

EMEA APPROVED NEW DRUG

Doribax (Doripenem)

New antibiotic developed from the carbapenem group of antibacterial agents

April of 2008, brought the arrival of another member to the carbapenem family. Doribax (Doripenem) marketed by Janssen-Cilag International NV for use in the treatment of nosocomial pneumonia (including ventilator-associated pneumonia), complicated intra-abdominal infections, and complicated urinary tract infections. Doripenem is a very broad spectrum beta-lactamase resistant synthetic carbapenem that works by inhibiting bacterial cell wall biosynthesis. It does this by inactivating multiple essential penicillin-binding proteins causing the inhibition of cell wall synthesis, leading to eventual cell death. Doripenem appears to have similar clinical efficacy and safety as meropenem. The compound has a low protein binding (8.1%) and a volume of distribution of 16.8 L, indicating a distribution over the extracellular fluid. In an attempt to preserve the activity of these valuable medications, carbapenems should be reserved for patients considered at high risk, or for the treatment of severe infections where alternative agents have been proven to be either more beneficial or ineffective, or with multi-resistant organisms (with the exception of methicillin-resistant *staphylococcus aureus*). The reason for limiting its use is because it has been shown that carbapenem treatment is connected with resistance development, in particular with *P. aeruginosa*. The bacteria *P. aeruginosa* is a Gram-negative pathogen that has been associated with increasing resistance to multiple drugs and it is one of the leading causes of nosocomial infections, including nosocomial pneumonia. Doripenem potentially has a lower minimum

inhibitory concentration required for *P. aeruginosa* and a lower likelihood of resistance development, which has been shown *in vitro*. These two potential benefits have yet to be proven through clinical studies. At this time the ultimate advantage of using doripenem is that it can be dosed three times a day as a 1-hour infusion compared to the usual four times a day like the other carbapenem products. At room temperature doripenem in solution is stable for eight hours in saline and four hours in glucose 5%. When refrigerated the solution is stable for at least 24 hours.

Final note, the FDA only approved doripenem for complicated intra-abdominal and urinary tract infections and NOT for use in nosocomial pneumonia due to lack of strength of the studies supporting that indication. Although EMEA has approved it for nosocomial pneumonia, it may be prudent when using doripenem for this condition to infuse the product over four hours due to its short half-life.

Source: EMEA

Mark Nolan, RPh
EJHP Editor

Snap Shot

Doribax (Doripenem)

Manufacturer:

Janssen-Cilag International NV

Drug Class: Carbapenem antibiotics

Indications: Nosocomial pneumonia, complicated intra-abdominal infection (cIAI), and complicated urinary tract infections (cUTI).

Dosage: Recommended dose is 500 mg every eight hours over one to four hours.

Of special note:

- To reduce the development of drug-resistant bacteria and maintain the effectiveness of Doripenem and other antibacterial drugs, Doripenem should be used only to treat infections proven or strongly suspected to be caused by susceptible bacteria.
- Based on Pharmacokinetic/Pharmacodynamic considerations, a 4-hour infusion time may be more suitable for infection with less sus-

ceptible pathogens and severe infections. The compound has a short elimination half-life of one hour.

- Usual treatment should be for 5–14 days.
- Do **NOT** use via inhalation!
- Preparing 500 mg dose:
 - Add 10 mL of sterile water for injection or sodium chloride 0.9% and shake gently to form a suspension
 - NOTE: Suspension is not for direct infusion
 - Withdraw suspension adding it to an infusion bag containing 100 mL of either sodium chloride 0.9% solution for injection or dextrose 5% solution for injection and mix to complete dissolution.
- See package insert for renal dosing.
- Doripenem is excreted via urine mostly unchanged and undergoes little to no CYP450 metabolism.

Patient Counselling

- Inform your doctor if you have had any side effects due to antibiotics, in particular penicillins, cephalosporins or carbapenems.
- Tell your doctor if you are taking a medicine called valproic acid (used to treat epilepsy, bipolar disorder, migraines or schizophrenia) or probenecid (used to treat gout).
- Inform the doctor if you have, or had any kidney problems, He/she may need to reduce the dose if you have.
- The most common side effects of this medication are headache, rash, diarrhoea, and fungal infections.