



Severn Pathology

North Bristol NHS Trust

Antimicrobial Reference Laboratory

GUIDELINE RANGES FOR TDM

2021 - 2022

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Antimicrobial Reference Laboratory – Guideline Ranges 2021 - 2022

Important Changes This Version	New Analytes Available (from May 2021)
ISAVUCONAZOLE now 2-4mg/L	ISONIAZID (+ N-Acetyl ISONIAZID)*

***ISONIAZID Sample Requirements:**

Blood drawn into Sodium Oxalate tube (Grey top)
Initial 2h post dose sample required. If slow absorption suspected a further 6h post dose sample may be drawn
Blood centrifuged in the laboratory and Plasma aliquoted into a secondary tube
Sent via Dx or Royal Mail
Plasma must reach ARL within 5 days at Room Temperature

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Version: 2021 - 2022
Issue date: 1st April 2021
Withdraw date: 1st April 2022

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Agent	Risk group	Expected levels (Guide-lines) (mg/L)	Re-assay interval* (days)
Aminoglycosides			
Gentamicin Tobramycin (Once-daily) ^a	All patients on 2nd-4th dose; earlier if changing renal function or other risk factors.	Pre <1 mg/L Post >10 mg/L or 8 h post (5 mg/kg) 1.5-6 mg/L or follow Hartford nomogram (but note this is for 7 mg/kg)	6-8
Gentamicin (Once-daily 5 mg/kg) ^b	Neonatal sepsis	Pre < 2mg/L BUT <1 mg/L after 3 rd dose Post >8mg/L	
Gentamicin Tobramycin (BD or TDS) ^{c-d}	All patients on 2nd-4th dose; earlier if changing renal function or other risk factors.	Gram Negative pneumonia Pre <2 mg/L Post >7 mg/L Infective endocarditis (IE) Pre <1 mg/L Post 3-5 mg/L	3-7
Amikacin (Once-daily) ^{a,f}		Pre <5 mg/L Post 40-45 [†] mg/L	6-8
Amikacin (BD or TDS) ^c		Pre <10 mg/L Post 20-30 mg/L	3-7
Streptomycin (7.5 mg/kg BD) ^{d-e}	All patients after 2nd-4th dose.	Infective endocarditis Pre <3.0 mg/L Post 10-25 mg/L	7-28
* Assuming initial results are within the expected range ^aNicolau et al. 1995. Antimicrobial Agents & Chemotherapy 39:650-655. ^bNICE Clinical Guideline 149, 2012. ^cBritish National Formulary, Edition 67. 2014 section 5.1.4. ^dElliott et al. 2004. Journal of Antimicrobial Chemotherapy 54: 971-81. ^eNote: these are different to the AHA Scientific Statement ranges. Baddour et al. 2015. Circulation 132:1435-86. ^fJenkins et al. 2016. Journal of Antimicrobial Chemotherapy 71: 2754-59. [†] Guideline levels not available; these are levels that are routinely seen. Hartford nomogram link https://clincalc.com/Aminoglycoside/			

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Glycopeptides/Lipopeptides/Oxazolidinones			
Vancomycin ^{a-d}	All patients on >2-4 days therapy. Patients receiving other nephrotoxic drugs. Assay at 2nd-4th dose.	Pre dose 10-15 mg/L but 15-20 mg/L in complicated infection OR Steady state during continuous infusion 20-25 mg/L	6-8
Teicoplanin ^{e-f}	a) Skin and soft tissue infection b) Bone and Joint infection d) Infective endocarditis e) OPAT on 25 mg/kg 3x per week	Pre 15-30 but <60 mg/L Pre 20-40 but <60 mg/L Pre 30-40 but <60 mg/L Pre 20-30 mg/L	6-8
Daptomycin ^g	Patients with CPK elevation, high dose therapy (>6 mg/kg) or renal impairment	Pre dose 5-20 mg/L or Pre dose 10-20mg/L in severe sepsis Pre dose levels >20 mg/L associated with increased risk of toxicity	6-8
Linezolid (600mg BD) ^{h-i}	Patients on long-term therapy (>28d) or if on agents with potential drug interactions	Pre 2-8 mg/L Post 12-26 mg/L	8-16
* Assuming initial results are within the expected range ^aJeffres et al. 2006. Chest 130: 947-55. Lodise et al. 2008. Antimicrobial Agents & Chemotherapy 52: 1330-1336. ^bBritish National Formulary. 2008. Number 55. Rybak et al. 2009. Am J Health-Syst Pharm. 66:82-98. ^cIngram et al. 2008. Journal of Antimicrobial Chemotherapy 62: 168-171. ^dWysocki et al, 2001. Antimicrobial Agents and Chemotherapy 45: 2460-2467. ^eTeicoplanin: Summary of Product Characteristics. 2013. European Medicines Agency. Assessment report: Targocid and associated names. 2014. EMEA/H/A-30/1301. European Medicines Agency. ^fLamont et al, 2009. Journal of Antimicrobial Chemotherapy 64: 181-187. ^gBhavnani et al. 2010. Clinical Infectious Diseases 50: 1568-74. Falcone et al. 2013. J. Infection Chemotherapy 19 :732-9, DiPaolo et al. 2013. Int J. Antimicrobial Agents 42 :250-5, Falcone et al. 2013. CID 57 :1568-76, Reiber et al. 2015 Therapeutic Drug Monitoring, 37 :634-40. . ^hPea et al. 2012. JAC 67:2034-42. Dong et al. 2014. Eur J. Clinical Microbiology & Infectious Diseases, Epub 12/02/14 ⁱMatsumoto et al. 2014. International Journal of Antimicrobial Agents 44:242-7. Cattaneo et al. 2016. Expert Opin Drug Metab. Toxicol. 12:533-44			

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Antifungal agents			
Flucytosine ^a	Routine within 72h of starting therapy.	Pre 20-50 mg/L; Post 50-100 mg/L Pre dose concentrations <20 mg/L have been associated with treatment failure and emergence of resistance. Post dose concentrations >100 mg/L have been associated with toxicity.	4-8
Isavuconazole ^e	Not routinely monitored but may be useful in complex cases or in renal impairment	Pre 2-4 mg/L (usually) [^]	4-8
Itraconazole ^{a-b}	Routine in 1 st week of therapy. Measure 4-7 days after starting therapy	By Chromatographic assay Prophylaxis: Pre 0.5-4.0 mg/L Therapy: Pre 1.0-4.0 mg/L All pre-dose levels to be kept below 4.0 mg/L	4-8
Fluconazole ^a	Not routinely monitored but may be useful in complex cases or renal failure	AUC:MIC ratio of >100, call for advice on sampling.	4-8
Posaconazole ^{a-c}	Routine in majority of patients. Measure 3-8 days after starting therapy	Prophylaxis: Pre 0.7-3.75 mg/L Therapy: Pre 1.0-3.75 mg/L All pre-dose levels to be kept below 3.75 mg/L	4-8
Voriconazole ^{a,b,d}	Routinely within 5d of starting therapy	Prophylaxis and therapy Pre 1.0-5.5 mg/L or 2.0-5.5 mg/L for bulky or disseminated infections	4-8
*Assuming initial results are within the expected range. ^aVermes et al. 2000. Journal of Antimicrobial Chemotherapy 46: 171-179. Ashbee et al. 2014. J. Antimicrobial Chemotherapy 69:1162-1176. ^bAndes et al. 2009. Antimicrobial Agents and Chemotherapy 53: 24-34. Dolton et al. 2015. Current Opinion in Infectious Diseases 27:493-500. Chau et al. 2014 Intern Med J 44:1364-88. ^cDolton et al. 2012. Antimicrobial Agents and Chemotherapy 56: 2806-2813. Dekkers et al. 2016. Curr Fung Infect Rep 10:51-61. ^dPascual et al. 2012. Clinical Infectious Diseases 55:381-90. ^eBorman et al. 2020. Med Mycol 58 (7): 996-999. [^] Levels that are routinely seen and not true expected levels.			

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Agents used in Mycobacterial infection^a			
Streptomycin ^b (15 mg/kg OD)	All patients after 2nd-4th dose.	Pre <5 mg/L in <50y patients Pre <1 mg/L in >50y patients Post 15-40 mg/L	7-28d
Streptomycin ^c (25 mg/kg BIW)	All patients after 2nd-4th dose.	Pre <1 mg/L Post 65-80 mg/L	7-28d
Rifampicin ^c	Patients with poor clinical progression	Pre <0.5mg/L (ideally) Post <4mg/L sub-therapeutic Post 4-8mg/L usually adequate Post 8-24mg/L ideal	Depending on levels & patient progression
ISONIAZID ^f (+N-Acetyl-ISONIAZID)	Patients with poor clinical progression + checking for acetylation status	Post (2hr) 3-5mg/L	Depending on levels & progression
Ethambutol ^c	Patients with poor clinical progression or significant renal dysfunction	Pre <1 mg/L Post 2-6 mg/L	Depending on levels & progression
Rifabutin ^d	Patients who fail to respond to treatment. Patients on agents with CYP P450 interactions	Pre <0.1mg/L (usually) Post 0.45-0.9 mg/L	Depending on levels & patient progression
Levofloxacin ^d	Patients being treated for MDR TB.	Pre 0.5-2 mg/L Post 8-13 mg/L	Depending on levels & progression
Cycloserine ^d	All patients after 4th-6th dose.	Pre 10-20mg/L Post (3-4h) 20-35mg/L Levels to be kept below 35 mg/L	10-30d
Moxifloxacin ^d	Patients being treated for MDR TB.	Pre 0.3-0.7 mg/L Post 3-5 mg/L	Depending on levels & progression
Linezolid ^e (600 mg OD oral) (600 mg BD oral)	Patients being treated for MDR TB.	Pre <5mg/L (ideally) Post 12-26mg/L Pre 2-8 mg/L (usually) Post 12-26 mg/L	Depending on levels & progression

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* Assuming initial results are within the expected range; BIW: twice a week

^a Assuming that patients are on standard (usually daily) therapy, for patients on intermittent therapy please call to discuss expected levels as these will vary depending on dosing regimen used.

^b British National Formulary, Edition 67. 2014 section 5.1.9.

^c Peloquin 2017. Microbiol Spectrum 5:1-8. Pasipanodya et al. 2013. J. Infectious Diseases 208:1464-73.

^d Holland et al. 2009. Pharmacotherapy 29:503-10. Srivastava et al. 2013. European Respiratory Journal, 42:1449-53.

Ramachandran et al, 2015, Drug Safety, 38:253-69. Peloquin 2017. Microbiol Spectrum 5:1-8. Hwang et al. 2013. Int J. Tuberc Lung Dis 17:1257-66. Park et al. 2017. AAC 59:4429-4435

^e Schecter et al. 2010. CID 50: 49-55; McGee et al. 2009. Antimicrobial Agents & Chemotherapy 53: 3981-3984. Dong et al. 2014. Eur J. Clinical Microbiology & Infectious Diseases, Epub 12/02/14

^f Potter et al, 2020. MDRTB ADR Monitoring Guidance. TB Drug Monographs

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Other agents			
Aciclovir and its metabolite CMMG ^f	Patients with renal impairment, on high dose therapy or exhibiting CNS effects	For aciclovir, interpretation of levels needs to be patient specific CMMG: Measured in Pre-dose levels ONLY. Pre dose CMMG ≤ 2.6 mg/L. Elevated CMMG levels are associated with increased risk of neurotoxicity.	6-8
Ganciclovir ^a	Young children, renally impairment or unstable renal function	Pre 0.5-1.0 mg/L Post 7-9 mg/L (ganciclovir) Post 5-7 mg/L (valganciclovir)	4-8
Chloramphenicol ^b	All patients but especially neonates.	Pre Ideally <10 mg/L but must be <15 mg/L Post (2h) 10-25 mg/L	5-7
Co-trimoxazole ^d (sulphamethoxazole + trimethoprim) ^c	High-dosage therapy (PCP) or renal impairment.	Sulphamethoxazole: Pre <100 mg/L, Post 120-150 but <200 mg/L Trimethoprim: Pre 5-7 mg/L, Post 5-10 but <20 mg/L	6-8
Colistin ^e	Patients on IV treatment	Pre 2-4 mg/L	Day 2-3 (if patient received a loading dose) Re-assay 5-7d
* Assuming initial results are within the expected range ^aLuck et al. 2011 International Journal of Antimicrobial Agents 37:445-448. ^bBritish National Formulary for Children. 2018-19 p354 ^cJoos et al. 1995. Antimicrobial Agents & Chemotherapy 39:2661-2666. ^dBrown. 2014. Ann Int Care 4:13-22 ^eNation et al. 2014. Lancet Infectious Diseases S1473-3099. Gregorie et al. 2017. Clin Pharmacokinet 56:1441-1460. ^fHellden et al. 2003. Nephrol. Dial. Transplant 18: 1135-1141			

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