

Critical values for therapeutic drug levels

The concept of critical values for drug levels was developed by Daniel M. Baer, MD, professor emeritus of laboratory medicine, Oregon Health Sciences University, Portland, OR, and first published in the April 1982 issue of *MLO*. This table is an expanded version of that publication and newly revised by Diane M. Lyle, PharmD, BCPS, Critical Care Clinical Pharmacy Specialist, Portland VA Medical Center. Dr. Baer is a member of *MLO's* Editorial Board and editor of *MLO's* "Tips from the Clinical Experts" department.

Drug	Indication	Therapeutic range	Critical Value	Clinical correlation		Comments
				Efficacy	Toxicity	
Acetaminophen	Analgesic	5-20 mcg/mL	>200 mcg/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 mcg/mL Trough: <10 mcg/mL	Trough >10mcg/mL	YES	YES	Peak: 1 hour after end of infusion Trough: before next dose
Amiodarone	Antiarrhythmic	0.5-2mcg/mL	>2.5mcg/mL	UNCLR	YES	Trough concentration Concentrations more accurate with chronic treatment (due to long half life of drug)
Amitriptyline	Antidepressant/analgesic (neuropathic pain)	125-250ng/mL	>500ng/mL	UNCLR	YES	Trough concentration Life threatening cardiac toxicity and/or seizures with concentration >1000 ng/mL
Carbamazepine	Antiepileptic/mood stabilizer	4-12mcg/mL	>20 mcg/mL	YES	YES	Trough concentrations preferred Correlate serum concentration with clinical presentation.
Cyclosporine	Immunosuppressant	100-400 mcg/mL	>500mcg/mL	YES	YES	Specific goal concentration dependent upon clinical situation. For concentrations drawn with intravenous therapy, blood should be drawn from sites other than that where drug is infusing. (cyclosporine adheres to plastic)
Digoxin	Inotropic, AV node blocker	0.8- 1.2 ng/mL* (immunoassay)	> 2.0ng/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	110-250ng/mL	>500ng/mL	UNCLR	YES	Trough concentration
Ethosuximide	Antiepileptic	40-100 mcg/mL	>200 mcg/mL	YES	YES	Trough concentration
Flecainide	Antiarrhythmic	0.2-1.0 mcg/mL	> 1.0mcg/mL	UNCLR	YES	Midpoint or trough concentration Monitoring recommended when given concurrently with medications that may decrease metabolism (increase concentrations)
Flucytosine	Antifungal	Not established	> 100-200 mcg/mL	NO	YES	Concentration should be a peak drawn 2 hours post dose.
Gentamicin, Tobramycin	Antimicrobial	Peaks 4-8mcg/mL - standard 8-12mcg/mL -once daily Trough <1.0 mcg/mL - standard <0.5 mcg/mL - once daily	Trough >2mcg/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	>180-240ng/mL	Not clear (>500ng/mL)	YES	YES	Concentration = imipramine + desipramine(metabolite)
Lamotrigine	Antiepileptic/mood stabilizer	1-4 mcg/mL	>20mcg/mL	UNCLR	UNCLR	Trough concentration. High concentrations generally associated with increased somnolence/osefulness.
Lidocaine	Antiarrhythmic	1.5-5mcg/mL	>6mcg/mL	YES	YES	Concentration can be drawn at any point (from separate IV line)
Lithium	Mood stabilizer	Acute: 1-1.8 mEq/L Chronic: 0.6-1.2 mEq/L	>2.0mEq/L >5mEq/L (potentially fatal)	YES	YES	Serum concentrations may increase in presence of hyponatremia. Concentration: 12 hours after dose
Nortriptyline	Antidepressant/analgesic (neuropathic pain)	50-150ng/mL	>500ng/mL	UNCLR	YES	Trough concentration
Phenobarbital	Antiepileptic	15-40mcg/mL	> 60 mcg/mL	YES	YES	Trough or mid interval concentration
Phenytoin	Antiepileptic	10-20mcg/mL	> 40 mcg/mL	YES	YES	Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free phenytoin.
Primidone	Antiepileptic	5-12mcg/mL	>24mcg/mL	YES	YES	Metabolized to Phenobarbital
Procainamide (PA) (metabolite: NAPA)	Antiarrhythmic	PA: 4-8mcg/mL (NAPA: 10-20mcg/mL)	>10mcg/mL (>40mcg/mL)	YES (NO)	YES (YES)	Use as an antiarrhythmic decreasing NAPA concentrations increase in renal insufficiency/failure Mid-point or trough concentration
Propranolol	Antidepressant	70-250ng/mL	>500ng/mL	UNCLR	YES	Trough concentration
Quinidine	Antiarrhythmic	2-5mcg/mL	>6mcg/mL	YES	YES	Midpoint or trough concentration
Salicylate	Analgesic/anti-inflammatory	10-30 mg/L	>40 mg/L	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.
Sildenafil	Immunosuppressant	5-15ng/mL	>15ng/mL	YES	YES	Trough concentration Whole blood samples
Tacrolimus	Immunosuppressant	5-20 ng/mL	>25ng/mL	NO	YES	Trough: 12 hours after given dose. Whole blood samples
Theophylline	Bronchodilator	5-20mcg/mL	>25mcg/mL	UNCLR	YES	Pulmonary literature suggest that concentrations 5-15mg/L may be as efficacious with less toxicity. Trough or mid-interval concentration depending upon drug formulation.
Valproic acid	Antiepileptic/mood stabilizer	50-125mcg/mL	>200mcg/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: 10-15mcg/mL Pneumonia: 15-20mcg/mL	Trough >20mcg/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 15-20mcg/mL for pneumonia have been proven to correlate. Trough: before next dose
Voriconazole	Antifungal	>0.5-1000 mcg/mL	>6 mcg/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.