Severn Pathology
North Bristol NHS Trust

Antimicrobial Reference Laboratory

GUIDELINE RANGES FOR TDM

2025 – 2026b

Antimicrobial Reference Laboratory – Guideline Ranges 2025 – 2026b

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Important Changes: This Version 2025-2026 & further updates * 2025-2026b

Updated with the following changes -

Page 2
Professor Elizabeth Johnson has retired from the Mycology Reference Laboratory, all clinical advice for antifungal assays needs to be directed to Professor Andy Borman – 0117 4146286.

Added contact emails for Labgnostic (formally known as NPEx).

Page 5
Gentamicin and Vancomycin assays removed.
The ARL no longer performs Gentamicin and Vancomycin Assays.

Page 6
Updated Daptomycin range for Pre dose level with upper limit as 24.3mg/L.

Page 6 & 8 updated Linezolid range. *Page 6 Linezolid guideline ranges reverted to version 2024-2025
Updated related reference.

Page 8
Updated Streptomycin added –
Pre <1mg/L in >50y patients or patients with renal impairment.
Updated related reference.

Page 8
Updated Ethambutol range added –
15mg/kg OD.
BIW 50mg/kg – Post: 4-12 mg/L.
Updated reference related.

*Page 9
New assay Bedaquiline introduced – please see website for sample test information

Please state if a non-serum/plasma sample is being sent clearly on the request form and if there is a biohazard risk.

For sample requirements, request form and further information please visit our website:

www.nbt.nhs.uk/severn-pathology/pathology-services/antimicrobial-reference-laboratory

TDM preface

Despite advances in antimicrobial therapy, a significant proportion of patients with infection suffer with negative clinical outcomes driven by non-modifiable factors such as age, co-morbidities and severity of infection. With rising antimicrobial resistance (AMR) and a decline in the availability of newer agents, optimising the existing therapeutic agents by applying pharmacokinetic/pharmacodynamic (PK/PD) principles has become a priority in clinical practice.

Therapeutic drug monitoring (TDM) of antimicrobial agents has been used for a number of antimicrobials for decades; mainly to monitor efficacy and prevent dose-related adverse drug reactions.

In recent years, application of TDM has been extended across a wider range of agents as an Antimicrobial Stewardship Strategy (AMS) against growing AMR.

Modern healthcare professionals/organisations are faced with more complex clinical needs with age (extremes of low and high), body habitus with a wide range of Body Mass Indices (BMI), multi-organ co-morbidities and polypharmacy leading to drug-drug interactions. There is a growing pressure amongst clinicians to adopt new technologies to achieve “precision dosing” with a widespread use of TDM in the belief that such intervention will improve patient outcomes. However, hard evidence in the form of Randomised Controlled Trials (RCT) to support such a notion are lacking.

Therefore, therapeutic ranges quoted in this document should be used as a “guide” in terms of patient management rather than as a therapeutic “target” to achieve taking into consideration all the infection related factors including host, pathogen, clinical and antimicrobial options.

We welcome discussion from clinicians in terms of indications, timings, sample type/container, logistics, transport, and interpretation of results on a case-by-case basis. Therefore, please do not hesitate to contact us with the above details during the days and timings specified in this document.

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Aminoglycosides

Agent	Risk group	Expected levels (Guidelines) (mg/L)	Re-assay interval* (days)
Tobramycin (Once-daily)[a]	All patients between 2nd-4th dose; earlier if changing renal function or other risk factors e.g. Age	Pre: <1 mg/L Post: >10 mg/L or 8h post (on 5 mg/kg dose): 1.5 - 6 mg/L or follow Hartford nomogram[a] (patient is on 7 mg/kg dose)	3
Tobramycin (BD or TDS)[b]	All patients on 2nd-4th dose; earlier if changing renal function or other risk factors.	Gram-negative sepsis or pneumonia Pre: <2 mg/L Post: 5 – 10 mg/L Infective endocarditis (IE) Pre: <1 mg/L Post: 3-5 mg/L	3
Amikacin (Once-daily)[a,c]		Pre: <5 mg/L Post: 40 - 45[†] mg/L	6-8
Amikacin (BD or TDS)[d]		Pre: <10 mg/L Post: 20 - 30 mg/L	3-7
Streptomycin (7.5 mg/kg BD)[b,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

[a]Nicolau et al. 1995. Antimicrobial Agents & Chemotherapy 39:650-655.

[b]Elliott et al. 2004. Journal of Antimicrobial Chemotherapy 54: 971-81.

[c]Jenkins et all. 2016. Journal of Antimicrobial Chemotherapy 71: 2754-59. [†] Guideline levels not available; these are levels that are routinely seen.

[d]British National Formulary, ©NICE; April 2025 https://bnf.nice.org.uk/drugs/amikacin/#monitoring-requirements

[e]Note: these are different to the AHA Scientific Statement ranges. Baddour et al. 2015. Circulation 132:1435-86.

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Glycopeptides/Lipopeptides/Oxazolidinones

Agent	Risk group	Expected levels (Guidelines) (mg/L)	Re-assay interval* (days)
Teicoplanin[a,b,c]	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[d]	Patients with CPK elevation, high dose therapy (>6 mg/kg) or renal impairment	(6 - 8mg/kg dose) Pre: 5 – 24.3 mg/L or Pre: 10 – 24.3 mg/L in severe sepsis or deep-seated infection Pre: >24.3 mg/L associated with increased risk of toxicity[d]	6-8
Linezolid (600mg BD)[e,f]	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

[a]Teicoplanin: Summary of Product Characteristics. 2013. European Medicines Agency. Assessment report: Targocid and associated names. 2014. EMEA/H/A-30/1301. European Medicines Agency.

[b]Lamont et al, 2009. Journal of Antimicrobial Chemotherapy 64: 181-187.

[c]Hanai et al. 2022. Journal Antimicrobial Chemotherapy 77: 869-879.

[d]Bhavnani 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.

[e]Pea et al. 2012. JAC 67:2034-42. Dong et al. 2014. Eur J. Clinical Microbiology & Infectious Diseases, Epub 12/02/14

[f]Matsumoto 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

Agent	Risk group	Expected levels (Guidelines) (mg/L)	Re-assay interval* (days)
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[b]	Not routinely monitored but may be useful in complex cases or in renal impairment	Pre: 2 - 4 mg/L (usually)	4-8
Itraconazole[a, c]	Routine in 1st week of therapy. Measure 4-7 days after starting therapy	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,d]	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,c,e]	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.

[a]Vermes et al. 2000. Journal of Antimicrobial Chemotherapy 46: 171-179. Ashbee et al. 2014. J. Antimicrobial Chemotherapy 69:1162-1176.

[b]Borman et al. 2020. Med Mycol 58 (7): 996-999. ^ Levels that are routinely seen and not true expected levels.

[c]Andes 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.

[d]Dolton et al. 2012. Antimicrobial Agents and Chemotherapy 56: 2806-2813. Dekkers et al. 2016. Curr Fung Infect Rep 10:51-61.

[e]Pascual et al. 2012. Clinical Infectious Diseases 55:381-90.

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Agents used in Mycobacterial infection[a]

Agent	Risk group	Expected levels (Guidelines) (mg/L)	Re-assay interval* (days)
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 or patients with renal impairment 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] ARL recommends: PRE dose sample: up to 1h before dose POST dose samples: ORAL 1, 2 and 4h after dose IV 1h after dose	Patients with poor clinical progression	Pre: <0.5 mg/L (ideally) Post: <4 mg/L sub-therapeutic Post: 4 - 8 mg/L usually adequate Post: 8 - 24 mg/L ideal	Depending on levels & progression
Ethambutol[c,d] (15mg/kg OD) (BIW 50mg/kg)	Patients with poor clinical progression or significant renal dysfunction	Pre: <1 mg/L Post: 2 - 6 mg/L Pre: <1 mg/L Post: 4-12 mg/L	Depending on levels & progression
Rifabutin[e] ARL recommends: PRE dose sample: up to 1h before dose POST dose samples: ORAL 1, 2 and 4h after dose IV 1h after dose	Patients who fail to respond to treatment. Patients on agents with CYP P450 interactions	Pre: <0.1 mg/L (usually) Post: 0.45 - 0.9 mg/L	Depending on levels & progression
Levofloxacin[e]	Patients being treated for MDR TB.	Pre: 0.5 - 2 mg/L Post: 8 - 13 mg/L	Depending on levels & progression
Cycloserine[e]	All patients after 4th-6th dose.	Pre: 10 - 20 mg/L Post: (3-4h) 20 - 35 mg/L Levels to be kept below 35 mg/L	10-30d
Moxifloxacin[e]	Patients being treated for MDR TB.	Pre: 0.3 - 0.7 mg/L Post: 3 - 5 mg/L	Depending on levels & progression
Linezolid[f,d] (600 mg OD oral) (600 mg BD oral)	Patients being treated for MDR TB.	Pre: <2 mg/L (ideally) Post: 12 - 26 mg/L Pre: 3 - 9 mg/L (usually) Post: 12 - 26 mg/L	Depending on levels & progression
Isoniazid[g] (+N-Acetyl-Isoniazid)	Patients with poor clinical progression + checking for acetylation status	Post: (2hr) 3 - 5 mg/L	Depending on levels & progression

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Agents used in Mycobacterial infection[a]

Continued….

Agent	Risk group	Expected levels (Guidelines) (mg/L)	Re-assay interval* (days)
Bedaquiline[d] (400mg OD for 2 weeks) and then (200mg TIW for 24 weeks)	Patients with poor clinical progression	TDM after 2 weeks Pre (24h): 0.73 - 0.96 mg/L Post (5-6h): 2.8 - 3.3 mg/L TDM after 8 weeks Pre (48h): 0.62 mg/L Post (5-6h): 1.7 mg/L (target values only stated as a guide) TDM after 24 weeks (48h) Pre (48h): 0.36 mg/L Post (5-6h): 1.3 mg/L (target values only stated as a guide)	Depending on levels & progression

* 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, ©NICE; April 2025

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

[d] Maranchick &Peloquin 2024 J Clin Tuberc Other Mycobact Dis 36: 100444

[e]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

[f]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

[g]Potter *et al*, 2020. MDRTB ADR Monitoring Guidance. TB Drug Monographs

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Other agents

Agent	Risk group	Expected levels (Guidelines) (mg/L)	Re-assay interval* (days)
Aciclovir and its metabolite CMMG[a]	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: CMMG ≤2.6 mg/L. Elevated CMMG levels are associated with increased risk of neurotoxicity.	6-8
Ganciclovir[b]	Young children, renally impairment or unstable renal function	Pre: 0.5 -1.0 mg/L (prophylaxis) Pre: 1.0 – 2.0 mg/L (therapy) Post: 7 - 9 mg/L (Ganciclovir) Post: 5 - 7 mg/L (Valganciclovir)	4-8
Chloramphenicol[c]	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)[e]	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[f]	Patients on IV treatment	Pre: 2 - 4 mg/L	Day 2-3 (if patient receives a loading dose) Re-assay 5-7d

*Assuming initial results are within the expected range

[a]Hellden et al. 2003. Nephrol. Dial. Transplant 18: 1135-1141

[b]Luck et al. 2011 International Journal of Antimicrobial Agents 37:445-448. Marston et al J Antimicrob Chemother 2021; 76: 2356–2363. Franck et al Clin Pharmacol Ther, 112: 233-276. https://doi.org/10.1002/cpt.2431

[c]British National Formulary for Children. 2018-19 p354

[d]Brown. 2014. Ann Int Care 4:13-22

[e]Joos et al. 1995. Antimicrobial Agents & Chemotherapy 39:2661-2666.

[f]Nation et al. 2014. Lancet Infectious Diseases S1473-3099. Gregorie et al. 2017. Clin Pharmacokinet 56:1441-1460.