DOSAGE OF ANTIBIOTICS (AVAILABLE IN BELGIUM) IN ADULT PATIENTS
INTEGRATING THE NEW EUCAST BREAKPOINT TABLES (VERSION 13;0 VALID AS FROM JANUARY 1ST 2023)

Introduction
Following the recommendations from the Belgian National Antiibiotic Committee (NAC), most microbiology laboratories in Belgium apply the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines for the interpretation and reporting of antimicrobial susceptibility testing (AST) results. The EUCAST recommendations have the advantage of considering microbiological, pharmacological, and clinical parameters in establishing breakpoints of sensitivity and resistance of bacteria to different antibiotics. Important changes in the interpretation of AST have been introduced by EUCAST in 2019 and mostly result from the introduction of a new “I” result category which now stands for “susceptible at increased exposure”. This new definition emphasizes the relationship between the concentration of the antimicrobial agent at the site of infection and the breakpoints for categorization (S, I and R).

There are now two categories of “susceptibility” which refers to the isolates categorized as S (susceptible at standard dosage) or I (susceptible at high dose). The latter highlights the importance of increasing the individual dose, the frequency of dosing, the route of administration and relying on the pharmacokinetics of agents at the infected site, which may all significantly increase the exposure. The creation of the new “I” category intends to promote the use of narrow-spectrum antibiotics with an “I” result by adjusting to the correct high posology, rather than switching to broader spectrum antibiotics prescribed at standard dosage (S result).

Below is a Belgian adaptation of the EUCAST recommendations and some dosages may not be identical to those in the EUCAST dosage table. These adaptations result from additional considerations: recent clinical data from the literature (e.g. temocillin and urinary tract infections) and/or specific therapeutical experience of nosocomial infections in Belgium for some agents (e.g. ceftazidime) leading to the general use of higher dosage instead of standard dosage recommended by EUCAST (expert opinion). High dosage regimens are still recommended for empirical treatment (without/before the susceptibility test results of the causative pathogen available).

How to read the table:
To achieve proper use of the new EUCAST definitions, one must ensure that the daily posology of antibiotics used locally matches with the dosage levels recommended. The table below shows the standard dosages and high dosages of each antibiotic (other than antimycobacterial agents). The standard dosages must be used for the treatment of infections with bacteria categorized as “susceptible to standard dosage” (S), and the high dosages are required for the treatment of infections with bacteria categorized as “susceptible to high dosage” (I).

These dosages apply to adult patients of normal weight (not obese), excluding the context of renal or hepatic impairment. They may not fully apply to specific clinical situations that require higher dosages such as septic shock, neutropenia, infective endocarditis, central nervous system infection, bone and joint infection, infection on prosthetic material, etc.

Higher dosages and/or longer infusion times for "time-dependent" antibiotics (β-lactams for example) can also make it possible to obtain the PK/PD targets of efficacy, but the risk of toxicity must be taken into account. For some antibiotics, proposed dosage regimens for continuous administration might require further adjustments, since the maximum duration of stability of the molecule must be considered. For some antibiotics, when there is no I result according to EUCAST breakpoints, no high dose is recommended in the table.

24-02-2023
1. A higher dosage is recommended in specific clinical conditions (endocarditis, meningitis, osteomyelitis, ...).

2. CNS = central nervous system, HD = high dosage, MIC = minimal inhibitory concentration, HAP = hospital acquired pneumonia, IA = intra-abdominal, MIU = million international units, MRSA = methicillin-resistant *Staphylococcus aureus*, SD = standard dosage, TDM = therapeutic drug monitoring, UTI = urinary tract infection, VAP = ventilator associated pneumonia.

3. No “I” results according to EUCAST breakpoints and/or no high dosage defined.
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<table>
<thead>
<tr>
<th>ANTI-INFECTIVE AGENT</th>
<th>STANDARD DOSAGE (SD) FOR EUCAST “S” STRAINS</th>
<th>HIGH DOSAGE (HD) FOR EUCAST “I” STRAINS</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEPHALOSPORINS (continued)</td>
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</tbody>
</table>
| Ceftriaxone iv.        | 2 g every 12 or 24 hours (see comments).  |                                        | • Standard dosage.  
|                       |                                           |                                        | o Meningitis and other CNS² infections, infections due to *Staphylococcus aureus*: 2 g every 12 hours.  
|                       |                                           |                                        | o Other infections: 2 g every 24 hours.  
|                       |                                           |                                        | • Uncomplicated gonorrhoea: single dose of 1 g im.  |
| Cefuroxime iv.        | 1.5 g every 8 hours.                      | 1.5 g every 8 hours.                   |          |
| Cefuroxime axetil po. | 500 mg every 8 hours.                    | 500 mg every 8 hours.                  |          |

<table>
<thead>
<tr>
<th>CARBAPENEMS, MONOBACTAMS</th>
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</thead>
<tbody>
<tr>
<td>Aztreonam iv.</td>
<td>1 to 2 g every 8 hours¹.</td>
<td>2 g every 6 hours.</td>
<td>• Severe infections due to <em>Pseudomonas aeruginosa</em>: 2 g every 6 hours by extended 3-hour infusions.</td>
</tr>
<tr>
<td>Meropenem iv.</td>
<td>1 g every 8 hours.</td>
<td>2 g every 8 hours by extended 3-hour infusions.</td>
<td></td>
</tr>
<tr>
<td>Meropenem-vaborbactam iv.</td>
<td>(2 g + 2 g) every 8 hours by extended 3-hour infusions.</td>
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<tr>
<th>AZALIDES, LINCOSAMIDES, (NEO)MACROLIDES</th>
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<tbody>
<tr>
<td>Azithromycin po.</td>
<td>500 mg every 24 hours.</td>
<td>None³.</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin po.</td>
<td>500 mg every 12 hours.</td>
<td>None³.</td>
<td></td>
</tr>
<tr>
<td>Clarithromycin iv.</td>
<td>500 mg every 12 hours.</td>
<td>None³.</td>
<td></td>
</tr>
<tr>
<td>Clindamycin iv.</td>
<td>600 mg every 8 hours.</td>
<td>None³.</td>
<td>• Dosages vary by indication [up to (900 mg every 8 hours) or (600 mg every 6 hours)].</td>
</tr>
<tr>
<td>Clindamycin po.</td>
<td>300 mg every 6 to 8 hours¹.</td>
<td>None³.</td>
<td>• Dosages vary by indication (up to 600 mg every 8 hours).</td>
</tr>
<tr>
<td>Erythromycin iv.</td>
<td>500 mg every 6 to 8 hours.</td>
<td>None³.</td>
<td>• Dosages vary by indication.</td>
</tr>
<tr>
<td>Roxithromycin po.</td>
<td>150 mg every 12 hours.</td>
<td>None³.</td>
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3. No “I” results according to EUCAST breakpoints and/or no high dosage defined.
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### MISCELLANEOUS ANTIBIOTICS (continued)

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<td>Linezolid po.</td>
<td>600 mg every 12 hours.</td>
<td>None³.</td>
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<tr>
<td>Metronidazole iv.</td>
<td>500 mg every 8 hours.</td>
<td>None³.</td>
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<tr>
<td>Metronidazole po.</td>
<td>500 mg every 8 hours.</td>
<td>None³.</td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin po.</td>
<td>100 mg every 6 to 8 hours.</td>
<td>None³.</td>
<td>Only indicated for the treatment of uncomplicated UTI².</td>
</tr>
<tr>
<td>Rifampicin iv.</td>
<td>600 mg every 24 hours.</td>
<td>None³.</td>
<td></td>
</tr>
<tr>
<td>Rifampicin po.</td>
<td>600 mg every 24 hours.</td>
<td>None³.</td>
<td></td>
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<td>Trimethoprim + sulfamethoxazole iv.</td>
<td>(160 mg + 800 mg) every 12 hours.</td>
<td>(240 mg + 1.2 g) every 12 hours.</td>
<td>Higher dosages (maximum 960 mg + 4.8 g per day) are required in some conditions:</td>
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<tr>
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<td>o Infections due to <em>Stenotrophomonas maltophilia</em>: (4 mg + 20 mg)/kg every 8 to 12 hours (maximum 960 mg + 4.8 g per day).</td>
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