THERAPEUTIC SERUM CONCENTRATIONS AND SAMPLING GUIDELINES

Drug	Usual Sample Time	Therapeutic Serum Concentration	Physicians' Routine Inpatient Orders	Comments
Amikacin **Extended Interval**	Pre: 18–24 hr after 2nd dose No peak level required	<2.5 mg/L	**Initial:** pre level 18–24 hr after 2nd dose **Maintenance:** Pre: once weekly. Administer over 30 minutes	- Half-life (t½) will be prolonged in patients with renal dysfunction - Levels are sent off-site for analysis; allow time for results
Amikacin **Traditional dosing**	Pre: 0-30 min. prior to next dose	2.5-10 mg/L	**Initial:** Pre and Post with third regular dose **Maintenance:** Pre and Post: Once weekly	- Half-life (t½) will be prolonged in patients with renal dysfunction - Levels are sent off-site for analysis; allow time for results
	Post: 30 min. after end of infusion	20-35 mg/L		
Carbamazepine (Tegretol®)	Pre: 0-30 min. prior to next dose	20-50 µmol/L	**Initial:** Pre: 3-7 days after final dosing alteration **Maintenance:** Pre: Only if patient still has seizures. If toxicity is suspected, take sample at time of symptoms, or 3 hours after the dose	- Enzyme auto-induction occurs so that t½ during chronic dosing may be much shorter than after first dose - Dose should be increased at 5-7 day intervals over a 4-6 week period and the first serum level measured at 5 weeks
Chloramphenicol	Post: 30 min. after end of infusion	15-25 mcg/mL	**Initial:** Post on Day 2 of therapy **Maintenance:** Post: Once weekly	- Pharmacokinetics in pediatric patients are highly variable and unpredictable - Levels are sent off-site for analysis; allow time for results

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Cyclosporine	Pre: 0-30 min. prior to next dose	**Renal Graft Rejection:** Time Post-transplant: 0-30 days: 200-250 µg/L 31-60 days:150-200 µg/L 61-90 days:100-150 µg/L > 91 days: 80-100 µg/L **Liver Graft rejection:** Time post transplant: <3 months: 240-320 µg/L 3-6 months: 160-240 µg/L > 6 months: 80-160 µg/L **GVHD Prophylaxis in BMT** 150-250 µg/L (levels at the higher end of the range are targeted in the early phase [3-4 weeks post BMT] and at the lower end of the range in the later phase but are dependent upon the protocol, presence/absence of GVHD and/or toxicity) **Aplastic Anemia (IST)** First month: 240-320 µg/L	**Initial:** Pre: Day 3 of therapy. **Maintenance:** Pre: Three times weekly during first 2-3 weeks, then twice weekly x 2-3 weeks then monthly	*Ranges have been adjusted (downwards by 20%) to reflect the method change to tandem mass spectrometry (VGH laboratory) in August 2010. This method measures parent drug and is free from metabolite interference. Methods susceptible to metabolite interference may give higher results - Monitoring is necessary to avoid extremely high or low levels which may precipitate nephrotoxicity or therapeutic failure, respectively. - See “Practical Guidelines for Tacrolimus and Cyclosporine Use” in white pages for information on AUC and dose adjustments - Monitoring may be less frequent if patient is stable. - IST = immune suppressant therapy

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Digoxin	Pre: 0-30 min. prior to next dose (Must be AT LEAST 8 hours postdose)	0.6-2.5 nmol/L	Pre levels should be drawn only if risk factors are present Risk factors include: • suspicion of toxicity • renal or hepatic impairment • poor response • drug interactions • suspected non-adherence • prematurity • hypokalemia	- The correlation between serum levels and therapeutic effect is not clearly defined - Digoxin therapy should be monitored by clinical effect rather than serum levels, unless toxicity is suspected - Digoxin serum levels are not useful after digoxin immune Fab (DigiFab^{R})

Drug	Usual Sample Time	Therapeutic Serum Concentration	Physicians' Routine Inpatient Orders	Comments
Gentamicin **Extended Interval** (outside of neonatal period)	Pre: 18–24 hr after 2nd dose No peak level required	≤ 1 mg/L	**Initial:** pre level 18–24 hr after 2nd dose **Maintenance:** Pre: once weekly. Administer over 30 minutes	- Refer to neonatal gentamicin monograph for monitoring extended interval gentamicin in neonates - If therapy is anticipated > 72 hours: ▪ Trough level prior to 3rd dose (18–24 hrs after 2nd dose) ▪ Administer 3rd dose ▪ Before giving 4th dose: - if level ≤ 1 mg/L: Administer next dose - if level > 1 mg/L: DO NOT administer next dose until pharmacy is consulted - For therapy beyond 7 days: ▪ Trough level once weekly
Gentamicin **Traditional dosing**	Pre: 0-30 min. prior to next dose	0.5-2 mg/L	**Initial:** Pre & post with 3rd dose. (See Comments.) **Maintenance:** Pre: Once weekly in stable patients. Pre & Post: As required in patients with unstable renal function	- No monitoring required for (patients with normal renal function): • uncomplicated UTIs • surgery prophylaxis < 72 hr • empiric therapy < 72 hr - t½ will be prolonged in patients with renal impairment
	Post: 30 min. after end of infusion	6-10 mg/L		

Drug	Usual Sample Time	Therapeutic Serum Concentration	Physicians' Routine Inpatient Orders	Comments
Itraconazole	Pre: 0-30 min. prior to next dose	**Prophylaxis**: >0.5 mg/L **Treatment**: >1 mg/L	**Initial:** >4-7 days after initiation of therapy **Maintenance:** As clinically indicated, at least 4-7 days after change in dose or formulation	- Pre concentrations > 3 mg/L may increase the risk of adverse effects - Itraconazole levels are variable. Consider monitoring levels when change in formulation (capsule vs. liquid), diet, or interacting drugs or in case of concerns about adherence adverse effects or lack of effectiveness - Liquid has higher bioavailability than capsules - Samples are sent to St. Paul's Hospital and processed on Thursday; send samples by Tuesday morning
Lithium	"Pre" level 30 min. prior to morning dose when administered BID, or 10-12 hours after dose when administered as a single HS dosage. Any time if suspected toxicity	0.8-1.2 mmol/L	**Initial:** 5 days after reaching initial estimated target dose, and following subsequent dose adjustments until patient is clinically stable **Maintenance:** every 6 months routinely and as needed if toxicity or non-adherence is suspected	- Steady state is reached after 5 days on a stable dosage - Serum level decreased with increased sodium intake and increased with dehydration- Serum level drawn following single daily HS dosage regimen may be 10-20% higher than when same daily dosage is given in divided doses BID - Samples are sent to VGH. Turn around time for STAT request is 2 hours. Please notify lab if stat levels will be required
Phenobarbital	Pre: 0-30 min. prior to next dose	65-170 µmol/L	**Initial:** Pre: After 10-14 days, unless toxicity is suspected or patient still has seizures	- Some patients may tolerate and benefit from levels that are significantly higher than the recommended maximum limit

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Phenytoin (Dilantin^{R})	Pre: 0-30 min. prior to next dose	40-80 µmol/L "free" phenytoin: 4-8 µmol/L	**Initial:** 1 hr. post IV load. Wait 7 days after each oral dosing change to measure pre level In acute management of seizures, where patient continues to seize, measure serum levels (pre) 1 or 2 times daily **Maintenance:** Pre: Only if patient still has seizures. If toxicity is suspected, take level at time of symptoms. **Fosphenytoin**: 2 hr. post IV load or 4 hr. post IM load	- Phenytoin exhibits dose dependent pharmacokinetics: plasma drug concentration may change disproportionately with dosage changes - Phenytoin is highly protein bound - Free phenytoin levels may be useful in monitoring patients with chronic renal failure (hypoalbuminemia), or who are receiving drugs that displace phenytoin from protein (e.g. valproic acid) or in disease states that may displace phenytoin from plasma protein (e.g. hyperbilirubinemia) - Free phenytoin levels are sent to VGH with turn around time approximately 8 hours. For ongoing monitoring in stable patients, free phenytoin can be calculated from total phenytoin by using percentage free phenytoin from a previous result
Posaconazole	Pre: 0-30 min. prior to next dose	**Prophylaxis**: ≥0.7 mg/L **Treatment**: ≥1 mg/L	**Initial:** >6-10 days after initiation of therapy **Maintenance:** As clinically indicated >6-10 days after dose change	- Posaconazole levels are variable with the liquid formulation and may be affected by diet. Consider monitoring levels when change in formulation (capsule vs. liquid) or interacting drugs - Samples are sent to St. Paul's Hospital and processed on Thursday; send samples by Tuesday morning
Salicylate (ASA)	JIA : Pre: 0-60 min. prior to next dose	1.1-2.2 mmol/L	**Initial:** Pre on Day 3 **Maintenance:** Pre: Once weekly	- For overdose, see BC Drug and Poison Information Centre Manual

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Sirolimus	Pre : 0-30 min. prior to next dose	Time post transplant: <3 months: 6-10 mcg/L ≥3 months: 4-6 mcg/L	**Initial:** 2-3 x weekly **Maintenance:** Q 2-4 weeks	- Samples are sent to VGH; allow time for results
Tacrolimus **(Prograf^{R}, FK506)**	For PO or intermittent IV dosing: Pre: 0-30 min. prior to morning dose For BMT patients receiving tacrolimus by continuous IV infusion, take sample from opposite lumen from which drug is infused. If patient has a single lumen CVC, draw a peripheral sample. Take sample at the same time each day, in the morning. This is essentially a steady state concentration but the same target levels apply.	**Renal transplant:** Time post transplant: 0-3 weeks: 10-12 mcg/L 4-11 weeks: 8-10 mcg/L 12-24 weeks: 6-8 mcg/L > 24 weeks: 5-7 mcg/L **Cardiac transplant:** Time post transplant: 0-6 months: 10-12 mcg/L 6-12 months: 8-10 mcg/L Year 2 and 3: 6-8 mcg/L > 3 years (if no rejection): 5-7 mcg/L **Liver transplant** 4-12 mcg/L **BMT:** 6-12 mcg/L (levels at the higher end of the range [8-12 mcg/L] are targeted in the early phase [3-4 weeks post BMT] and at the lower end of the range in the later phase but are dependent upon the protocol, presence/absence of GVHD and/or toxicity)	Renal Transplant: **Initial:** 2 – 3 x weekly **Maintenance:** Q 2-4 weeks BMT: Twice weekly while hospitalized, then weekly or monthly thereafter unless a change in medication (eg azole antifungal) or renal function may result in a change in tacrolimus level	- Samples are sent to VGH; allow time for results - Frequency of monitoring during maintenance treatment is guided by patient-specific factors - See “Practical Guidelines for Tacrolimus and Cyclosporine Use” in white pages for information

Drug	Usual Sample Time	Therapeutic Serum Concentration	Physicians' Routine Inpatient Orders	Comments
Theophylline	Timing depends on route of administration and dosage form.	55-110 µmol/L		- Refer to white pages in print copy for more details on theophylline - Samples are sent to VGH. Turn around time for STAT request is 2 hours. Please notify lab if stat levels will be required
Tobramycin **Extended interval** (outside of neonatal period)	Pre: 18 – 24 hr after 2nd dose No peak level required	≤ 1 mg/L	**Initial:** pre level 18 – 24 hr after 2nd dose **Maintenance:** Pre: once weekly. Administer over 30 minutes	- Refer to neonatal tobramycin monograph for monitoring extended interval tobramycin in neonates - If therapy is anticipated > 72 hours: ▪ Trough level prior to 3rd dose (18 – 24 hrs after 2nd dose) ▪ Administer 3rd dose ▪ Before giving 4th dose: - if level ≤ 1 mg/L: Administer next dose - if level > 1 mg/L: DO NOT administer next dose until pharmacy is consulted - For therapy beyond 7 days: ▪ Trough level weekly
Tobramycin **(Traditional dosing)**	Pre: 0-30 min. prior to next dose	0.6-2 mg/L	**Initial:** Pre & post with 3rd dose. (See Comments.) Maintenance: **Pre:** Once weekly in stable patients **Pre & Post:** As required in patients with unstable renal function	- No monitoring required for (patients with normal renal function): • uncomplicated UTIs • surgery prophylaxis < 72 hr • empiric therapy < 72 hr. - Half-life will be prolonged in patients with renal impairment
	Post: 30 min. after end of infusion	6-10 mg/L		
	Cystic Fibrosis	10-15 mg/L		

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Valproic Acid [687] **(Depakene^{R}, Epival^{R})**	Pre: 0-30 min. prior to next dose	350-700 µmol/L (epilepsy) 350-870 µmol/L (bipolar disorder)	**Maintenance:** **Epilepsy:** Pre: Only if patient still has seizures **Bipolar Disorder:** Every 3-6 months If toxicity is suspected, take sample at time of symptoms	- Half-life may be longer in patients with hepatic disease and may be shorter in patients receiving other anticonvulsant drugs - Some patients may tolerate higher levels (700-1000 µmol/L)
Vancomycin	Pre: 0-30 min. prior to next dose	8-15 mg/L	**Pre & Post:** With 3rd or 4th dose	- AUC:MIC monitoring recommended. Target AUC 400-600 mg.h/L Contact clinical pharmacist if MIC > 1 mg/L - No monitoring required for (patients with normal renal function): •surgery prophylaxis < 72 hrs •empiric therapy < 72 hrs - Half-life will be prolonged in patients with renal impairment - If AUC monitoring is not available, contact pharmacist for recommendations about when to draw pre and post levels
	Post: 1-2 hr. after end of infusion	25-40 mg/L		
Voriconazole [688]	Pre : 0-30 min. prior to next dose	1-5.5 mg/L	**Initial:** pre ≥ 4 days after onset of treatment or change in dose. **Maintenance:** Once weekly until therapeutic, then once every 2 weeks or monthly unless clinical changes or interacting meds are changed	- Samples are sent to St. Paul's Hospital and processed on Thursday; send samples by Tuesday morning