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 antimicrobials (Belgian specialties) in adult patients integrating the new EUCAST breakpoint tables*
*(version 13.0 valid from 01.01.2023)

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 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 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.

Antimicrobial	Standard Dosage (SD) (for EUCAST S result)	High Dosage (HD) (for EUCAST I result)	Comments
PENICILLINS			
Benzylpenicillin (Penicillin G) (i.v.)	2 MU every 6h[1]	2-4 MU every 4h	MU: million units - For meningitis caused by S. pneumoniae: for a dose of 4 MU x 6 iv, isolates with MIC ≤0.06 mg/L are susceptible - For pneumococcal non-meningitis, dosage can be adjusted to minimal inhibitory concentration (MIC) result *if available*. MIC ≤ 0.5 mg/L: 2 MU x 4 iv, MIC 1 mg/L: 4 MU g x 4 iv or 2 MU x 6 iv MIC 2 mg/L: 4 MU x 6 iv
Amoxicillin (i.v.)	1-2 g every 8h[1]	2 g every 4h	
Amoxicillin (p.o.)	500 mg every 8h[1]	1 g every 8h	For *Enterobacterales* , SD can only be used for uncomplicated UTI[2]
Amoxicillin-clavulanic acid (i.v.)	1 g/200 mg every 6-8h	2 g/200 mg every 8h or 1 g/200 mg every 4h	
Amoxicillin-clavulanic acid (p.o.)	500 mg/125 mg every 8h	875 mg/125 mg every 8h	For *Enterobacterales* , SD can only be used for uncomplicated UTI
Flucloxacillin (i.v.)	1-2 g every 6h[1]	No I results	Dosage vary by indication (up to 2g every 4h)
Flucloxacillin (p.o.)	1 g every 8h	No I results	
Temocillin (i.v.)	No more S results for *Enterobacterales*	2 g every 12h* 2 g every 8h**	* 2 g every 12h may be used in the context of: - uncomplicated UTI[2] - complicated UTI[2] with bacteremia and with a MIC ≤ 8 mg/L ** Other situations: 2 g every 8h (or 6g/d in continuous infusion after a loading dose of 2g)
Piperacillin-tazobactam (i.v.)	4 g/500 mg every 6h or every 8h by extended 4h infusion	4 g/500 mg every 6h by extended 4h infusion or 16 g/d by continuous infusion (after a loading dose of 4g in 30 min)	

Antimicrobial	Standard Dosage (STD) (for EUCAST S result)	High Dosage (for EUCAST I result)	Comments
CEPHALOSPORINS			
Cefadroxil (p.o)	500 mg–1g every 12h	NONE[3]	
Cefalexin (p.o.)	500 mg every 6h	NONE[3]	
Cefazolin (i.v.)	1g every 8h[1]	2 g every 8h	
Cefepime (i.v.)	2 g every 8h (1g/8h ou 2g/12h if stable patient , non-complicated infection, non obese, …)	2 g every 8h	Severe P. aeruginosa infections: 2 g x 3 with extended 4-hour infusion or continue infusion 6g/d after a loading dose of 2g in 30 min
Cefotaxime (i.v.)	2 g every 8h	2 g every 8h in 30 min. or by extended 4h*	*Meningitis, central nervous system infection: 2 g every 4h*
Ceftaroline (i.v.)	600 mg every 12h over 1h	600 mg every 8h over 2h	
Ceftazidime (i.v.)	2 g every 8h (1g/8h if stable patient, non-complicated infection, non obese, …)	2 g every 8h	Severe P. aeruginosa infections: 2 g every 8h with extended 4-hour infusion or continue infusion 6g/d after a loading dose of 2g in 30 min
Ceftazidime-avibactam (i.v.)	2 g/500 mg every 8h over 2h	NONE[3]	
Ceftriaxone (i.v.)	2 g every 24h*	2 g every 12h	*Meningitis, central nervous system infection, *S. aureus*: 2 g every 12h Uncomplicated gonorrhoea: 1 g IM as a single dose
Cefiderocol (i.v.)	2 g every 8h by extended 3h infusion	NONE[3]	Currently not marketed in Belgium (import)
Cefuroxime (i.v.)	1.5 g every 8h	1.5 g every 8h	
Cefuroxime (p.o.)	500 mg every 8h	500 mg every 8h	
Ceftolozane-tazobactam (i.v.)	1 g/500 mg every 8h° by extended 1h infusion or 2 g/1 g every 8h # by extended 1h infusion	NONE[3]	°Intra-abdominal infections and urinary tract infections #Hospital acquired pneumonia, including ventilator associated pneumonia
CARBAPENEMS			
Meropenem (i.v.)	1 g every 8h	2 g every 8h over 3h	
Meropenem-vaborbactam (i.v.)	2 g/2 g every 8h by extended 3h infusion	NONE[3]	
MONOBACTAMS			
Aztreonam (i.v.)	1-2 g every 8h[1]	2 g every 6h	Severe P. aeruginosa infections: 2 g x 4 with extended 3-hour infusion
MACROLIDES AND LINCOSAMIDES			
Azithromycin (p.o.)	500 mg every 24h	NONE[3]	
Clarithromycin (i.v.)	500 mg every 12h	No I result	
Clindamycin (i.v.)	600 mg every 8h[1]	No I result	Dosage vary by indication (up to 600 every 6h or 900 mg every 8h)

Clindamycin (p.o.)	300 mg every 6-8h[1]	No I result	Dosage vary by indication (up to 600 mg every 8h)
Erythromycin (i.v.)	500 mg every 8-6h	No I result	Dosage vary by indication
Erythromycin (p.o.)	500 mg every 6-12h	No I result	Dosage vary by indication
Roxithromycin (i.v.)	150 mg every 12h	NONE[3]	

Antimicrobial	Standard Dosage (SD) (for EUCAST S result)	High Dosage (HD) (for EUCAST I result)	Comments
TETRACYCLINES			
Doxycycline (p.o.)	100 mg every 12h	No I result	
Minocycline (p.o)	100 mg every 12h	No I result	
Tigecycline (i.v.)	100 mg loading dose followed by 50 mg every 12h	No I result	
FLUROQUINOLONES			
Ciprofloxacin (i.v.)	400 mg every 12h	400 mg every 8h	
Ciprofloxacin (p.o.)	500 mg every 12h	750 mg every 12h	
Levofloxacin (i.v.)	500 mg every 24h	500 mg every 12h	
Levofloxacin (p.o.)	500 mg every 24h	500 mg every 12h	
Moxifloxacin (i.v.)	400 mg every 24h	NONE[3]	
Moxifloxacin (p.o.)	400 mg every 24h	NONE[3]	
Ofloxacin (p.o.)	400 mg every 12h	400 mg every 12h	
AMINOGLYCOSIDES			
Amikacin (i.v.)	25-30 mg/kg every 24h	NONE[3]	
Gentamicin (i.v.)	5-7 mg/kg every 24h	NONE[3]	For endocarditis: 3 mg/kg every 24h or in 3 doses
Tobramycin (i.v.)	5-7 mg/kg every 24h	NONE[3]	
GLYCOPEPTIDES			
Teicoplanin (i.v.)	6-12 mg/kg every 24h[1] after loading dose of 10-12 mg/kg/12h for 5 doses	No I result	Dosage vary by indication Target trough concentrations of 15–30 mg/L are recommended for the treatment of non-complicated MRSA infection, 20–40 mg/L in patients with serious and/or complicated MRSA infections (first TDM[4] not before D4)
Vancomycin (i.v.)	Loading dose of 25-30mg/kg then 15 mg/kg every 12h by discontinuous infusion or 30-40 mg/kg every 24h by continuous infusion, then based on TDM[4]	NONE[3]	Dosage vary by indication Target trough concentrations of 15–30 mg/L are recommended in case of intermittent injection and between 20-30 mg/L in continuous infusion
OXAZOLIDINONES			

Linezolid (i.v.)	600 mg every 12h	NONE[3]	
Linezolid (p.o.)	600 mg every 12h	NONE[3]	

Antimicrobial	Standard Dosage (STD) (for EUCAST S result)	High Dosage (for EUCAST I result)	Comments
MISCELLANEOUS AGENTS			
Colistin (i.v.)	Loading dose of 9 MU followed by 4.5 MU every 12h	NONE[3]	
Fidaxomycin (p.o.)	200 mg every 12h	NONE[3]	
Fosfomycin (p.o.)	3 g as a single dose	NONE[3]	Only for non complicated UTI[2]
Fosfomycin (i.v.)	16-18 g/day divided in 3-4 doses	NONE[3]	Dosage vary by indication Currently not marketed in Belgium (import
Metronidazole (i.v.)	500 mg every 8h	NONE[3]	
Metronidazole (p.o.)	500 mg every 8h	NONE[3]	
Nitrofurantoin (p.o.)	100 mg every 6-8h	NONE[3]	Only for non complicated UTI[2]
Rifampicin (i.v.)	600 mg every 24h[1]	NONE[3]	…
Rifampicin (p.o.)	600 mg every 24h[1]	NONE[3]	
Trimethoprim – sulfamethoxazole (i.v.)	160 mg/800 mg every 12h	240 mg/1.2 g every 12h	Higher dosage used in some indications: *Stenotrophomonas maltophilia* infections 8-12 mg/kg/d of TMP every 12-8h. *Pneumocystis jirovecii:* 15-20* mg/kg/d every 6h of TMP * based on trimethoprim dosage
Trimethoprim – sulfamethoxazole (p.o.)	160 mg/800 mg every 12h	240 mg/1.2 g every 12h	Higher dosage used in certain conditions: *Stenotrophomonas maltophilia* infections 8-12 mg/kg/d of TMP every 12-8h (max 960 mg trimethoprim). *Pneumocystis jirovecii:* 15-20* mg/kg/d of TMP every 6h * based on trimethoprim dosage

[1]Higher dosage recommended in specific clinical situations (such as meningitis, endocarditis, ostéomyelitis…)
[2]UTI: urinary tract infections
[3]NONE = no high dosage defined

[4]TDM: Therapeutic drug monitoring

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