Table 2

Pharmacologic, Pharmokinetic, Clinical Properties of Doripenem

Brand/Generic	Doribax™ (Doripenem)
Classification	Carbapenem ß-lactam
Mechanism of Action	Inhibits bacterial cell wall synthesis and causes cell death by binding to and inactivating penicillin-binding proteins (PBPs)
Spectrum of Activity	• Aerobic facultative gram-negative microorganisms - Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa • Aerobic and facultative gram-positive microorganisms - Streptococcus constellatus, Streptococcus intermedius • Anaerobic microorganisms - Bacteroides caccae, Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Peptostreptococcus micros
FDA Indications	• Complicated Intra-Abdominal Infections • Complicated Urinary Tract Infections, Including Pyelonephritis • NDA submitted for use in nosocomial and ventilator-associated pneumonia For complicated intra-abdominal infections and complicated urinary tract infections (UTI), including
Pharmacokinetics	**Half-life:** 1h; **Biliary/fecal excretion:** <1%; **Recovered unchanged in urine:** 70% of total dose as unchanged doripenem; **Vd (L):** 16.8; **Protein Bound:** 8.1%; **Hepatic Metabolis:** Minimal; inactive ring-opened metabolite (doripenem-M1) via dehydropeptidase-I
Dosage	pyelonephritis in patients 18 years and older: • 500 mg IV every 8 hours infused over 1 hour • Recommended duration of treatment for complicated intra-abdominal infections: 5-14 days • Recommended duration of treatment for complicated UTI, including pyelonephritis: 10-14 days • A switch to oral therapy is possible after 3 days of IV therapy if patient displays clinical improvement.
Dosage Adjustment	**Renal** • CrCl > 50 ml/min: No dose adjustment required • CrCl 30-50 ml/min: 250 mg IV (over 1 hour) every 8 hours • CrCl 10-30 ml/min: 250 mg IV (over 1 hour) every 12 hours **Note: 52% of dose removed after 4 hour HD. No recommendations on dosing in HD or CAPD pts.** **Hepatic** No dosage adjustment is required.
Monitoring Requirements	• Serum creatinine/BUN
Contraindications	• Previous hypersensitivity to doripenem, to other drugs in same class, or in patients who have had naphylactic reactions to beta-lactams
Precautions/Warnings	• **Hypersensitivity reaction** - Serious and fatal hypersensitivity reactions are reported with ß-lactam antibiotics. Reactions are more likely to occur in patients with a history of sensitivity to multiple allergens. If allergic reaction occurs, discontinue drug immediately and consider emergency measures if patient is undergoing anaphylaxis. • **Clostridium difficile-associated Colitis** - Ranges in severity from mild to fatal. Patients who develop diarrhea should be monitored. • **Seizures** - May reduce serum valproic acid concentration resulting in loss of seizure control. Monitor serum valproic acid levels more frequently.
Adverse Effects	Most commonly observed in Phase III clinical studies: • Headache (4-16%) • Nausea (4-12%) • Diarrhea (6-11%) • Rash (1-5%) • Phlebitis (4-8%)
Drug Interactions	• Carbapenem antibiotics may cause a clinically significant reduction in serum valproic concentrations and may prevent seizure control. • Probenecid may interfere with tubular secretion of doripenem resulting in increased plasma concentration and AUC (75%) and prolonging the half-life of Doripenem
How Supplied	• Single-use clear glass vials containing 500mg of sterile doripenem powder
Storage/Administration	**Storage** • Prior to reconstitution, store vial at 250C (770 F); excursions permitted to 150 to 300 C (590 to 850 F) • Diluted IV infusion can be stored at room temperature for 8h if prepared in normal saline or for 4h if prepared in 5% dextrose (D5W) and refrigerated (20 to 80 C (360 to 460F)) for up to 24h **Administration** • Reconstitute with 10 mL of sterile water for injection or 0.9% sodium chloride (NS) injection • Withdraw the reconstituted suspension and add to a 100 mL NS or D5W bag (maximum concentration: 4.5 mg/mL) • Infuse over 1 hour

Table 2...*continued from previous page*

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Pregnancy Category	• Pregnancy category B • Excretion in human milk is unknown. Use caution in nursing women.
Lactation Daily Cost[a]	• Doripenem 500 mg IV Q 8h = $114.99 • Imipenem/Cilistatin 500 mg IV Q 6 h to 1 g IV Q 8h $103.16-$154.74 • Meropenem 500 mg - 1 g IV Q 8h = $62.55 - $125.10 • Ertapenem 1 g IV Q 24 = $44.46

[a] Wholesale and novation pricing information accessed on February 26, 2008 (from Purchasing Department at Santa Clara Valley Medical Center, San Jose, CA