MEMORANDUM

Date October 16th, 2008

To: Fraser Health Medical Directors, Heads of ICU, Emergency, Surgery, Internal Medicine and Hospitalists.

From: Dr. Yasemin Arikan, Co-Chair, Fraser Health Infectious Diseases Subcommittee

CC: Pharmacy Clinical Practice Leaders and Pharmacy Site Managers

Re: Meropenem Dosing Strategy for Fraser Health

As many of you are aware, the Infectious Diseases Subcommittee recently performed an extensive chart review in Fraser Health to determine the pattern of use of Meropenem. Five sites chosen for this review were Royal Columbian Hospital, Surrey Memorial Hospital, Burnaby Hospital, Chilliwack General Hospital, and the MSA General Hospital (ARHCC). The results are available on Power Point presentation and can be presented to your group by any ID subcommittee member at your request. In summary, the results indicate that Meropenem is prescribed for many types of infections, and at a variety of dosage regimens. Currently, this drug is the most frequently prescribed broad spectrum agent in Fraser Health. The ID subcommittee has developed guidelines for the use of Meropenem, which are based on a thorough review of the literature and also a review of Fraser Health susceptibility patterns of common organisms targeted with this drug.

The Meropenem Guidelines are two fold, focusing on both indication and dose (see next page for details).

INDICATION: Recommended prescribing indications for Meropenem emphasize reserving this drug for most severe infections, ensuring that it is administered without any delays in such circumstances.

DOSING GUIDELINES: This focuses on how to optimize the treatment by using the most effective dose of Meropenem for serious infections in the acute care setting. This is based on Meropenem pharmacodynamics and pharmacokinetics, which have been studied in various modeling studies and applied successfully in various clinical settings. The dosing strategy presented in Table 1 has already been successfully implemented in many Canadian hospitals and has been formally adopted by one of the ICUs within Fraser Health. The ID subcommittee would like to recommend that any protocols or pre-printed doctor’s orders containing Meropenem be re-evaluated and modified to reflect these new guidelines.

Finally, on day-to-day orders for Meropenem, we have recommended that clinical pharmacists assess the patients and discuss the cases with the prescribing physicians to consider changing Meropenem dosing as per the attached Meropenem Dosing Guideline (Table 1).

The ID subcommittee team, which is comprised of ID specialists, medical microbiologists, respirologist/intensive care physician, and clinical pharmacists, will continue to monitor the trends of multiple resistant organisms and the effectiveness of the available broad spectrum antibiotics. As a reminder, please refer or discuss all cases of multiple resistant infections with the ID specialists or the medical microbiologist.

If you have any questions, please direct them to Dr. Anisha Lakhani at anisha.lakhani@fraserhealth.ca so that your queries can be addressed by the ID subcommittee.
Guidelines for Use of Meropenem

Part 1: Indication

Meropenem should be reserved for the most serious and life-threatening infections as follows:

- Documented Gram negative infections involving multiple resistant organisms where other agents are either ineffective due to resistance or cannot be used due to intolerance.
- Empiric therapy for severe, life threatening infections where multiple resistant organisms may be suspected, such as:
  - Severe sepsis
  - Cystic fibrosis
  - Febrile neutropenia

Note:
- Antimicrobial therapy for all serious infections should be administered without delay and reassessed within 2-3 days to determine if step down to narrower regimen is possible.
- Ertapenem has shown efficacy against resistant organisms and is a good alternative to Meropenem. Note that it is not effective against Pseudomonas aeruginosa or Acinetobacter spp.
- For severe gastrointestinal or any serious post surgical infections consider using other effective antibiotics such as Piperacillin/tazobactam or combination regimens.

Part 2: Meropenem Dosing (Adults)

Table 1: Meropenem Dosing Guideline

<table>
<thead>
<tr>
<th>Estimated GFR (ml/min)</th>
<th>≥ 50</th>
<th>25-49</th>
<th>10-24</th>
<th>&lt;10*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>500 mg IV Q6H</td>
<td>500 mg IV Q8H</td>
<td>500 mg IV Q12H</td>
<td>500 mg IV Q24H</td>
</tr>
</tbody>
</table>

Note: Dosing substitution may be performed by a clinical pharmacist on consultation with MD

EXCEPTIONS:

1. Following are exempt from dosing substitution because higher doses are needed for drug penetration. Use 1 gram dose and dosing interval indicated in Table 1 above for:
   - Cystic Fibrosis (1g IV Q6H)
   - Meningitis or CNS infections (may use 1g IV Q6H or maximum 2 g IV Q8H)
   - Obese patients with actual weight twice their calculated ideal body weight

2. Patients on dialysis: Treatment will be guided by the intensive care and renal dialysis medical/clinical pharmacy teams. Dosing regimen can vary day-to-day based on dialysis schedules as well as clinical progress. General dosing guidelines are as follows:
   - Hemodialysis: Meropenem 500 mg IV every 24 hours administered post dialysis
   - Continuous renal replacement therapy (CRRT): Meropenem 500 mg IV Q8H
REFERENCES


10. Zanetti G et al. Meropenem (1.5 g/day) is as effective as imipenem/cilastatin (2 g/day) for the treatment of moderately severe intra-abdominal infections. International Journal of Antimicrobial Agents 1999; 11:107-13.
