Société belge d'infectiologie et de microbiologie clinique
Belgische vereniging voor infectiologie en klinische microbiologie

IGGI
Infectiologiegids - Guide d'infectiologie

National Antibiogram Committee

# 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 Antibiogram 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 susceptibility 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 categorisation ("S", "I" and "R").
**There are now two categories of "susceptibility" which refer to the isolates categorised 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).**
The table 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 mentioned in the table.
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| ANTI-INFECTIVE AGENT | STANDARD DOSAGE (SD) FOR EUCAST "S" STRAINS | HIGH DOSAGE (HD) FOR EUCAST "I" STRAINS | COMMENTS |
|---|---|---|---|
| **PENICILLINS** | | | |
| **Amoxicillin iv.** | 1 to 2 g every 8 hours[1]. | 2 g every 4 hours. | |
| **Amoxicillin po.** | 500 mg every 8 hours[1]. | 1 g every 8 hours. | • Infections due to *Enterobacterales*: the SD[2] can only be used to treat uncomplicated UTI[2]. |
| **Benzylpenicillin iv (penicillin G).** | 2 MIU[2] every 6 hours[1] . | 2 to 4 MIU[2] every 4 hours. | • Meningitis due to *Streptococcus pneumoniae*: strains with a MIC[2] ≤ 0.06 µg/ml are susceptible to doses of 4 MIU[2] every 4 hours.<br>• Other infections due to *Streptococcus pneumoniae*: the dosage can be adjusted to the MIC[2] (if available):<br>○ MIC[2] < 0.5 µg/ml: 2 MIU[2] every 6 hours.<br>○ MIC[2] 1 µg/ml: 4 MIU every 6 hours or 2 MIU[2] every 4 hours.<br>○ MIC[2] 2 µg/ml: 4 MIU[2] every 4 hours. |
| **Amoxicillin-clavulanate iv.** | (1 g + 200 mg) every 6 to 8 hours. | [(2 g + 200 mg) every 8 hours] or [1 g + 200 mg) every 4 hours]. | |
| **Amoxicillin-clavulanate po.** | (500 mg + 125 mg) every 8 hours. | (875 mg + 125 mg) every 8 hours. | • Infections due to *Enterobacterales*: the SD[2] can only be used to treat uncomplicated UTI[2] (urinary tract infections). |
| **Flucloxacillin iv.** | 1 to 2 g every 6 hours[1]. | None[3]. | • Dosages vary be indication (up to 2 g every 4 hours). |
| **Flucloxacillin po.** | 1 g every 8 hours. | None[3]. | |
| **Piperacillin-tazobactam iv.** | [(4 g + 500 mg) every 6 hours] or [(4 g + 500 mg) every 8 hours by extended 4-hour infusions]. | [(4 g + 500 mg) every 6 hours by extended 4-hour infusions] or [(16 g + 2 g)/day by continuous infusion]. | |
| **Temocillin iv.** | No more "S" results reported for *Enterobacterales*. | 2 g every 8 or 12 hours. | • 2 g every 12 hours may be used in the context of uncomplicated UTI[2] and of complicated UTI[2] with bacteraemia due to strains with a MIC[2] < 8 µg/ml.<br>• Other infections: (2 g every 8 hours) or [6 g/day by continuous infusion (after a loading dose of 2 g)]. |

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.

| ANTI-INFECTIVE AGENT | STANDARD DOSAGE (SD) FOR EUCAST "S" STRAINS | HIGH DOSAGE (HD) FOR EUCAST "I" STRAINS | COMMENTS |
|---|---|---|---|
| **CEPHALOSPORINS** | | | |
| **Cefadroxil po.** | 500 mg to 1 g every 12 hours. | None[3]. | |
| **Cefalexin po.** | 500 mg every 6 hours. | None[3]. | |
| **Cefazolin iv.** | 1 g every 8 hours[1]. | 2 g every 8 hours. | |
| **Cefepime iv.** | 2 g every 8 hours [(1 g every 8 hours) or (2 g every 12 hours) in stable, non-obese patients with uncomplicated infections, …]. | 2 g every 8 hours. | • Severe infections due to *Pseudomonas aeruginosa*: [2 g every 8 hours by extended 4-hour infusions] or [6 g/day by continuous infusion (after a loading dose of 2 g over 30 minutes)]. |
| **Cefotaxime iv.** | 2 g every 8 hours. | (2 g every 8 hours over 30 minutes) or (2 g every 8 hours by extended 4-hour infusions). | • Meningitis and other CNS[2] infections: 2 g every 4 hours. |
| **Ceftaroline iv.** | 600 mg every 12 hours over 1 hour. | 600 mg every 8 hours over 2 hours. | |
| **Ceftazidime iv.** | 2 g every 8 hours [(1 g every 8 hours) or (2 g every 12 hours) in stable, non-obese patients with uncomplicated infections, …]. | 2 g every 8 hours. | • Severe infections due to *Pseudomonas aeruginosa*: [2 g every 8 hours by extended 4-hour infusions] or [6 g/day by continuous infusion (after a loading dose of 2 g over 30 minutes)]. |
| **Ceftazidime-avibactam iv.** | (2 g + 500 mg) every 8 hours over 2 hours. | None[3]. | |
| **Ceftriaxone iv.** | 2 g every 12 or 24 hours (see comments). | 2 g every 12 hours. | • Standard dosage:.<br>  ○ Meningitis and other CNS[2] infections, infections due to *Staphylococcus aureus*: 2 g every 12 hours.<br>  ○ Other infections: 2 g every 24 hours.<br>• Uncomplicated gonorrhoea: single dose of 1 g im. |
| **Cefiderocol iv.** | 2 g every 8 hours by extended 8-hour infusions. | None[3]. | • Currently not marketed in Belgium (consult hospital pharmacist). |

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3. No "I" results according to EUCAST breakpoints and/or no high dosage defined.

| ANTI-INFECTIVE AGENT | STANDARD DOSAGE (SD) FOR EUCAST "S" STRAINS | HIGH DOSAGE (HD) FOR EUCAST "I" STRAINS | COMMENTS |
|---|---|---|---|
| **CEPHALOSPORINS (continued)** | | | |
| **Ceftolozane-tazobactam iv.** | [(1 g + 500 mg) every 8 hours by extended infusion over 1 hour] or [(2 g + 1 g) every 8 hours over 1 hour] (see comments). | None[3]. | • Standard dosage.<br>○ IA[2] infections and UTI[2]: [(1 g + 500 mg) every 8 hours by extended infusion over 1 hour.<br>○ HAP[2] (including VAP[2]): (2 g + 1 g) every 8 hours over 1 hour. |
| **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. | |
| **CARBAPENEMS, MONOBACTAMS** | | | |
| **Aztreonam iv.** | 1 to 2 g every 8 hours[1]. | 2 g every 6 hours. | • Severe infections due to *Pseudomonas aeruginosa*: 2 g every 8 hours by extended 3-hour infusions. |
| **Meropenem iv.** | 1 g every 8 hours. | 2 g every 8 hours by extended 3-hour infusions. | |
| **Meropenem-vaborbactam iv.** | (2 g + 2 g) every 8 hours by extended 3-hour infusions. | None[3]. | |
| **AZALIDES, (NEO)MACROLIDES, LINCOSAMIDES** | | | |
| **Azithromycin po.** | 500 mg every 24 hours. | None[3]. | |
| **Clarithromycin iv.** | 500 mg every 12 hours. | None[3]. | |
| **Clarithromycin po.** | 500 mg every 12 hours. | None[3]. | |
| **Clindamycin iv.** | 600 mg every 8 hours[1]. | None[3]. | • Dosages vary by indication [up to (900 mg every 8 hours) or (600 mg every 6 hours)]. |
| **Clindamycin po.** | 300 mg every 6 to 8 hours[1]. | None[3]. | • Dosages vary by indication (up to 600 mg every 8 hours). |
| **Erythromycin iv.** | 500 mg every 6 to 8 hours. | None[3]. | • Dosages vary by indication. |
| **Erythromycin iv.** | 500 mg every 8 to 12 hours. | None[3]. | • Dosages vary by indication. |
| **Roxithromycin po.** | 150 mg every 12 hours. | None[3]. | |

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3. No "I" results according to EUCAST breakpoints and/or no high dosage defined.

| ANTI-INFECTIVE AGENT | STANDARD DOSAGE (SD) FOR EUCAST "S" STRAINS | HIGH DOSAGE (HD) FOR EUCAST "I" STRAINS | COMMENTS |
|---|---|---|---|
| **TETRACYCLINES** | | | |
| **Doxycycline po.** | 100 mg every 12 hours. | None[3]. | |
| **Minocycline po.** | 100 mg every 12 hours. | None[3]. | |
| **Tigecycline iv.** | 1 loading dose of 100 mg, followed, starting 12 hours after the start of the loading dose, by 50 mg every 12 hours. | None[3]. | |
| **FLUOROQUINOLONES** | | | |
| **Ciprofloxacin iv.** | 400 mg every 12 hours. | 400 mg every 8 hours. | |
| **Ciprofloxacin po.** | 500 mg every 12 hours. | 750 mg every 12 hours. | |
| **Levofloxacin iv.** | 500 mg every 24 hours. | 500 mg every 12 hours. | |
| **Levofloxacin po.** | 500 mg every 24 hours. | 500 mg every 12 hours. | |
| **Moxifloxacin iv.** | 400 mg every 24 hours. | None[3]. | |
| **Moxifloxacin po.** | 400 mg every 24 hours. | None[3]. | |
| **Ofloxacin po.** | 400 mg every 12 hours. | 400 mg every 12 hours. | |
| **AMINOGLYCOSIDES** | | | |
| **Amikacin iv.** | 25 to 30 mg/kg every 24 hours. | No high dosage defined. | • If treatment duration exceeds 3 days, TDM[2] indicated. |
| **Gentamicin iv.** | 5 to 7 mg/kg every 24 hours. | No high dosage defined. | • (3 mg/kg every 24 hours) or (1 mg/kg every 8 hours) for the treatment of endocarditis. TDM[2] indicated.<br>• If treatment duration exceeds 3 days (other indications than endocarditis), TDM[2] indicated. |
| **Tobramycin iv.** | 5 to 7 mg/kg every 24 hours. | No high dosage defined. | • If treatment duration exceeds 3 days, TDM[2] indicated.. |

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| **GLYCOPEPTIDES** | | | |
| **Teicoplanin iv.** | 5 loading doses of 10 to 12 mg/kg administered with intervals of 12 hours on days 1 to 3, followed, as from day 4, by TDM[2] guided doses of 6 to 12 mg/kg every 24 hours[1]. | None[3]. | • Dosages vary by indication.<br>• Target trough concentration for uncomplicated infections due to MRSA[2] : 15 to 30 µg/ml.<br>• Target trough concentration in patients with severe or complicated infections due to MRSA: 20 to 40 µg/ml.<br>• TDM[2] should not be started during the first 4 treatment days. |
| **Vancomycin iv.** | • 1 loading dose of 25 to 30 mg/kg over 2 hours, followed immediately by a TDM[2] guided continuous infusion of 30 to 40 mg/kg/day.<br>• 1 loading dose of 25 to 30 mg/kg over 1 hour, followed (12 hours after the start of the loading dose) by a TDM[2] guided intermittent infusion of ± 15 mg/kg every 12 hours. | None[3]. | • Dosages vary by indication.<br>• Target concentration of 20 to 30 µg/ml in case of TDM[2] guided continuous infusion.<br>• Target trough concentration of 15 to 20 µg/ml in case of TDM[2] guided intermittent infusions. |
| **MISCELLANEOUS ANTIBIOTICS** | | | |
| **Colistin iv.** | 1 loading dose of 9 MIU[2], followed, starting 8 hours after the start of the loading dose, by 4.5 MIU[2] every 8 hours. | None[3]. | |
| **Fidaxomicin po.** | 200 mg every 12 hours. | None[3]. | |

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| **MISCELLANEOUS ANTIBIOTICS (continued)** | | | |
| **Fosfomycin iv.** | 16 to 15 g/day div in 3 or 4 doses. | None[3]. | • Dosages vary by indication.<br>• Currently not marketed in Belgium (consult hospital pharmacist). |
| **Fosfomycin (trometamol) po.** | Single dose of 3 g. | None[3]. | • Only indicated for the treatment of uncomplicated UTI[2]. |
| **Linezolid iv.** | 600 mg every 12 hours. | None[3]. | |
| **Linezolid po.** | 600 mg every 12 hours. | None[3]. | |
| **Metronidazole iv.** | 500 mg every 8 hours. | None[3]. | |
| **Metronidazole po.** | 500 mg every 8 hours. | None[3]. | |
| **Nitrofurantoin po.** | 100 mg every 6 to 8 hours. | None[3]. | • Only indicated for the treatment of uncomplicated UTI[2]. |
| **Rifampicin iv.** | 600 mg every 24 hours. | None[3]. | |
| **Rifampicin po.** | 600 mg every 24 hours. | None[3]. | |
| **Trimethoprim-sulfamethoxazole (TMP-SMX) iv.** | (160 mg + 800 mg) every 12 hours. | (240 mg +1.2 g) every 12 hours. | • Higher dosages (maximum 960 mg + 4.8 g per day) are required in some conditions:<br>  ○ Infections due to *Stenotrophomonas maltophilia*: (4 mg + 20 mg)/kg every 8 to 12 hours (maximum 960 mg + 4.8 g per day).<br>  ○ Infections due to *Pneumocystis jirovecii*: (4 to 5 mg + 20 to 25 mg)/kg every 6 hours. |
| **Trimethoprim- sulfamethoxazole (TMP-SMX) po.** | (160 mg + 800 mg) every 12 hours. | (240 mg + 1.2 g) every 12 hours. | • Higher dosages (maximum 960 mg + 4.8 g per day) are required in some conditions:<br>  ○ Infections due to *Stenotrophomonas maltophilia*: (4 mg + 20 mg)/kg every 8 to 12 hours (maximum 960 mg + 4.8 g per day).<br>  ○ Infections due to *Pneumocystis jirovecii*: (4 to 5 mg + 20 to 25 mg)/kg every 6 hours. |

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