

CRITICAL VALUES FOR THERAPEUTIC DRUG LEVELS

The concept of critical values for drug levels was originally developed by the late Daniel M. Baer, MD, and first published in the April 1982 issue of *MLO*. This table lists the critical values for common therapeutic drugs updated in 2023 by Rajasri Chandra, MS, MBA.

DRUG	INDICATION	THERAPEUTIC RANGE	CRITICAL VALUE	COMMENTS
Acetaminophen	Analgesic	5-20 µg/mL	>200 µg/mL *drawn 4 hours after ingestion	*Determination if a concentration is toxic is dependent upon when it is drawn in relation to the time of ingestion of the dose. Multiple serum concentrations will be needed to monitor improvement and removal of drug.
Amikacin	Antimicrobial	Peak: 15-30 µg/mL Trough: 4-8 µg/mL	>10 µg/mL	Peak: 30 minutes after end of infusion. Trough: before next dose. Conventional dosing protocol.
Amiodarone	Antiarrhythmic	0.5-2 µg/mL	>2.5 µg/mL	Trough concentration. Serum amiodarone levels >2.5 µg/mL had a positive predictive value of 76% for adverse drug events.
Amitriptyline	Antidepressant/analgesic (neuropathic pain)	125-250 ng/mL	>500 ng/mL	Trough concentration. Life threatening cardiac toxicity and/or seizures with concentration >1000 ng/mL.
Busulfan (IV)	Anti-leukemic, Hematopoietic cell transplantation conditioning	900-1350 µMOL/MIN	>1500 µmol/min	Area Under the Curve (AUC) calculations based on post-infusion sampling and dosing protocols vary by institution.
Carbamazepine	Antiepileptic/mood stabilizer	4-12 µg/mL	>20 µg/mL	Trough concentrations. Correlate serum concentration with clinical presentation.
Cyclosporine	Immunosuppressant	100-400 ng/mL	>500 ng/mL	Specific concentration goal dependent upon clinical situation. For concentrations drawn with intravenous therapy, blood should be drawn from site other than that where drug is infusing. (Cyclosporine adheres to plastic.) TDM levels are dependent on transplant type. Blood concentrations can be method (immunoassay or mass spectrometry) dependent.
Digoxin	Inotrope, AV node blocker	0.5-2.0 ng/mL*	>2.5 ng/mL	Samples should be drawn >8 hours after last dose. *Concentrations >1.5 ng/mL may be associated with higher mortality.
Doxepin	Antidepressant	110-250 ng/mL	>500 ng/mL	Trough concentration.
Ethosuximide	Antiepileptic	40-100 µg/mL	>200 µg/mL	Trough concentration.
Everolimus	Immunosuppressant	3-8 ng/mL	>15 ng/mL	Trough concentration. Varies by transplant protocol.
Flecainide	Antiarrhythmic	0.2-1.0 µg/mL	>1.0 µg/mL	Midpoint or trough concentration. Monitoring recommended when given concurrently with medications that may decrease metabolism (increase concentrations).
Fluconazole	Antifungal	4.0-20.0 µg/mL	None established	Limited TDM utility except in patients receiving hemodialysis.
Flucytosine	Antifungal	25-50 µg/mL	>100-200 µg/mL	Concentration should be a peak drawn 2 hours post dose.
Gentamicin	Antimicrobial	Peak: 5-10 µg/mL Trough: <2 µg/mL	Peak: >12 µg/mL Trough: >2 µg/mL	Peak: 1 hour after infusion. Trough: before next dose. Conventional dosing protocol.
Hydroxyl itraconazole	Antifungal	Not established	None established	Active metabolite of itraconazole.
Imipramine	Antidepressant	>180-240 ng/mL	>500 ng/mL	Concentration = imipramine + desipramine (metabolite).
Itraconazole	Antifungal	>0.5 µg/mL (localized) >1.0 µg/mL (systemic)	None established	Large PK variability. Should be measured within 5-7 after initiation of therapy.
Lamotrigine	Antiepileptic/mood stabilizer	1-15 µg/mL	>20 µg/mL	Trough concentration. High concentrations generally associated with increased somnolence/confusion.
Lidocaine	Antiarrhythmic	1.5-5 µg/mL	>6 µg/mL	Concentration can be drawn at any point (from separate IV line).
Lithium	Mood stabilizer	Acute: 1-1.6 mmol/L Chronic: 0.6-1.2 mmol/L	>2.0 mmol/L >5 mmol/L potentially fatal	Serum concentrations may increase in presence of hyponatremia. Concentration: 12 hours after dose.
Nortriptyline	Antidepressant/analgesic (neuropathic pain)	50-150 ng/mL	>500 ng/mL	Trough concentration.
Phenobarbital	Antiepileptic	15-40 µg/mL	>60 µg/mL	Trough concentration. Do not collect before steady state achieved.
Phenytoin	Antiepileptic	10-20 µg/mL	>20 µg/mL	Trough concentrations. Toxic >20 µg/mL (lateral nystagmus), >40 µg/mL (decreased mentation). Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free phenytoin.
Posaconazole	Antifungal	>0.7 µg/mL	None established	Should be measured within 7 days of initiation therapy.
Primidone	Antiepileptic	5-12 µg/mL	>15 µg/mL	Metabolized to phenobarbital.
Procainamide (PA) (metabolite: NAPA)	Antiarrhythmic	PA: 4-8 µg/mL NAPA: 10-20 µg/mL	>10 µg/mL >40 µg/mL	Mid-point or trough concentration. Procainamide monitoring is particularly important in patients who might be fast acetylators (60% to 70% of northern Europeans, and 50% of black and white Americans) and in patients with renal impairment. Procainamide and N-acetylprocainamide levels should always be measured on the same sample.
Protriptyline	Antidepressant	50-170 ng/mL	>500 ng/mL	Trough concentration.
Quinidine	Antiarrhythmic	2-5 µg/mL	>6 µg/mL	Midpoint or trough concentration.
Salicylate	Analgesic, antipyresis, Anti-inflammatory	20-100 µg/mL 100-200 µg/mL	Vertigo, tinnitus 150-300 µg/mL Nausea, vomiting, hyper-ventilation 250-400 µg/mL Toxicity >500 µg/mL	Serum concentration should be used in conjunction with clinical presentation to make decision on therapy. Multiple serum concentrations will be necessary to monitor improvement and removal of drug.
Sirolimus	Immunosuppressant	4-20 ng/mL	>25 µg/mL	Trough concentration. Whole blood samples. Therapeutic levels can be lower when used in combination with other immunosuppressants. Blood concentrations can be method (immunoassay or mass spectrometry) dependent. Therapeutic levels depend on type of transplant, time post transplant, and other concomitant drug therapy.
Tacrolimus	Immunosuppressant	5-20 ng/mL	>25 ng/mL	Whole blood samples collected as trough. Therapeutic levels can be lower when used in combination with other immunosuppressants. Bias may be present between immunoassay and LC/MS methods.
Theophylline	Bronchodilator	10-20 µg/mL	>25 µg/mL	Pulmonary literature suggest that concentrations 5-15 mg/L may be as efficacious with less toxicity. Trough concentration dependent upon drug formulation.
Tobramycin	Antibacterial	Peak: 4-8 µg/mL Trough: <1.0 µg/mL	>12 µg/mL >2 µg/mL	Peak: 1 hour after end of infusion. Trough: before next dose. Conventional dosing protocol.
Valproic acid	Antiepileptic/mood stabilizer	50-125 µg/mL	>200 µg/mL	Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free valproic acid. Trough concentration preferred.
Vancomycin	Antimicrobial	Trough concentrations: General: 5-15 µg/mL Pneumonia: 15-20 µg/mL	Trough: >30 µg/mL	Monitoring of peaks no longer recommended. Goal trough concentration dependent upon indication. Trough: before next dose.
Voriconazole	Antifungal	1.0-5.5 µg/mL	>6 µg/mL	Should be measured within 7 days of initiation therapy.

Ranges are approximate and may vary with laboratory and/or assay. Proper interpretation of therapeutic drug concentrations requires that the specimen be drawn at an appropriate time in relation to drug administration.