

# 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 is an expanded version of that publication and newly revised for 2009-2010 by Yash Pal Agrawal, MD, PhD; associate professor of Clinical Pathology and Laboratory Medicine; director, Central Laboratory; director Point-of-Care Testing Services; Department of Pathology and Laboratory Medicine, New York Presbyterian Hospital-Cornell Campus, New York, NY.

Drug	Indication	Therapeutic range	Critical Value	Clinical correlation		Comments
				Efficacy	Toxicity	
Acetaminophen	Analgesic	5-20 µg/mL	>200 µg/mL *drawn 4 hours after ingestion	UNCLR	YES	Determination of 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: <10 µg/mL	Trough >4-8 µg/mL	YES	YES	Peak: 1 hour after end of infusion Trough: before next dose
Amiodarone	Antiarrhythmic	0.5-2 µg/mL	>2.5 µg/mL	UNCLR	YES	Trough concentration Concentrations more accurate with chronic treatment (due to long half life of drug)
Amitriptyline	Antidepressant/analgesic (neuropathic pain)	125-250 ng/mL	>500 ng/mL	UNCLR	YES	Trough concentration Life threatening cardiac toxicity and/or seizures with concentration >1000 ng/mL
Carbamazepine	Antiepileptic/mood stabilizer	4-12 µg/mL	>20 µg/mL	YES	YES	Trough concentrations preferred Correlate serum concentration with clinical presentation.
Cyclosporine	Immunosuppressant	100-400 µg/mL	>500 µg/mL	YES	YES	Specific goal concentration 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.
Digoxin	Inotrope, AV node blocker	0.8- 1.2 ng/mL* (immunoassay)	>2.5 ng/mL	UNCLR	YES	Concentrations should be drawn >8 hours after last dose. *Concentrations >1.5 in heart failure patients may be associated with higher mortality. Consult assay instructions for potential interfering factors.
Doxepin	Antidepressant	110-250 ng/mL	>500 ng/mL	UNCLR	YES	Trough concentration
Ethosuximide	Antiepileptic	40-100 µg/mL	>200 µg/mL	YES	YES	Trough concentration
Flecainide	Antiarrhythmic	0.2-1.0 µg/mL	>1.0 µg/mL	UNCLR	YES	Midpoint or trough concentration Monitoring recommended when given concurrently with medications that may decrease metabolism (increase concentrations)
Flucytosine	Antifungal	25-50 µg/mL	>100-200 µg/mL	NO	YES	Concentration should be a peak drawn 2 hours post dose.
Gentamicin, Tobramycin	Antimicrobial	Peaks 4-8 µg/mL – standard 8-12 µg/mL-once daily  Trough <1.0 µg/mL – standard <0.5 µg/mL – once daily	Trough >2 µg/mL	YES	YES	Goal concentration (peak and trough) dependent upon dosing method. Peak: 1 hour after end of infusion Trough: before next dose
Imipramine	Antidepressant	>180-240 ng/mL	Not clear (>500 ng/mL)	YES	YES	Concentration = imipramine + desipramine(metabolite)
Lamotrigine	Antiepileptic/mood stabilizer	1-4 µg/mL	>20 µg/mL	UNCLR	UNCLR	Trough concentration. High concentrations generally associated with increased somnolence/confusion.
Lidocaine	Antiarrhythmic	1.5-5 µg/mL	>6 µg/mL	YES	YES	Concentration can be drawn at any point (from separate IV line)
Lithium	Mood stabilizer	Acute: 1-1.6 mEq/L Chronic: 0.6-1.2 mEq/L	>2.0 mEq/L  >5 mEq/L potentially fatal	YES	YES	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	UNCLR	YES	Trough concentration
Phenobarbital	Antiepileptic	15-40 µg/mL	>60 µg/mL	YES	YES	Trough or mid interval concentration
Phenytoin	Antiepileptic	10-20 µg/mL	>40 µg/mL	YES	YES	Toxic >20 µg/mL Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free phenytoin.
Primidone	Antiepileptic	5-12 µg/mL	>24 µg/mL	YES	YES	Metabolized to Phenobarbital
Procainamide (PA) (metabolite: NAPA)	Antiarrhythmic	PA: 4-8 µg/mL (NAPA: 10-20 µg/mL)	>10 µg/mL (>40 µg/mL)	YES (NO)	YES (YES)	Use as an antiarrhythmic decreasing NAPA concentrations increase in renal insufficiency/failure Mid-point or trough concentration
Protriptyline	Antidepressant	70-250 ng/mL	>500 ng/mL	UNCLR	YES	Trough concentration
Quinidine	Antiarrhythmic	2-5 µg/mL	>6 µg/mL	YES	YES	Midpoint or trough concentration
Salicylate	Analgesic/anti-inflammatory	10-30 mg/dL	>40 mg/dL	NO	YES – weakly	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	5-15 ng/mL	>15 ng/mL	YES	YES	Trough concentration Whole blood samples
Tacrolimus	Immunosuppressant	5-20 ng/mL	>25 ng/mL	NO	YES	Trough: 12 hours after given dose. Whole blood samples
Theophylline	Bronchodilator	5-20 µg/mL	>25 µg/mL	UNCLR	YES	Pulmonary literature suggest that concentrations 5-15 mg/L may be as efficacious with less toxicity. Trough or mid-interval concentration depending upon drug formulation.
Valproic acid	Antiepileptic/mood stabilizer	50-125 µg/mL	>200 µg/mL	YES* As anti-epileptic	YES	Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free valproic acid. Trough concentration preferred.
Vancomycin	Antimicrobial	Trough concentrations: General: 10-15 µg/mL Pneumonia: 15-20 µg/mL	Trough >30 µg/mL  *Daily dose may correlate more with toxicity than trough	UNCLR*	UNCLR	Monitoring of peaks no longer recommended. Goal trough concentration dependent upon indication. *Only trough concentrations of 15-20 µg/mL for pneumonia have been proven to correlate. Trough: before next dose
Voriconazole	Antifungal	>0.25-1000 µg/mL	>6 µg/mL	UNCLR	YES	Trough concentration preferred. Steady state trough achieved after 7 days of therapy.

UNCLR = unclear

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.