volgende neem:
- valproïensuur of natriumdivalproeks (medisyne wat gebruik word vir die behandeling van epilepsie, bipolêre versteuring, migraine of skisofrenie)
- probenesied ('n medisyne vir jig).

Dit is omdat INVABEX die manier waarop sommige ander medisynes werk, kan beïnvloed. U dokter sal besluit of u INVABEX in kombinasie met ander medisyne kan gebruik.

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is of u baba borsvoed, vermoed dat u swanger is, of 'n baba beplan, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgverskaffer vir advies, voordat u INVABEX ontvang.

Veiligheid tydens swangerskap is nie vasgestel nie.
INVABEX word uitgeskei in menslike borsmelk. Veiligheid by moeders wie borsvoed, is nie vasgestel nie. Indien u INVABEX ontvang, moet u nie u baba borsvoed nie, want die baba kan aangetas word.

Daar is geen inligting omtrent die effek van INVABEX op vrugbaarheid by mans en vroue nie.

Bestuur en hantering van masjiene
Geen navorsing op die vermoë om te bestuur en masjiene te hanteer, is uitgevoer nie.
Duiseligheid en slaperigheid mag newe-effekte van INVABEX wees. Indien u hierdie newe-effekte ervaar, moet u nie bestuur, of gereedskap of masjinerie hanteer nie.
Dit is nie altyd moontlik om te voorspel tot watter mate INVABEX met die daaglikse aktiwiteite van 'n pasiënt inmeng nie. Pasiënte moet verseker dat hulle nie by bogenoemde aktiwiteite betrokke raak, totdat hulle bewus is tot watter mate INVABEX hulle beïnvloed nie.

INVABEX bevat natrium
INVABEX bevat ongeveer 137 mg (ongeveer 6,0 millimol) natrium (hoofkomponent van kook/tafelsout) in elke flessie. Dit is gelykstaande aan 6,85 % van die aanbevole maksimum daaglikse dieetinname van natrium vir 'n volwassene.

3. Hoe om INVABEX te neem
Moenie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie.
Daar sal nie van u verwag word om INVABEX aan uself toe te dien nie. Dit sal aan u toegedien word deur 'n gekwalifiseerde persoon.
U gesondheidsorgverskaffer sal INVABEX voorberei en dit intraveneus (in 'n aar) of intramuskulêr (in 'n spier) aan u toedien.

Volwassenes en adolessente, 13 jaar oud en ouer:
Die aanbevole INVABEX dosis vir volwassenes en adolessente 13 jaar en ouer is 1 gram (g) wat een keer per dag toegedien word.

Kinders, 3 maande - 12 jaar oud:
Die aanbevole dosis vir kinders van 3 maande - 12 jaar oud, is 15 mg/kg, wat twee keer per dag toegedien word (nie meer as 1 g/dag nie).

U dokter sal egter 'n dosis voorskryf wat geskik is vir u of u kind. Die dosis sal afhang van die tipe infeksie wat u het en die toestand van u niere.
U dokter sal besluit vir hoe lank u of u kind moet behandel word. Die tydsduur sal afhang van die tipe infeksie en u reaksie op die behandeling.
Dit is baie belangrik dat u voortgaan om INVABEX te ontvang vir solank as wat u dokter dit voorskryf.
Indien u onder die indruk is dat die effek van INVABEX té sterk, of té swak is, vertel u dokter of apteker.

Indien meer INVABEX aan u toegedien word as wat u moes ontvang
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal of gifbeheersentrum.

Aangesien 'n gesondheidsorgdeskundige INVABEX sal toedien, sal hy/sy die dosis beheer. In geval van oordosering sal u dokter egter die oordosering hanteer.

Indien u 'n INVABEX dosis oorgeslaan het
Aangesien 'n gesondheidsorgdeskundige INVABEX sal toedien, is dit onwaarskynlik dat 'n dosis oorgeslaan sal word.

4. Moontlike newe-effekte
INVABEX kan newe-effekte hê.
Nie alle newe-effekte wat vir INVABEX aangemeld is, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid versleg, of u enige ongunstige effekte ervaar terwyl u INVABEX ontvang, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgdeskundige vir advies.

Indien enige van die volgende gebeur, staak die gebruik van INVABEX en vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal:
- swelling van die hande, voete, enkels, gesig lippe, mond, of keel, wat sluk of asemhaling mag bemoeilik
- DRESS ('n geneesmiddel uitslag met eosinofilie en sistemiese simptome): Dit is 'n ernstige of lewensgevaarlike allergiese reaksie wat u vel, of ander gedeeltes van u liggaam, soos u lewer of bloedselle, mag aantas. U kan koors, gevoelige geswelde kliere in die nek, oksels en lies ondervind en 'n uitslag kry
- ernstige velaandoenings, soos blase of afskilfering van die vel, Stevens-Johnson-sindroom ('n komplekse allergiese reaksie met letsels op die vel en slymvliesmembrane, wat ernstig kan word en noodlottig mag wees).
- erg omgekrapte maag (pseudomembraneuse kolitis) U kan inflammasie van die derms, wat lewensbedreigend mag wees, ondervind. Die simptome mag erge buikpyn en diarree, of diarree met bloed bevlek, braking en koors, insluit.

Hierdie is alles baie ernstige newe-effekte. Indien u dit ondervind, kon u moontlik 'n ernstige allergiese reaksie teenoor INVABEX ervaar het. U mag dringende mediese aandag, of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
Volwassenes 18 jaar oud en ouer:
- vergeling van die oë en vel (geelsug, of 'n lewerversteuring)
- aanval, tremor
- stadige harttempo, onreëlmatige hartklop, vinnige hartklop
- lae of hoë bloeddruk
- 'n allergiese reaksie wat Kounis sindroom genoem word (u mag simptome soos borsongemak, akute borspyn, lighoofdigheid, hoofpyn, naarheid en dispnee, ervaar)
- nierfunksie word aangetas. Probleme om te urineer, of voldoende te urineer (akute renale ontoereikendheid)
- hallusinasies (hoor en sien dinge wat nie bestaan nie)
- verandering in u geestestoestand (insluitend aggressie, versteuring van geestesvermoë, disoriëntasie, verwarring, geheueverlies, persoonlikheidsveranderinge)
- afname in die bewussynsvlak.

Kinders en adolessente (3 maande - 17 jaar oud):
- hallusinasies
- verandering in geestestoestand (insluitend aggressie)
- hoë bloeddruk.

Hierdie is alles ernstige newe- effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende opmerk:
Algemene newe-effekte:
Volwassenes 18 jaar oud en ouer:
- hoofpyn
- probleme met die aar waarin die medisyne toegedien word (insluitend inflammasie, vorming van 'n knop, swelling by die inspuitplek)
- diarree, naarheid, braking
- jeuk, uitslag
- toename in verskeie lewerensieme. Sommige van die tekens kan wees dat die vel en wit gedeeltes van die oë, geel verkleur, pyn of swelling in die buik, naarheid en braking, donker urine, bleek-kleurige stoelgange.
- verhoogde bloedplaatjietelling. Sommige van die tekens kan hoofpyn, gevoelloosheid van die hande of voete, swakheid, bloeding in die mond of tandvleis, bloederige stoelgang, maklike bloeding of kneusing, neusbloedings, insluit
- spierkramp, skouerpyn.

Kinders en adolessente (3 maande - 17 jaar oud):
- diarree, braking
- luieruitslag, uitslag
- pyn by die inspuitingsplek
- veranderinge in witbloedseltelling, veranderinge in lewerfunksietoetse.

Minder algemene newe-effekte:
Volwassenes 18 jaar oud en ouer:
- infeksies, soos mondsproei, vaginale sproei, gis- en swaminfeksies, wondinfeksie na 'n operasie, urienweginfeksie
- laboratoriumtoetse kan 'n baie lae aantal witbloedselle of bloedplaatjies toon (wat tot meer infeksies of bloeding mag lei)
- anoreksie (eetversteuring)
- lae bloedsuiker
- slaperigheid, slapeloosheid
- angs, depressie
- verandering in smaaksensasie
- veranderinge in die wit gedeelte van die oog
- bloeding
- asemnood, seer keel, neuskongestie, hoes, abnormale asemhalingsgeluide, gehyg
- neusbloeding
- hardlywigheid
- buikpyn, inflammasie van die buikmembrane in die bekkenarea
- suur terugstroming, indigestie, droë mond, problematiese sluk
- fekale inkontinensie
- inflammasie van die lewer en/of galblaas
- rooiheid van die vel, inflammasie
- velblase in 'n trosformasie op die gesig en moontlik die perineum, wat mag versprei na die ledemate, bolyf, hande, voete en kopvel (linière IgA bulleuse siekte)
- miskraam, genitale bloeding
- uitputting
- lekkasie van vloeistof in die weefsel en vel, rondom die inspuitingsplek
- koors, voel ongesteld, swelling, borspyn
- veranderinge in verskeie laboratorium bloed- en urientoetse, wat byvoorbeeld effekte op die lewer, niere, suiker, bloedchemie, cholesterol, aandui.

Kinders en adolessente (3 maande - 17 jaar oud):
- hoofpyn
- warm gloed
- verkleurde stoelgang, swart, teeragtige stoelgang
- rooiheid van die vel, veluitslag, klein pers, rooi, of bruin kolletjies op die vel
- branderigheid, jeukerigheid, rooiheid en hitte by die plek van infusie, rooiheid by die inspuitingsplek
- verhoging in plaatjietelling en veranderinge in bloedstollingstoetse.

Die volgende newe-effekte is aangemeld, maar die frekwensie van voorkoms is onbekend:
Volwassenes 18 jaar oud en ouer:
- onbeheerde, onwillekeurige beweging, spasmodiese, rukkerige kontraksies
- wankelrige loop
- gevlekte tande
- swak spiere.

Indien u enige newe-effekte opmerk, wat nie in hierdie inligtingsblad genoem word nie, lig asseblief u dokter, of apteker in.

Aanmelding van newe-effekte
Indien u newe-effekte ervaar, praat met u dokter, apteker of verpleegkundige. U kan ook newe-effekte by SAHPRA via die Med Safety toepassing (Medsafety X SAHPRA) en eReporting platform (who-umc.org), wat op SAHPRA se webtuiste gevind kan word, aanmeld.
Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van INVABEX te verskaf.
U kan ook 'n e-pos direk aan die maatskappy stuur, pharmacovigilance@pharmadynamics.co.za, om die veiligheid van die produk te verseker.

5. Hoe om INVABEX te bewaar
Bewaar alle medisyne buite bereik van kinders.

Flessie met poeier:
Bewaar teen of benede 25 °C. Moenie vries nie.
Moenie INVABEX na die vervaldatum wat op die flessie en die kartonhouer aangedui word, gebruik nie. Die vervaldatum verwys na die laaste dag van daardie maand.

Na hersamestelling:
Slegs vir eenmalige gebruik.

Hersaamgestelde oplossings
Vanuit 'n mikrobiologiese oogpunt, moet die produk dadelik gebruik word.

Hersaamgestelde intramuskulêre inspuiting oplossing
Die hersaamgestelde IM oplossing, moet binne 1 uur na voorbereiding, gebruik word.

Hersaamgestelde intraveneuse infusie oplossing
Indien dit nie dadelik gebruik word nie, is die in-gebruik bergingstye en toestande voor gebruik, die verantwoordelikheid van die gebruiker en sal dit gewoonlik nie langer as 24 uur teen 2 - 8 °C wees nie, tensy hersamestelling/verdunning onder gekontroleerde en gevalideerde aseptiese toestande plaasgevind het.
Verdunde oplossings (ongeveer 20 mg/mL ertapenem) is fisies en chemies stabiel vir 6 uur teen of benede 25 °C en vir 24 uur teen 2 - 8 °C (in 'n yskas). Oplossings moet binne 4 uur nadat dit uit die yskas verwyder is, gebruik word. Moenie INVABEX oplossings vries nie.
Moenie INVABEX gebruik, indien u deeltjies en verkleuring in die hersaamgestelde oplossings opmerk nie.
Neem alle ongebruikte medisyne terug na u apteker.
Moenie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette) weggooi nie.

6. Verpakkingsinhoud en ander inligting
Wat INVABEX bevat:
Die aktiewe bestanddeel is ertapenem.
Elke flessie INVABEX bevat natriumertapenem gelykstaande aan ertapenem 1 g.
Die ander bestanddele is natriumwaterstofkarbonaat en natriumhidroksied (vir pH aanpassing).

Hoe INVABEX lyk en die verpakkingsinhoud
INVABEX is 'n steriele wit tot gelerige poeier vir oplossing vir inspuiting of infusie.
Oplossings van INVABEX wissel van kleurloos tot liggeel en is vry van sigbare deeltjies.
INVABEX word in 20 mL kleurlose, deursigtige, Tipe I flessies met chloorbutielrubberproppe en aluminium/gelakte opskiet verseëlings voorsien.
Verskaf in verpakkings van 1 of 10 flessies.
Nie alle verpakkingshoeveelhede word noodwendig bemark nie.

Houer van die registrasiesertifikaat
Pharma Dynamics (Edms.) Bpk.
1ste Vloer Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Kaapstad, Suid-Afrika
Tel: +27 21 707 7000
of 0860-PHARMA (742 762)

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