Severn Pathology

Antimicrobial Reference Laboratory

Guideline Ranges for TDM

2016-17

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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 (4.5 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 3rd 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.	Gm- pneumonia Pre <2 mg/L Post >7 mg/L Infective endocarditis (IE) Pre <1mg/L Post 3-5 mg/L	3-7
Amikacin (Once-daily)[a]		Pre <5, Post >50	6-8
Amikacin (BD or TDS)[c]		Pre <10, Post >20	3-7
Streptomycin (7.5 mg/kg BD)[d]	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] NICE Clinical Guideline 149, 2012.

[c] British National Formulary, Edition 67. 2014 section 5.1.4.

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

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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 15-25 mg/L	6-8
Teicoplanin[e-f]	*Staph. aureus* 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	6-8
Linezolid (600mg BD)[h,i]	Patients on long-term therapy (>28d) or if on agents with potential drug interactions (eg: omeprazole, clarithromycin, rifampicin)	Pre 3-8 mg/L	8-16

*Assuming initial results are within the expected range

[a]Jeffres et al. 2006. Chest 130: 947-55. Lodise et al. 2008. Antimicrobial Agents & Chemotherapy 52: 1330-1336.

[b]British National Formulary. 2008. Number 55. Rybak et al. 2009. Am J Health-Syst Pharm. 66:82–98.

[c]Ingram et al. 2008. Journal of Antimicrobial Chemotherapy 62: 168-171.

[d]Wysocki et al, 2001. Antimicrobial Agents and Chemotherapy 45: 2460-2467.

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

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

[g]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. .

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

[i]Matsumoto et al. 2014. International Journal of Antimicrobial Agents 44:242-7.

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Antifungal agents			
Flucytosine[a]	Routine with 72h of starting therapy; in changing renal function, bone marrow suppression, those receiving amphotericin B	Pre 20-40 mg/L Post 50-100mg/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
Itraconazole[a-b]	Routine in 1st week of therapy, lack of clinical response, gastrointestinal dysfunction, co-medication. Measure 4-7 days after starting therapy	By Chromatographic assay Prophylaxis pre 0.5-1.0 mg/L Therapy pre 1.0-2.0mg/L NB. These guidelines are different to those achieved by bio-assay.	4-8
Posaconazole[a-c]	Routine in majority of patients, lack of clinical response, gastrointestinal dysfunction, therapy with proton pump inhibitors. Measure 3-8 days after starting therapy	Prophylaxis: Pre 0.7-1.5 mg/L Therapy: Pre 1.0-2.0 mg/L	4-8
Voriconazole[a,b,d,e]	Routinely within 5d of starting therapy, lack of clinical response, gastrointestinal dysfunction, co-medications.	Prophylaxis and therapy Pre 1.0-4.5 mg/L	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]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.
[c]Dolton et al. 2012. Antimicrobial Agents and Chemotherapy 56: 2806-2813.
[d]Pascual et al. 2012. Clinical Infectious Diseases 55:381-90.
[e]Jin et all. 2016 Journal Antimicrobial Chemotherapy 71:1772-1785

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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
Rifampicin[c]	Patients with poor clinical progression	Pre <0.5mg/L Post <4mg/L sub-therapeutic Post 4-8mg/L usually adequate Post 8-15mg/L ideal	Depending on levels & patient progression
Rifabutin[d]	Patients who fail to respond to treatment. Patients on agents with P450 interactions	Pre <0.1mg/L Post 0.3-0.9 mg/L	Depending on levels & patient progression
Levofloxacin[d]	Patients being treated for MDR TB.	Pre 0.5-2 mg/L Post 8-12 mg/L	Depending on levels & patient progression
Cycloserine[e]	All patients after 4th-6th dose.	Pre 10-20mg/L Post (3-4h) 20-35mg/L	10-30
Moxifloxacin[d]	Patients being treated for MDR TB.	Pre 0.3-0.7 mg/L, Post 3-5 mg/L	Depending on levels & patient progression
Linezolid[d] (600 mg OD oral)	Patients being treated for MDR TB.	Pre <5mg/L Post 12-24mg/L	Depending on levels & patient progression

* Assuming initial results are within the expected range

[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] Alsutan et al. 2014. Drugs 74:839-54. 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. Alsultan et al. 2015. Antimicrobial Agents & Chemotherapy, 59:3800-7. Ramachandran et al, 2015, Drug Safety, 38:253-69.

[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

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Other agents			
Aciclovir	Patients with renal impairment or on high dose therapy	There are too many dose regimens used to give single guideline ranges and interpretation of levels needs to be patient specific	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 <10, Post (2h) 10-25	5-7
Co-trimoxazole (sulphamethoxazole + trimethoprim)[c]	High-dosage therapy (PCP) or renal impairment.	Sulphamethoxazole: Pre <100, Post 120-150 but <200 Trimethoprim: Pre 5-7, Post 5-10 but <20	6-8
Colistin[d]	Patients on IV treatment	Pre 2-4 mg/L	14-28

- Assuming initial results are within the expected range

[a] Luck et al. 2011 International Journal of Antimicrobial Agents 37:445-448.
[b] British National Formulary, Edition 67. 2014 section 5.1.7
[c] Joos et al. 1995. Antimicrobial Agents & Chemotherapy 39:2661-2666.
[d] Nation et al. 2014. Lancet Infectious Diseases S1473-3099.

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