MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA

INVANZ®
(ERTAPENEM FOR INJECTION)

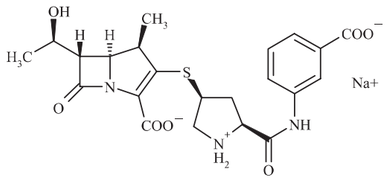
To reduce the development of drug-resistant bacteria and maintain the effectiveness of INVANZ and other antibacterial drugs, INVANZ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

For Intravenous or Intramuscular Use

DESCRIPTION

INVANZ* (Ertapenem for Injection) is a sterile, synthetic, parenteral, 1-β methyl-carbapenem that is structurally related to beta-lactam antibiotics.

Chemically, INVANZ is described as [4*R*-[3(3*S**,5*S**),4α,5β, 6β(*R**)]]-3-[[5-[[(3-carboxyphenyl)amino]carbonyl]-3-pyrrolidinyl]thio]-6-(1-hydroxyethyl)-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid monosodium salt. Its molecular weight is 497.50. The empirical formula is $C_{22}H_{24}N_3O_7SNa$, and its structural formula is:



Ertapenem sodium is a white to off-white hygroscopic, weakly crystalline powder. It is soluble in water and 0.9% sodium chloride solution, practically insoluble in ethanol, and insoluble in isopropyl acetate and tetrahydrofuran.

INVANZ is supplied as sterile lyophilized powder for intravenous infusion after reconstitution with appropriate diluent (see DOSAGE AND ADMINISTRATION, PREPARATION OF SOLUTION) and transfer to 50 mL 0.9% Sodium Chloride Injection or for intramuscular injection following reconstitution with 1% lidocaine hydrochloride. Each vial contains 1.046 grams ertapenem sodium, equivalent to 1 gram ertapenem. The sodium content is approximately 137 mg (approximately 6.0 mEq).

Each vial of INVANZ contains the following inactive ingredients: 175 mg sodium bicarbonate and sodium hydroxide to adjust pH to 7.5.

CLINICAL PHARMACOLOGY

Pharmacokinetics

Average plasma concentrations (mcg/mL) of ertapenem following a single 30-minute infusion of a 1 g intravenous (IV) dose and administration of a single 1 g intramuscular (IM) dose in healthy young adults are presented in Table 1.

Table 1
Plasma Concentrations of Ertapenem After Single Dose Administration

	Average Plasma Concentrations (mcg/mL)								
Dose/Route	0.5 hr	1 hr	2 hr	4 hr	6 hr	8 hr	12 hr	18 hr	24 hr
1 g IV*	155	115	83	48	31	20	9	3	1
1 g IM	33	53	67	57	40	27	13	4	2

*Infused at a constant rate over 30 minutes

The area under the plasma concentration-time curve (AUC) of ertapenem increased less-than dose-proportional based on total ertapenem concentrations over the 0.5 to 2 g dose range, whereas the AUC increased greater-than dose proportional based on unbound ertapenem concentrations. Ertapenem exhibits non-linear pharmacokinetics due to concentration-dependent plasma protein binding at the proposed therapeutic dose. (See CLINICAL PHARMACOLOGY, *Distribution*.)

There is no accumulation of ertapenem following multiple IV or IM 1 g daily doses in healthy adults.

Absorption

Ertapenem, reconstituted with 1% lidocaine HCl injection, USP (in saline without epinephrine), is almost completely absorbed following intramuscular (IM) administration at the recommended dose of 1 g. The mean bioavailability is approximately 90%. Following 1 g daily IM administration, mean peak plasma concentrations (C_{max}) are achieved in approximately 2.3 hours (T_{max}).

Distribution

Ertapenem is highly bound to human plasma proteins, primarily albumin. In healthy young adults, the protein binding of ertapenem decreases as plasma concentrations increase, from approximately 95% bound at an approximate plasma concentration of <100 micrograms (mcg)/mL to approximately 85% bound at an approximate plasma concentration of 300 mcg/mL.

The apparent volume of distribution at steady state (V_{ss}) of ertapenem is approximately 8.2 liters.

The concentrations of ertapenem achieved in suction-induced skin blister fluid at each sampling point on the third day of 1 g once daily IV doses are presented in Table 2. The ratio of $AUC_{0\text{-}24}$ in skin blister fluid/$AUC_{0\text{-}24}$ in plasma is 0.61.

Table 2
Concentrations (mcg/mL) of Ertapenem in Skin Blister Fluid at each Sampling Point on the Third Day of 1-g Once Daily IV Doses

0.5 hr	1 hr	2 hr	4 hr	8 hr	12 hr	24 hr
7	12	17	24	24	21	8

The concentration of ertapenem in breast milk from 5 lactating women with pelvic infections (5 to 14 days postpartum) was measured at random time points daily for 5 consecutive days following the last 1 g dose of intravenous therapy (3-10 days of therapy). The concentration of ertapenem in breast milk within 24 hours of the last dose of therapy in all 5 women ranged from <0.13 (lower limit of quantitation) to 0.38 mcg/mL; peak concentrations were not assessed. By day 5 after discontinuation of therapy, the level of ertapenem was undetectable in the breast milk of 4 women and below the lower limit of quantitation (<0.13 mcg/mL) in 1 woman.

Metabolism

In healthy young adults, after infusion of 1 g IV radiolabeled ertapenem, the plasma radioactivity consists predominantly (94%) of ertapenem. The major metabolite of ertapenem is the inactive ring-opened derivative formed by hydrolysis of the beta-lactam ring.

In vitro studies in human liver microsomes indicate that ertapenem does not inhibit metabolism mediated by any of the following cytochrome p450 (CYP) isoforms: 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4. (See DRUG INTERACTIONS.)

In vitro studies indicate that ertapenem does not inhibit P-glycoprotein-mediated transport of digoxin or vinblastine and that ertapenem is not a substrate for P-glycoprotein-mediated transport. (See PRECAUTIONS, *Drug Interactions*.)

Elimination

Ertapenem is eliminated primarily by the kidneys. The mean plasma half-life in healthy young adults is approximately 4 hours and the plasma clearance is approximately 1.8 L/hour.

Following the administration of 1 g IV radiolabeled ertapenem to healthy young adults, approximately 80% is recovered in urine and 10% in feces. Of the 80% recovered in urine, approximately 38% is excreted as unchanged drug and approximately 37% as the ring-opened metabolite.

In healthy young adults given a 1 g IV dose, the mean percentage of the administered dose excreted in urine was 17.4% during 0-2 hours postdose, 5.4% during 4-6 hours postdose, and 2.4% during 12-24 hours postdose.

Special Populations

Renal Insufficiency

Total and unbound fractions of ertapenem pharmacokinetics were investigated in 26 adult subjects (31 to 80 years of age) with varying degrees of renal impairment. Following a single 1 g IV dose of ertapenem, the unbound AUC increased 1.5-fold and 2.3-fold in subjects with mild renal insufficiency (CL_{CR} 60-90 mL/min/1.73 m^2) and moderate renal insufficiency (CL_{CR} 31-59 mL/min/1.73 m^2), respectively, compared with healthy young subjects (25 to 45 years of age). No dosage adjustment is necessary in patients with CL_{CR} ≥31 mL/min/1.73 m^2. The unbound AUC increased 4.4-fold and 7.6-fold in subjects with advanced renal insufficiency (CL_{CR} 5-30 mL/min/1.73 m^2) and end-stage renal insufficiency (CL_{CR} <10 mL/min/1.73 m^2), respectively, compared with healthy young subjects. The effects of renal insufficiency on AUC of total drug were of smaller magnitude. The recommended dose of ertapenem in patients with CL_{CR} ≤30 mL/min/1.73 m^2 is 0.5 grams every 24 hours. Following a single 1 g IV dose given immediately prior to a 4 hour hemodialysis session in 5 patients with end-stage renal insufficiency, approximately 30% of the dose was recovered in the dialysate. A supplementary dose of 150 mg is recommended if ertapenem is administered within 6 hours prior to hemodialysis. (See DOSAGE AND ADMINISTRATION.)

Hepatic Insufficiency

The pharmacokinetics of ertapenem in patients with hepatic insufficiency have not been established. However, ertapenem does not appear to undergo hepatic metabolism based on *in vitro* studies and approximately 10% of an administered dose is recovered in the feces. (See PRECAUTIONS and DOSAGE AND ADMINISTRATION.)

Gender

The effect of gender on the pharmacokinetics of ertapenem was evaluated in healthy male (n=8) and healthy female (n=8) subjects. The differences observed could be attributed to body size when body weight was taken into consideration. No dose adjustment is recommended based on gender.

Geriatric Patients

The impact of age on the pharmacokinetics of ertapenem was evaluated in healthy male (n=7) and healthy female (n=7) subjects ≥65 years of age. The total and unbound AUC increased 37% and 67%, respectively, in elderly adults relative to young adults. These changes were attributed to age-related changes in creatinine clearance. No dosage adjustment is necessary for elderly patients with normal (for their age) renal function.

Pediatric Patients

The pharmacokinetics of ertapenem in pediatric patients have not been established.

Microbiology

Ertapenem has *in vitro* activity against gram-positive and gram-negative aerobic and anaerobic bacteria. The bactericidal activity of ertapenem results from the inhibition of cell wall synthesis and is mediated through ertapenem binding 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 is stable against hydrolysis by a variety of beta-lactamases, including penicillinases, and cephalosporinases and extended spectrum beta-lactamases. Ertapenem is hydrolyzed by metallo-beta-lactamases.

Ertapenem has been shown to be active against most strains of the following microorganisms *in vitro* and in clinical infections. (See INDICATIONS AND USAGE):

Aerobic gram-positive microorganisms:
Staphylococcus aureus (methicillin susceptible strains only)
Streptococcus agalactiae
Streptococcus pneumoniae (penicillin susceptible strains only)
Streptococcus pyogenes
Note: Methicillin-resistant staphylococci and *Enterococcus* spp. are resistant to ertapenem.

Aerobic gram-negative microorganisms:
Escherichia coli
Haemophilus influenzae (Beta-lactamase negative strains only)
Klebsiella pneumoniae
Moraxella catarrhalis

Anaerobic microorganisms:
Bacteroides fragilis
Bacteroides distasonis
Bacteroides ovatus
Bacteroides thetaiotaomicron
Bacteroides uniformis
Clostridium clostridioforme
Eubacterium lentum
Peptostreptococcus species
Porphyromonas asaccharolytica
Prevotella bivia

The following *in vitro* data are available, **but their clinical significance is unknown**.

At least 90% of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for ertapenem; however, the safety and effectiveness of ertapenem in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical studies:

Aerobic gram-positive microorganisms:
Streptococcus pneumoniae (penicillin-intermediate strains only)

Aerobic gram-negative microorganisms:
Citrobacter freundii
Citrobacter koseri
Enterobacter aerogenes
Enterobacter cloacae
Haemophilus influenzae (Beta-lactamase positive strains)
Haemophilus parainfluenzae
Klebsiella oxytoca (excluding ESBL producing strains)
Morganella morganii
Proteus mirabilis
Proteus vulgaris
Serratia marcescens

Anaerobic microorganisms:
Clostridium perfringens
Fusobacterium spp.

Susceptibility Tests:

When available, the results of *in vitro* susceptibility tests should be provided to the physician as periodic reports which describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting the most effective antimicrobial.

Dilution Techniques:

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a broth dilution method[1,4] or equivalent with standardized inoculum concentrations and standardized concentrations of ertapenem powder. The MIC values should be interpreted according to the following criteria:

For testing Enterobacteriaceae and *Staphylococcus* spp.:

MIC (μg/mL)	Interpretation
≤2.0	Susceptible (S)
4.0	Intermediate (I)
≥8.0	Resistant (R)

Note: *Staphylococcus* spp. can be considered susceptible to ertapenem if the penicillin MIC is ≤ 0.12 μg/mL. If the penicillin MIC is >0.12 μg/mL, then test oxacillin. *Staphylococcus aureus* can be considered susceptible to ertapenem if the oxacillin MIC is ≤2.0 μg/mL and resistant to ertapenem if the oxacillin MIC is ≥4.0 μg/mL. Coagulase negative staphylococci can be considered susceptible to ertapenem if the oxacillin MIC is ≤0.25 μg/mL and resistant to ertapenem if the oxacillin MIC ≥0.5 μg/mL.

For testing *Haemophilus* spp.[a]:

MIC (μg/mL)	Interpretation[b]
≤0.5	Susceptible (S)

[a] This interpretive standard is applicable only to broth microdilution susceptibility tests with *Haemophilus* spp. using *Haemophilus* Test Medium (HTM)[1] inoculated with a direct colony suspension and incubated in ambient air at 35°C for 20-24 hrs.

[b] The current absence of data in resistant strains precludes defining any results other than "Susceptible". Strains yielding MIC results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

For testing *Streptococcus pneumoniae*[c,d]:

MIC (μg/mL)	Interpretation[b]
≤1.0	Susceptible (S)

[c] This interpretive standard is applicable only to broth microdilution susceptibility tests using cation-adjusted Mueller-Hinton broth with 2-5% lysed horse blood inoculated with direct colony suspension and incubated in ambient air at 35°C for 20-24 hrs.

[d] *Streptococcus pneumoniae* that are susceptible to penicillin (penicillin MIC ≤0.06 μg/mL) can be considered susceptible to ertapenem. Testing of ertapenem against penicillin-intermediate or penicillin-resistant isolates is not recommended since reliable interpretive criteria for ertapenem are not available.

For testing *Streptococcus* spp. other than *Streptococcus pneumoniae*[c,e]:

MIC (μg/mL)	Interpretation[b]
≤1.0	Susceptible (S)

[e] *Streptococcus* spp. that are susceptible to penicillin (MIC ≤0.12 μg/mL) can be considered susceptible to ertapenem. Testing of ertapenem against penicillin-intermediate or penicillin-resistant isolates is not recommended since reliable interpretive criteria for ertapenem are not available.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in blood reaches the concentrations usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body

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sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Quality control microorganisms are specific strains of organisms with intrinsic biological properties. QC strains are very stable strains which will give a standard and repeatable susceptibility pattern. The specific strains used for microbiological quality control are not clinically significant. Standard ertapenem powder should provide the following MIC values.

Microorganism	MIC Range (μg/mL)
Enterococcus faecalis ATCC 29212	4.0-16.0
Escherichia coli ATCC 25922	0.004-0.016
Haemophilus influenzae[f] ATCC 49766	0.016-0.06
Pseudomonas aeruginosa ATCC 27853	2.0-8.0
Staphylococcus aureus ATCC 29213	0.06-0.25
Streptococcus pneumoniae[g] ATCC 49619	0.03-0.25

[f] This quality control range is applicable to only *H. influenzae* ATCC 49766 tested by the broth microdilution procedure using HTM[1] inoculated with a direct colony suspension and incubated in ambient air at 35°C for 20-24 hrs.

[g] This quality control range is applicable to only *S. pneumoniae* ATCC 49619 tested by a broth microdilution procedure using cation-adjusted Mueller-Hinton broth with 2-5% lysed horse blood inoculated with a direct colony suspension and incubated in ambient air at 35°C for 20-24 hrs.

Diffusion Techniques:

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure[2,4] requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 10-μg ertapenem to test the susceptibility of microorganisms to ertapenem.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 10-μg ertapenem disk should be interpreted according to the following criteria:

For testing Enterobacteriaceae and *Staphylococcus* spp.:

Zone Diameter (mm)	Interpretation
≥19	Susceptible (S)
16-18	Intermediate (I)
≤15	Resistant (R)

Note: *Staphylococcus* spp. can be considered susceptible to ertapenem if the penicillin (10 U disk) zone is ≥29 mm. If the penicillin zone is ≤28 mm, then test oxacillin by disk diffusion (1 μg disk). *Staphylococcus aureus* can be considered susceptible to ertapenem if the oxacillin (1 μg disk) zone is ≥13 mm and resistant to ertapenem if the oxacillin zone is ≤10 mm. Coagulase negative staphylococci can be considered susceptible to ertapenem if the oxacillin zone is ≥18 mm and resistant to ertapenem if the oxacillin (1 μg disk) zone is ≤17 mm.

For testing *Haemophilus* spp.[h]:

Zone Diameter (mm)	Interpretation[b]
≥19	Susceptible (S)

[h] This zone diameter standard is applicable only to tests performed by disk diffusion with *Haemophilus* spp. using HTM[2] inoculated with a direct colony suspension and incubated in 5% CO_2 at 35°C for 16-18 hrs.

For testing *Streptococcus pneumoniae*[i,j]:

Zone Diameter (mm)	Interpretation[b]
≥19	Susceptible (S)

[i] These zone diameter standards apply only to tests performed using Mueller-Hinton agar supplemented with 5% sheep blood inoculated with a direct colony suspension and incubated in 5% CO_2 at 35°C for 20-24 hrs.

[j] *Streptococcus pneumoniae* that is susceptible to penicillin (1-μg oxacillin disk zone diameter ≥20 mm), can be considered susceptible to ertapenem. Isolates with 1-μg oxacillin zone diameter ≤19 mm should be tested against ertapenem using an MIC method.

For testing *Streptococcus* spp. other than *Streptococcus pneumoniae*[k,l]:

Zone Diameter (mm)	Interpretation[b]
≥19	Susceptible (S)

[k] These zone diameter standards apply only to tests performed using Mueller-Hinton agar supplemented with 5% sheep blood inoculated with a direct colony suspension and in ambient air at 35°C for 20-24 hrs.

[l] Beta-hemolytic *Streptococcus* spp. that are susceptible to penicillin (10-units penicillin disk zone diameter ≥24 mm), can be considered susceptible to ertapenem. Isolates with 10-units penicillin disk zone diameter <24 mm should be tested against ertapenem using an MIC method. Penicillin disk diffusion interpretive criteria are not available for viridans group streptococci and they should not be tested against ertapenem.

Interpretation should be as stated above for results using dilution techniques. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for ertapenem.

As with standardized dilution techniques, diffusion methods require the use of laboratory control microorganisms that are used to control the technical aspects of the laboratory procedures. Quality control microorganisms are specific strains of organisms with intrinsic biological properties. QC strains are very stable strains that will give a standard and repeatable susceptibility pattern. The specific strains used for microbiological quality control are not clinically significant. For the diffusion technique, the 10-μg ertapenem disk should provide the following zone diameters in these laboratory quality control strains:

Microorganism	Zone Diameter Range (mm)
Escherichia coli ATCC 25922	29-36
Haemophilus influenzae[m] ATCC 49766	27-33
Pseudomonas aeruginosa ATCC 27853	13-21
Staphylococcus aureus ATCC 25923	24-31
Streptococcus pneumoniae[n] ATCC 49619	28-35

[m] This quality control range is applicable to *Haemophilus influenzae* ATCC 49766 tested by disk diffusion using HTM[2] agar inoculated with a direct colony suspension and incubated in 5% CO_2 at 35°C for 16-18 hrs.

[n] This quality control range is applicable to *Streptococcus pneumoniae* ATCC 49619 tested by disk diffusion using Mueller-Hinton agar supplemented with 5% sheep blood inoculated with a direct colony suspension and incubated in 5% CO_2 at 35°C for 20-24 hrs.

Anaerobic Techniques:

For anaerobic bacteria, the susceptibility to ertapenem as MICs can be determined by standardized test methods[3]. The MIC values obtained should be interpreted according to the following criteria:

MIC (μg/mL)	Interpretation
≤4.0	Susceptible (S)
8.0	Intermediate (I)
≥16.0	Resistant (R)

Interpretation is identical to that stated above for results using dilution techniques.

As with other susceptibility techniques, the use of laboratory control microorganisms is required to control the technical aspects of the laboratory standardized procedures. Standardized ertapenem powder should provide the following MIC values:

Microorganism	MIC[o] (μg/mL)
Bacteroides fragilis ATCC 25285	0.06-0.25
Bacteroides thetaiotaomicron ATCC 29741	0.25-1.0
Eubacterium lentum ATCC 43055	0.5-2.0

[o] These quality control ranges are applicable only to agar dilution using *Brucella* agar supplemented with hemin, vitamin K1 and 5% defibrinated or laked sheep blood inoculated with a direct colony suspension or a 6- to 24-hour fresh culture in enriched thioglycollate medium and incubated in an anaerobic jar or chamber at 35-37°C for 42-48 hrs.

INDICATIONS AND USAGE

INVANZ is indicated for the treatment of adult patients with the following moderate to severe infections caused by susceptible strains of the designated microorganisms. (See DOSAGE AND ADMINISTRATION):

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 due to *Staphylococcus aureus* (methicillin susceptible strains only), *Streptococcus pyogenes*, *Escherichia coli*, or *Peptostreptococcus* species.

Community Acquired Pneumonia due to *Streptococcus pneumoniae* (penicillin susceptible strains only) including cases with concurrent bacteremia, *Haemophilus influenzae* (beta-lactamase negative strains only), or *Moraxella catarrhalis*.

Complicated Urinary Tract Infections including pyelonephritis due to *Escherichia coli*, including cases with concurrent bacteremia, or *Klebsiella pneumoniae*.

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

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 INVANZ (ertapenem) may be initiated empirically before results of these tests are known; once results become available, antimicrobial therapy should be adjusted accordingly.

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

CONTRAINDICATIONS

INVANZ is contraindicated in patients with known hypersensitivity to any component of this product or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta-lactams.

Due to the use of lidocaine HCl as a diluent, INVANZ administered intramuscularly is contraindicated in patients with a known hypersensitivity to local anesthetics of the amide type. (Refer to the prescribing information for lidocaine HCl.)

WARNINGS

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. 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 INVANZ, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, OTHER BETA-LACTAMS AND OTHER ALLERGENS. IF AN ALLERGIC REACTION TO INVANZ OCCURS, DISCONTINUE THE DRUG IMMEDIATELY. **SERIOUS ANAPHYLACTIC REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE, OXYGEN, INTRAVENOUS STEROIDS, AND AIRWAY MANAGEMENT, INCLUDING INTUBATION. OTHER THERAPY MAY ALSO BE ADMINISTERED AS INDICATED.**

Seizures and other CNS adverse experiences have been reported during treatment with INVANZ. (See PRECAUTIONS and ADVERSE REACTIONS.)

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including ertapenem, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis".

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Lidocaine HCl is the diluent for intramuscular administration of INVANZ. Refer to the prescribing information for lidocaine HCl.

PRECAUTIONS

General

During clinical investigations in adult patients treated with INVANZ (1 g once a day), seizures, irrespective of drug relationship, occurred in 0.5% of patients during study therapy plus 14-day follow-up period. (See ADVERSE REACTIONS.) These experiences have occurred most commonly in patients with 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 disorders. If focal tremors, myoclonus, or seizures occur, patients should be evaluated neurologically, placed on anticonvulsant therapy if not already instituted, and the dosage of INVANZ re-examined to determine whether it should be decreased or the antibiotic discontinued. Dosage adjustment of INVANZ is recommended in patients with reduced renal function. (See DOSAGE AND ADMINISTRATION.)

As with other antibiotics, prolonged use of INVANZ 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.

Prescribing INVANZ in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Caution should be taken when administering INVANZ intramuscularly to avoid inadvertent injection into a blood vessel. (See DOSAGE AND ADMINISTRATION.)

Lidocaine HCl is the diluent for intramuscular administration of INVANZ. Refer to the prescribing information for lidocaine HCl for additional precautions.

Information for patients

Patients should be counseled that antibacterial drugs including INVANZ should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When INVANZ is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by INVANZ or other antibacterial drugs in the future.

Laboratory Tests

While INVANZ possesses toxicity similar to the beta-lactam group of antibiotics, periodic assessment of organ system function, including renal, hepatic, and hematopoietic, is advisable during prolonged therapy.

Drug Interactions

When ertapenem is co-administered with probenecid (500 mg p.o. every 6 hours), probenecid competes for active tubular secretion and reduces the renal clearance of ertapenem. Based on total ertapenem concentrations, probenecid increased the AUC by 25% and reduced the plasma and renal clearances by 20% and 35%, respectively. The half-life increased from 4.0 to 4.8 hours. Because of the small effect on half-life, the coadministration with probenecid to extend the half-life of ertapenem is not recommended.

In vitro studies indicate that ertapenem does not inhibit P-glycoprotein-mediated transport of digoxin or vinblastine and that ertapenem is not a substrate for P-glycoprotein-mediated transport. *In vitro* studies in human liver microsomes indicate that ertapenem does not inhibit metabolism mediated by any of the following six cytochrome p450 (CYP) isoforms: 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4. Drug interactions caused by inhibition of P-glycoprotein-mediated drug clearance or CYP-mediated drug clearance with the listed isoforms are unlikely. (See CLINICAL PHARMACOLOGY, *Distribution* and *Metabolism*.)

Other than with probenecid, no specific clinical drug interaction studies have been conducted.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies in animals have been performed to evaluate the carcinogenic potential of ertapenem.

Ertapenem was neither mutagenic nor genotoxic in the following *in vitro* assays: alkaline elution/rat hepatocyte assay, chromosomal aberration assay in Chinese hamster ovary cells, and TK6 human lymphoblastoid cell mutagenesis assay; and in the *in vivo* mouse micronucleus assay.

In mice and rats, IV doses of up to 700 mg/kg/day (for mice, approximately 3 times the recommended human dose of 1 g based on body surface area and for rats, approximately 1.2 times the human exposure at the recommended dose of 1 g based on plasma AUCs) resulted in no effects on mating performance, fecundity, fertility, or embryonic survival.

Pregnancy: Teratogenic Effects

Pregnancy Category B: In mice and rats given IV doses of up to 700 mg/kg/day (for mice, approximately 3 times the recommended human dose of 1 g based on body surface area and for rats, approximately 1.2 times the human exposure at the recommended dose of 1 g based on plasma AUCs), there was no evidence of developmental toxicity as assessed by external, visceral, and skeletal examination of the fetuses. However, in mice given 700 mg/kg/day, slight decreases in average fetal weights and an associated decrease in the average number of ossified sacrocaudal vertebrae were observed. Ertapenem crosses the placental barrier in rats.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Ertapenem is excreted in human breast milk. (See CLINICAL PHARMACOLOGY, *Distribution*.) Caution should be exercised when INVANZ is administered to a nursing woman. INVANZ should be administered to nursing mothers only when the expected benefit outweighs the risk.

Labor and delivery

INVANZ has not been studied for use during labor and delivery.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established. Therefore, use in patients under 18 years of age is not recommended.

Geriatric Use

Of the 1,835 patients in Phase IIb/III studies treated with INVANZ, approximately 26 percent were 65 and over, while approximately 12 percent were 75 and over. No overall differences in safety or effectiveness were observed between these patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

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

Hepatic Insufficiency

The pharmacokinetics of ertapenem in patients with hepatic insufficiency have not been established. Of the total number of patients in clinical studies, 37 patients receiving ertapenem 1 g daily and 36 patients receiving comparator drugs were considered to have Child-Pugh Class A, B, or C liver impairment. The incidence of adverse experiences in patients with hepatic impairment was similar between the ertapenem group and the comparator groups.

ANIMAL PHARMACOLOGY

In repeat-dose studies in rats, treatment-related neutropenia occurred at every dose-level tested, including the lowest dose (2 mg/kg, 12 mg/m^2).

Studies in rabbits and Rhesus monkeys were inconclusive with regard to the effect on neutrophil counts.

ADVERSE REACTIONS

Clinical studies enrolled 1954 patients treated with ertapenem; in some of the clinical studies, parenteral therapy was followed by a switch to an appropriate oral antimicrobial. (See CLINICAL STUDIES.) Most adverse experiences reported in these clinical studies were described as mild to moderate in severity. Ertapenem was discontinued due to adverse experiences in 4.7% of patients. Table 3 shows the incidence of adverse experiences reported in ≥1.0% of patients in these studies. The most common drug-related adverse experiences in patients treated with INVANZ, including those who were switched to therapy with an oral antimicrobial, were diarrhea (5.5%), infused vein complication (3.7%), nausea (3.1%), headache (2.2%), vaginitis in females (2.1%), phlebitis/thrombophlebitis (1.3%), and vomiting (1.1%).

Table 3
Incidence (%) of Adverse Experiences Reported During Study Therapy Plus 14-Day Follow-Up in ≥1.0% of Patients Treated With INVANZ in Clinical Studies

Adverse Events	INVANZ* 1 g daily (N=802)	Piperacillin/ Tazobactam* 3.375 g q6h (N=774)	INVANZ† 1 g daily (N=1152)	Ceftriaxone† 1 or 2 g daily (N=942)
Local:				
Extravasation	1.9	1.7	0.7	1.1
Infused vein complication	7.1	7.9	5.4	6.7
Phlebitis/thrombophlebitis	1.9	2.7	1.6	2.0
Systemic:				
Asthenia/fatigue	1.2	0.9	1.2	1.1
Death	2.5	1.6	1.3	1.6
Edema/swelling	3.4	2.5	2.9	3.3
Fever	5.0	6.6	2.3	3.4
Abdominal pain	3.6	4.8	4.3	3.9
Chest pain	1.5	1.4	1.0	2.5
Hypertension	1.6	1.4	0.7	1.0
Hypotension	2.0	1.4	1.0	1.2
Tachycardia	1.6	1.3	1.3	0.7
Acid regurgitation	1.6	0.9	1.1	0.6
Oral candidiasis	0.1	1.3	1.4	1.9
Constipation	4.0	5.4	3.3	3.1
Diarrhea	10.3	12.1	9.2	9.8
Dyspepsia	1.1	0.6	1.0	1.6
Nausea	8.5	8.7	6.4	7.4
Vomiting	3.7	5.3	4.0	4.0
Leg pain	1.1	0.5	0.4	0.3
Anxiety	1.4	1.3	0.8	1.2
Altered mental status‡	5.1	3.4	3.3	2.5
Dizziness	2.1	3.0	1.5	2.1
Headache	5.6	5.4	6.8	6.9
Insomnia	3.2	5.2	3.0	4.1
Cough	1.6	1.7	1.3	0.5
Dyspnea	2.6	1.8	1.0	2.4
Pharyngitis	0.7	1.4	1.1	0.6
Rales/rhonchi	1.1	1.0	0.5	1.0
Respiratory distress	1.0	0.4	0.2	0.2
Erythema	1.6	1.7	1.2	1.2
Pruritus	2.0	2.6	1.0	1.9
Rash	2.5	3.1	2.3	1.5
Vaginitis	1.4	1.0	3.3	3.7

* Includes Phase IIb/III Complicated intra-abdominal infections, Complicated skin and skin structure infections and Acute pelvic infections studies

† Includes Phase IIb/III Community acquired pneumonia and Complicated urinary tract infections, and Phase IIa studies

‡ Includes agitation, confusion, disorientation, decreased mental acuity, changed mental status, somnolence, stupor

In patients treated for complicated intra-abdominal infections, death occurred in 4.7% (15/316) of patients receiving ertapenem and 2.6% (8/307) of patients receiving comparator drug. These deaths occurred in patients with significant co-morbidity and/or severe baseline infections. Deaths were considered unrelated to study drugs by investigators.

In clinical studies, seizure was reported during study therapy plus 14-day follow-up period in 0.5% of patients treated with ertapenem, 0.3% of patients treated with piperacillin/tazobactam and 0% of patients treated with ceftriaxone. (See PRECAUTIONS.)

Additional adverse experiences that were reported with INVANZ with an incidence >0.1% within each body system are listed below:

Body as a whole: abdominal distention, pain, chills, septicemia, septic shock, dehydration, gout, malaise, necrosis, candidiasis, weight loss, facial edema, injection site induration, injection site pain, flank pain, and syncope;

Cardiovascular System: heart failure, hematoma, cardiac arrest, bradycardia, arrhythmia, atrial fibrillation, heart murmur, ventricular tachycardia, asystole, and subdural hemorrhage;

Digestive System: gastrointestinal hemorrhage, anorexia, flatulence, *C. difficile* associated diarrhea, stomatitis, dysphagia, hemorrhoids, ileus, cholelithiasis, duodenitis, esophagitis, gastritis, jaundice, mouth ulcer, pancreatitis, and pyloric stenosis;

Nervous System & Psychiatric: nervousness, seizure (see WARNINGS and PRECAUTIONS), tremor, depression, hypesthesia, spasm, paresthesia, aggressive behavior, and vertigo;

Respiratory System: pleural effusion, hypoxemia, bronchoconstriction, pharyngeal discomfort, epistaxis, pleuritic pain, asthma, hemoptysis, hiccups, and voice disturbance;

Skin & Skin Appendage: sweating, dermatitis, desquamation, flushing, and urticaria;

Special Senses: taste perversion;

Urogenital System: renal insufficiency, oliguria/anuria, vaginal pruritus, hematuria, urinary retention, bladder dysfunction, vaginal candidiasis, and vulvovaginitis.

Post-Marketing Experience:

The following post-marketing adverse experiences have been reported:

Immune System: anaphylaxis including anaphylactoid reactions (very rare)

Nervous System & Psychiatric: hallucinations (very rare)

Adverse Laboratory Changes

Laboratory adverse experiences that were reported during therapy in ≥1.0% of patients treated with INVANZ in clinical studies are presented in Table 4. Drug-related laboratory adverse experiences that were reported during therapy in ≥1.0% of patients treated with INVANZ, including those who were switched to therapy with an oral antimicrobial, in clinical studies were ALT increased (6.0%), AST increased (5.2%), serum alkaline phosphatase increased (3.4%), platelet count increased (2.8%), and eosinophils increased (1.1%). Ertapenem was discontinued due to laboratory adverse experiences in 0.3% of patients.

Table 4
Incidence* (%) of Specific Laboratory Adverse Experiences Reported During Study Therapy Plus 14-Day Follow-Up in ≥1.0% of Patients Treated With INVANZ in Clinical Studies

Adverse laboratory experiences	INVANZ‡ 1 g daily (n^1=766)	Piperacillin/ Tazobactam‡ 3.375 g q6h (n^1=755)	INVANZ§ 1 g daily (n^1=1122)	Ceftriaxone§ 1 or 2 g daily (n^1=920)
ALT increased	8.8	7.3	8.3	6.9
AST increased	8.4	8.3	7.1	6.5
Serum albumin decreased	1.7	1.5	0.9	1.6
Serum alkaline phosphatase increased	6.6	7.2	4.3	2.8
Serum creatinine increased	1.1	2.7	0.9	1.2
Serum glucose increased	1.2	2.3	1.7	2.0
Serum potassium decreased	1.7	2.8	1.8	2.4
Serum potassium increased	1.3	0.5	0.5	0.7
Total serum bilirubin increased	1.7	1.4	0.6	1.1
Eosinophils increased	1.1	1.1	2.1	1.8
Hematocrit decreased	3.0	2.9	3.4	2.4
Hemoglobin decreased	4.9	4.7	4.5	3.5
Platelet count decreased	1.1	1.2	1.1	1.0
Platelet count increased	6.5	6.3	4.3	3.5
Segmented neutrophils decreased	1.0	0.3	1.5	0.8
Prothrombin time increased	1.2	2.0	0.3	0.9
WBC decreased	0.8	0.7	1.5	1.4
Urine RBCs increased	2.5	2.9	1.1	1.0
Urine WBCs increased	2.5	3.2	1.6	1.1

* Number of patients with laboratory adverse experiences/Number of patients with the laboratory test

† Number of patients with one or more laboratory tests

‡ Includes Phase IIb/III Complicated intra-abdominal infections, Complicated skin and skin structure infections and Acute pelvic infections studies

§ Includes Phase IIb/III Community acquired pneumonia and Complicated urinary tract infections, and Phase IIa studies

Additional laboratory adverse experiences that were reported during therapy in >0.1% but <1.0% of patients treated with INVANZ in clinical studies include: increases in BUN, direct and indirect serum bilirubin, serum sodium, monocytes, PTT, urine epithelial cells; decreases in serum bicarbonate.

OVERDOSAGE

No specific information is available on the treatment of overdosage with INVANZ. Intentional overdosing of INVANZ is unlikely. Intravenous administration of INVANZ at a dose of 2 g over 30 min or 3 g over 1-2h in healthy volunteers resulted in an increased incidence of nausea. In clinical studies, inadvertent administration of three 1 g doses of INVANZ in a 24 hour period resulted in diarrhea and transient dizziness in one patient.

In the event of an overdose, INVANZ should be discontinued and general supportive treatment given until renal elimination takes place.

INVANZ can be removed by hemodialysis; the plasma clearance of the total fraction of ertapenem was increased 30% in subjects with end-stage renal insufficiency when hemodialysis (4 hour session) was performed immediately following administration. However, no information is available on the use of hemodialysis to treat overdosage.

DOSAGE AND ADMINISTRATION

The dose of INVANZ in adults is 1 gram (g) given once a day.

INVANZ may be administered by intravenous infusion for up to 14 days or intramuscular injection for up to 7 days. When administered intravenously, INVANZ should be infused over a period of 30 minutes.

Intramuscular administration of INVANZ may be used as an alternative to intravenous administration in the treatment of those infections for which intramuscular therapy is appropriate.

DO NOT MIX OR CO-INFUSE INVANZ WITH OTHER MEDICATIONS. DO NOT USE DILUENTS CONTAINING DEXTROSE (α-D-GLUCOSE).

Table 5 presents dosage guidelines for INVANZ.

Table 5
Dosage Guidelines for Adults With Normal Renal Function* and Body Weight

Infection†	Daily Dose (IV or IM)	Recommended Duration of Total Antimicrobial Treatment
Complicated intra-abdominal infections	1 g	5 to 14 days
Complicated skin and skin structure infections	1 g	7 to 14 days
Community acquired pneumonia	1 g	10 to 14 days‡
Complicated urinary tract infections, including pyelonephritis	1 g	10 to 14 days‡
Acute pelvic infections including postpartum endomyometritis, septic abortion and post surgical gynecologic infections	1 g	3 to 10 days

* defined as creatinine clearance >90 mL/min/1.73 m^2

† due to the designated pathogens (see INDICATIONS AND USAGE)

‡ duration includes a possible switch to an appropriate oral therapy, after at least 3 days of parenteral therapy, once clinical improvement has been demonstrated.

Patients with Renal Insufficiency: INVANZ may be used for the treatment of infections in patients with renal insufficiency. In patients whose creatinine clearance is >30 mL/min/1.73 m^2, no dosage adjustment is necessary. Patients with advanced renal insufficiency (creatinine clearance ≤30 mL/min/1.73 m^2) and end-stage renal insufficiency (creatinine clearance ≤10 mL/min/1.73 m^2) should receive 500 mg daily.

Patients on Hemodialysis: When patients on hemodialysis are given the recommended daily dose of 500 mg of INVANZ within 6 hours prior to hemodialysis, a supplementary dose of 150 mg is recommended following the hemodialysis session. If INVANZ is given at least 6 hours prior to hemodialysis, no supplementary dose is needed. There are no data in patients undergoing peritoneal dialysis or hemofiltration.

When only the serum creatinine is available, the following formula** may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function.

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

Females: (0.85) x (value calculated for males)

Patients with Hepatic Insufficiency: No dose adjustment recommendations can be made in patients with impaired hepatic function. (See CLINICAL PHARMACOLOGY, *Special Populations, Hepatic Insufficiency* and PRECAUTIONS.)

No dosage adjustment is recommended based on age or gender. (See CLINICAL PHARMACOLOGY, *Special Populations*.)

PREPARATION OF SOLUTION

Preparation for intravenous administration:

DO NOT MIX OR CO-INFUSE INVANZ WITH OTHER MEDICATIONS. DO NOT USE DILUENTS CONTAINING DEXTROSE (α-D-GLUCOSE).

INVANZ MUST BE RECONSTITUTED AND THEN DILUTED PRIOR TO ADMINISTRATION.

1. Reconstitute the contents of a 1 g vial of INVANZ with 10 mL of one of the following: Water for Injection, 0.9% Sodium Chloride Injection or Bacteriostatic Water for Injection.
2. Shake well to dissolve and immediately transfer contents of the reconstituted vial to 50 mL of 0.9% Sodium Chloride Injection.
3. Complete the infusion within 6 hours of reconstitution.

Preparation for intramuscular administration:

INVANZ MUST BE RECONSTITUTED PRIOR TO ADMINISTRATION.

1. Reconstitute the contents of a 1 g vial of INVANZ with 3.2 mL of 1.0% lidocaine HCl injection*** (**without epinephrine**). Shake vial thoroughly to form solution.
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**.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to use, whenever solution and container permit. Solutions of INVANZ range from colorless to pale yellow. Variations of color within this range do not affect the potency of the product.

STORAGE AND STABILITY

Before reconstitution

Do not store lyophilized powder above 25°C (77°F).

Reconstituted and infusion solutions

The reconstituted solution, immediately diluted in 0.9% Sodium Chloride Injection (see DOSAGE AND ADMINISTRATION, PREPARATION OF SOLUTION), **may be stored at room temperature (25°C) and used within 6 hours or stored for 24 hours under refrigeration (5°C) and used within 4 hours after removal from refrigeration. Solutions of INVANZ should not be frozen.**

HOW SUPPLIED

INVANZ is supplied as a sterile lyophilized powder in single dose vials containing ertapenem for intravenous infusion or for intramuscular injection as follows:

No. 3843—1 g ertapenem equivalent
NDC 0006-3843-71 in trays of 10 vials
No. 3843—1 g ertapenem equivalent
NDC 0006-3843-45 in trays of 25 vials.

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

*** Refer to the prescribing information for lidocaine HCl.

CLINICAL STUDIES

Complicated Intra-Abdominal Infections

Ertapenem was evaluated in adults for the treatment of complicated intra-abdominal infections in a clinical trial. This study compared ertapenem (1 g intravenously once a day) with piperacillin/tazobactam (3.375 g intravenously every 6 hours) for 5 to 14 days and enrolled 665 patients with localized complicated appendicitis, and any other complicated intra-abdominal infection including colonic, small intestinal, and biliary infections and generalized peritonitis. The combined clinical and microbiologic success rates in the microbiologically evaluable population at 4 to 6 weeks posttherapy (test of cure) were 83.6% (163/195) for ertapenem and 80.4% (152/189) for piperacillin/tazobactam.

Complicated Skin and Skin Structure Infections

Ertapenem was evaluated in adults for the treatment of complicated skin and skin structure infections in a clinical trial. This study compared ertapenem (1 g intravenously once a day) with piperacillin/tazobactam (3.375 g intravenously every 6 hours) for 7 to 14 days and enrolled 540 patients including patients with deep soft tissue abscess, posttraumatic wound infection and cellulitis with purulent drainage. The clinical success rates at 10 to 21 days posttherapy (test of cure) were 83.9% (141/168) for ertapenem and 85.3% (145/170) for piperacillin/tazobactam.

Community Acquired Pneumonia

Ertapenem was evaluated in adults for the treatment of community acquired pneumonia in two clinical trials. Both studies compared ertapenem (1 g parenterally once a day) with ceftriaxone (1 g parenterally once a day) and enrolled a total of 866 patients. Both regimens allowed the option to switch to oral amoxicillin/clavulanate for a total of 10 to 14 days of treatment (parenteral and oral). In the first study the primary efficacy parameter was the clinical success rate in the clinically evaluable population and success rates were 92.3% (168/182) for ertapenem and 91.0% (183/201) for ceftriaxone at 7 to 14 days posttherapy (test of cure). In the second study the primary efficacy parameter was the clinical success rate in the microbiologically evaluable population and success rates were 91% (91/100) for ertapenem and 91.8% (45/49) for ceftriaxone at 7 to 14 days posttherapy (test of cure).

Complicated Urinary Tract Infections Including Pyelonephritis

Ertapenem was evaluated in adults for the treatment of complicated urinary tract infections including pyelonephritis in two clinical trials. Both studies compared ertapenem (1 g parenterally once a day) with ceftriaxone (1 g parenterally once a day) and enrolled a total of 850 patients. Both regimens allowed the option to switch to oral ciprofloxacin (500 mg twice daily) for a total of 10 to 14 days of treatment (parenteral and oral). The microbiological success rates (combined studies) at 5 to 9 days posttherapy (test of cure) were 89.5% (229/256) for ertapenem and 91.1% (204/224) for ceftriaxone.

Acute Pelvic Infections Including Endomyometritis, Septic Abortion And Post-Surgical Gynecological Infections

Ertapenem was evaluated in adults for the treatment of acute pelvic infections in a clinical trial. This study compared ertapenem (1 g intravenously once a day) with piperacillin/tazobactam (3.375 g intravenously every 6 hours) for 3 to 10 days and enrolled 412 patients including 350 patients with obstetric/postpartum infections and 45 patients with septic abortion. The clinical success rates in the clinically evaluable population at 2 to 4 weeks posttherapy (test of cure) were 93.9% (153/163) for ertapenem and 91.5% (140/153) for piperacillin/tazobactam.

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