Carbapenems STEPS

Recommendation	All the carbapenems exhibit broad-spectrum coverage, but there are some differences. Imipenem and meropenem exhibit similar activity and provide anti-pseudomonal coverage whereas ertapenem does not. Ertapenem offers the advantage of once-daily dosing and an IM formulation, both of which are useful in outpatient and long-term care facility population. Imipenem and meropenem have broader spectrums of action and more clinical utility (for empiric therapy in nosocomial infections and febrile neutropenia), and therefore should be the preferred agents in the hospital setting		
Brand Name **Generic Name**	**Invanz** **Ertapenem**	**Primaxin IV** **Imipenem/Cilastatin**	**Merrem IV** **Meropenem**
Safety	=	-	=
Drug Interactions	Probenicid increases levels – concomitant use not recommended. Serum levels of valproic acid may be decreased.	Ganciclovir may increase risk of seizures. Probenicid increases levels. Concurrent cyclosporine use may increase neurotoxic effects. Serum levels of valproic acid may be decreased	Probenicid may increase levels. May decrease valproic acid levels.
Pregnancy/Lactation	Category B Enters breast milk/use caution	Category C Enters breast milk/use caution	Category B Excretion in breast milk unknown
Look-alike Sound-alike ~ (confused with)	*Invanz~Avinza*	*Primaxin~Primacor, Premarin*	
Pediatric	Safety and efficacy in children 3 months to 17 years. Not recommended for meningitis because of lack of sufficient CSF penetration	Evidence for use in neonates to 16 years of age (with non-CNS infections). Not recommended in pediatric patients with CNS infections because of seizure risk. Not recommended in pediatric patients <30kg and impaired renal function because of lack of data	Safety and efficacy established for those 3 months or greater
Elderly	No differences identified	No differences identified	No differences identified
Renal/Hepatic impairment	If CrCl is < 30ml/min reduce dose to 500mg daily	Dose reduction necessary if CrCl < 70ml/min. Adjusted dose is determined based on severity and site of infection as well as body weight. See prescribing information for detailed chart.	If CrCl <51ml/min adjust dose as follows: CrCl 50 – 26ml/min: 1g IV q12h; CrCl 10–25ml/min: 500mg IV q12h; CrCl <10ml/min: 500mg IV q24h
Contraindications	Hypersensitivity, anaphylactic rxns to other beta-lactams. Lidocaine required for IM administration – IM form contraindicated in patients hypersensitive to amide type local anesthetics	Hypersensitivity. Patients with meningitis – safety and efficacy not established	Hypersensitivity, anaphylactic rxns to other beta-lactams
Precautions	Serious and occasionally fatal anaphylactic reactions have occurred. Seizures may occur, especially in patients with history or at higher than recommended doses. Prolonged use may result in super-infection. Pseudomembranous colitis has been reported with nearly all antibacterial agents. Use in the absence of proven or strongly suspected bacterial infection increases risk of development of drug-resistant bacteria. Periodic assessments of organ system function, including renal, hepatic, and hematopoietic, is recommended in prolonged therapy		
	Seizure risk 0.5%	Seizure risk (0.4-3%). Use with caution in patients with history of hypersensitivity or seizures with beta-lactams. Adjust dose for patients < 70kg. Not for IM use.	Seizure risk 0.7%. Overall less CNS adverse effects than with imipenem. Thrombocytopenia reported in patients with renal dysfunction

Brand Name **Generic Name**	**Invanz** **Ertapenem**	**Primaxin IV** **Imipenem/Cilastatin**	**Merrem IV** **Meropenem**
Tolerability	=	-	=
	Most common: N/V/D (10%), phlebitis, headache (5.8%), vaginitis, infused vein complications Others: platelet count increased, altered mental status, rash, chest pain, edema, hyper or hypotension, LFT elevations	Most common: N/V/D (2%), phlebitis (3%). Slow infusion rate to reduce nausea Others: Confusion, drug fever, hallucinations, pancytopenia, psychic disturbances, acute renal failure, seizure	Most common: N/V/D (5-8%), headache, phlebitis Others: LFT elevations, neutropenia, thrombocytopenia, acute renal failure, seizures, angioedema, Stevens-Johnson syndrome
Efficacy	-	+	=
FDA-approved indications	Indicated for moderate-to-severe infections • Complicated intra-abdominal • Complicated skin/skin structure • CAP • Complicated UTI/pyelonephritis • Acute pelvic infections (postpartum endomyometritis, septic abortion and post-surgical gynecologic • Prophylaxis of surgical site infection following elective colorectal surgery	Indicated for serious infections • Lower respiratory tract • UTI (complicated and uncomplicated) • Intra-abdominal infections • Gynecologic • Bacterial septicemia • Bone/joint • Skin/skin structure • Endocarditis • Polymicrobic	Indicated as single-agent therapy: • Intra-abdominal (complicated appendicitis and peritonitis) • Meningitis • Complicated skin/skin structure
Microbiology	Activity against a wide range of gram-negative and Gram-positive aerobic and anaerobic microorganisms. Imipenem and meropenem may be synergistic with aminoglycosides against *Pseudomonas*. Ertapenem is not active against *Pseudomonas*, *Enterococcus sp*, or *Acinetobacter* as are the other carbapenems. Ertapenem is less active against gram positives, particularly penicillin-resistant pneumococci. In vitro studies indicate that ertapenem may be more active than imipenem and equal to meropenem against enterobacteriaceae. None of the carbapenems should be used for MRSA, *Enterococcus faecium* or *Stenotrophomonas maltophilia*. Cilstatin prevents renal metabolism of imipenem.		
Penetration to tissues		Rapidly distributes to most tissues and fluids. Highest concentrations in pleural, interstitial, peritoneal fluids, bone and reproductive organs. Low concentration in CSF.	Penetrates well into most body tissues and fluids. CSF concentrations approximate those of plasma.

Brand Name **Generic Name**	**Invanz** **Ertapenem**	**Primaxin IV** **Imipenem/Cilastatin**	**Merrem IV** **Meropenem**
Clinical Studies	***Ertapenem vs. Ceftriaxone for CAP***. J Antimicrob Chemother. 2004;53(Suppl 2):ii59-66. Hospitalized adult patients were randomized to receive ertapenem or ceftriaxone both 1g IV daily. Cure rates were 91.9 and 92% respectively. Both agents were comparable in efficacy. ***Imipenem vs meropenem for Intra-abdominal infections***. Int J Antimicrob Agents. 1999;11:107-13. Patients with moderately severe infections received meropenem 500mg IV q8h or imipenem 500mg IV q6h. Clinical cure or improvement occurred in 91.6 and 93.8% respectively. Meropenem was as clinically effective as imipenem. ***Ertapenem vs Zosyn for polymicrobial infections***. J Antimicrob Chemother. 2004;53(Suppl 2)ii51-7. Post hoc analysis of three large, randomized, double-blind trials comparing ertapenem 1g IV daily and piperacillin/tazobactam 3.375g IV q6h for treatment of polymicrobial complicated intra-abdominal, complicated skin/skin structure, and acute pelvic infections. Both agents were equally effective.		
Price	+	=	=
Usual Dose for Intra-abdominal infections	1gram IV daily x 5-14days	500mg IV q6h	1g IV q8h
Relative cost for treatment course	10days: $	10 days: $$	10 days: $$

	Drug Regimen	**Price**
Comparison of regimens for CAP	Ertapenem 1gm IV q24h + azithromycin 500mg IV q24h x10days	$$$$$$
	Ceftriaxone 2gm IV q24h + azithromycin 500mg IV q24h x10days	$$
	Moxifloxacin 400mg IV q24h x 10 days	$
Comparison for prophylaxis following colorectal surgery	Ertapenem 1 gm IV x1dose pre-op	$$$
	Cefoxitin 1gm IV q6h x 24h	$
Comparison of regimens for acute pelvic infections	Cefoxitin 2gm IV q6h x10day	$$
	Unasyn 3gm IV q6h x 10days	$
	Zosyn 3.375gm IV q6h x10days	$$
	Ertapenem 1gm IV q24h x10days	$$

Simplicity	+	-	=
	Once daily dosing Doses do not require adjustment until CrCl < 30ml/min Dosage form can be used IV or IM	Do not administer IVP Doses≤500mg infuse over 20-30min Dose≥750mg infuse over 40-60min Complex renal impairment dosing guidelines	Multiple doses/day May be given over 30min or as a bolus over 3 – 5min