6.2.1 Imipenem and Cilastatin
(Proposed for deletion 2003)

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BRIEF COMMENTARY

Reasons for reviewing Imipenem and Cilastatin
Imipenem and Cilastatin is included in the complementary list of the EML as a reserve antimicrobial. Its public health relevance as an essential medicine, was questioned at the 2003 Meeting of the Expert Committee.

General considerations
Imipenem is an antimicrobial that belongs to the group of carbapenems, and is very active against a wide variety of infections including urinary tract, lower respiratory, intra-abdominal and gynecological infections. It is also active on skin, soft tissue, bone and joints infections. It is administered parenterally. There is an extensive body of evidence about the good benefit/risk ratio of the use of imipenem-cilastatin in treatment of severe infections caused for multidrug-resistant microorganisms. Imipenem/Cilastatin is an antimicrobial indispensable for use in hospital settings and its main indications are treatment of infections with wide spectrum activity on several bacteria including aerobic and anaerobic, gram positive and gram negative microorganisms, especially multidrug-resistant (P. aeruginosa, Acinetobacter baumanii and Klebsiella sp). These bacteria show an increasing pattern of resistance to other antimicrobials: ceftazidime, amikacin and ciprofloxacin. Bacteroides fragilis is also susceptible. This agent is not active against Enterococcus faecium, Staphlococcus resistant to oxacilin, Stenotrophomonas maltophilia and Burkholderia cepacia.

Place in therapeutics. Nosocomial environment of multidrug-resistant species.
Nosocomial infections, specially in intensive care units, are frequently caused by multi-drug resistant microorganisms. Bacterial resistance to antimicrobials is a worldwide problem that threatens the successful treatment of a growing number of infections caused by nosocomial isolates. In developing countries this situation is magnified. This escalating scenario requires the use of broad-spectrum carbapenems as adequate therapy for many infections that threatens the lives of critically ill patients. On the other hand, and in the same way that happens with long time and extent use of any antimicrobial, increasing the use of imipenem in these settings is promoting the emergence of resistant mutants, notably during therapy for P. aeruginosa and Enterobacter infections. There are a variety of mechanisms described to be responsible for the development of such resistance. (3-4)
Another Gram-negative bacilli, Acinetobacter strains, represents a great problem in certain geographic regions such as Latin America. They have unique characteristics among nosocomial Gram-negative bacteria that favor their persistence in the hospital environment, where they are commonly more resistant to antimicrobial agents, and spread easily from patient to patient \(^{(5)}\) (Table 1).

Because no new classes of antibacterial agents effective against multi-drug resistant gram-negative bacteria are likely to become available within the next few years, imipenem plus cilastatin (and other carbapenems) will continue to be used with increasing frequency. \(^{(3,6,7)}\)

**Activity of six selected antimicrobial agents tested against nosocomial and all Acinetobacter species**
(SENTRY. Antimicrobial Surveillance Programme in the United States and Canada compared with Latin America, January 1997 – December 1999). Table 1 \(^{(5)}\)

<table>
<thead>
<tr>
<th>Antimicrobial agent (*)</th>
<th>United States - Canada</th>
<th>Latin America</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Susceptible %</td>
<td>Resistant %</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>65.3</td>
<td>24.0</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>70.0</td>
<td>28.0</td>
</tr>
<tr>
<td>Imipenem</td>
<td>88.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Amikacin</td>
<td>91.3</td>
<td>4.0</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>71.3</td>
<td>25.3</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>70.7</td>
<td>20.7</td>
</tr>
</tbody>
</table>

\(^{(5)}\) all antimicrobial tested are included in the EML

**CONCLUSION**

We should emphasize that in the most critical situations where severe infections with multi-drug resistant bacteria can threaten the lives of patients, it is indispensable that drugs like imipenem are made available.

**RECOMMENDATION**

Imipenem/cilastatin should be kept as a complementary medicine in the EML.
REFERENCES


4. Livermore DM. Multiple mechanisms of antimicrobial resistance in *P. Aeruginosa*: our worst nightmare?. *Clinical Infectious Diseases. 2002; 34:634-40*

