

CANADIAN QUICK REFERENCE GUIDE to PSYCHIATRIC MEDICATION

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Please note, P450 & Special Considerations sections are designed to contain helpful clinical information, and are not designed to be comprehensive. Medication interactions mediated by P450 enzyme sub-systems can be derived from the P450 information sections of the guide. Selected other clinically significant medication interactions are referred to in the Special Considerations columns.

ANTIDEPRESSANTS	Total Daily Dose Range (mg)	Dosing	t ^{1/2} (hours)	P450 Systems (primary enzymes only)		Special Considerations (Class Effects Boxed) (Avoid, Caution, Risk of)
				Substrate of:	Inhibits or Induces	
Citalopram (Celexa)	20 - 60	od or qhs	30	2C19, 3A4, 2D6		Avoid MAOI's or Ergot compounds Risk SIADH (elderly) Sexual dysfunction common, may be unreported Avoid MAOIs Avoid MAOIs, fluvoxamine, Risk Seizures Avoid sympathomimetics, clomipramine or opioids Caution high tyramine foods Avoid MAOIs Narrow therapeutic Index, Avoid MAOIs Caution antiarrhythmics & sympathomimetics Class Effects Above + Caution methadone Dietary restrictions, Extreme Caution with opioids Serotonergic drugs, sympathomimetics, OTC meds Avoid with HTN, Vascular disease, Pregnancy
Paroxetine (Paxil)	20 - 60	od (or qhs)	30 - 65	2D6	2D6	
Sertraline (Zoloft)	50 - 200	od or qhs	25	3A4		
Fluoxetine (Prozac)	20 - 80	od (or qhs)	330	2D6, 2C9	2D6, 2C9, 2C19	
Fluvoxamine (Luvox)	100 - 300	od or qhs	17 - 22	2D6, 2C9	2D6, 1A2, 2C19, 3A4	
Venlafaxine XR (Effexor XR)	75 - 225	od	15	2D6, 3A3/4		
Bupropion SR (Wellbutrin SR)	150 - 300	150mg/dose	11 - 14	2B6	2D6	
Moclobemide (Manerix)	450 - 900	od or bid	1 - 3	2C19	1A2, 2C19	
Mirtazapine (Remeron)	30 - 60	qhs	20 - 40	2D6, 3A4		
Amitriptyline (Elavil)	100 - 300	qhs	10 - 46	2D6, 2C, 1A2, 3A4	2D6	
Imipramine (Tofranil)	100 - 300	qhs	4 - 34	1A2, 2C19, 3A4	2D6	
Clomipramine (Anafranil)	100 - 300	qhs	17 - 37	2C19, 2D6		
Nortriptyline (Aventyl)	75 - 200	qhs	13 - 88	2D6	2D6, 3A4, 2C	
Desipramine (Norpramin)	100 - 300	qhs	12 - 76	2D6	2D6	
Phenelzine (Nardil)	30 - 90	bid (before 1pm)	1 - 4	2E1		
Tranylcypromine (Parnate)	20 - 80	bid (before 1pm)	2 - 4		2C19, 2D6, 2A6	

Note: Many antidepressants should be tapered gradually to avoid discontinuation syndromes

ANTIPSYCHOTICS	Total Daily Dose Range (mg)	Dosing	t ^{1/2} (hours)	P450 Systems		Special Considerations ¹ (Avoid, Caution with, Risk of) Check CYP interactions of all below & Avoid rapid withdrawal
				Substrate of:	Inhibits or Induces	
Risperidone (Risperdal)	2 - 6	qhs or bid	20 - 24	2D6	2D6	Risk EPS, hyperprolactenemia, NMS, Caution hypotensives Risk weight gain, NMS, transient transaminase abnormalities
Olanzapine (Zyprexa) po, *IM or Zydys (dissolvable wafer)	10 - 20	qhs	21 - 54	1A2		
Quetiapine (Seroquel)	300 - 800+	bid or qhs	6 - 7	3A4		Risk NMS, Caution hypotensives, Cataracts in humans not proven Use titration & Monitoring schedule, Caution fluvoxamine, BZD, LI, hypotensives Risk weight gain, seizures, aganulocytosis, cardiac effects, NMS Pregnancy & Lactation, Risk QT prolongation, TD, EPS, NMS, seizures Caution fluvoxamine, Risk TD, NMS, Highest risk EPS, hyperprolactinemia Risk TD, NMS, moderate risk EPS, Hyperprolactinemia Risk TD, NMS, moderate risk EPS, Hyperprolactinemia Risk TD, NMS, moderate risk EPS, Hyperprolactinemia Caution hypotensives, Risk EPS, TD, NMS, weight gain, seizures, hypotension
Clozapine (Clozaril)	300 - 900	qhs	5 - 16	1A2		
Haloperidol (Haldol) po or IM	2 - 10	qhs or od	12 - 36	3A4	2D6	
Zuclopenthixol (Clopixol) po	20 - 60	qhs or od	12 - 28	2D6	2D6	
Loxapine (Loxapac) po or IM	15 - 50	qhs or bid	8 - 30	1A2, 2D6, 3A4		
Perphenazine (Trilafon) po preferred	4 - 16	qhs or bid	9 - 21	2D6	2D6	
Chlorpromazine (Largactil) po or IM	100 - 500	qhs or bid	16 - 30	1A2, 2D6	2D6	

¹ With atypical antipsychotics monitor glucose & lipids IM formulations indicated for acute use; bioavailability up to double that of oral dose.

DEPOT ANTIPSYCHOTICS	Dose Range in mg (IM)	t ^{1/2} (hours)	Clinical Equivalence (Estimated, mg)
Haloperidol decanoate (Haldol LA)	50 - 300mg q 4 weeks	18 - 21 days	40 q 4 wk
Fluphenazine decanoate (Modectate)	12.5 - 100mg q 4 weeks	14 - 102 days	15 q 4 wk
Flupenthixol decanoate (Fluanxol inj)	20 - 100mg q 2 - 3 weeks	8 - 17 days	24 q 4 wk
Zuclopenthixol decanoate (Clopixol depot) (Only medium potency depot)	150 - 300mg q 2 weeks	19 days	120 q 4 wk
Zuclopenthixol acetate (Clopixol acuphase)	50 - 100mg q 2 - 3 days ¹	36 hours	15 q 3 days

¹ Short term use only: Maximum 4 injections

ANXIOLYTICS & SEDATIVES	Dose Range Anxiolytic	BZD Dose Sedative	Equiv. (mg)	t ^{1/2} (Hours)	P450 Systems		Special Considerations (Class Effects Boxed) (Avoid, Caution with, Risk of)
					Substrate of:	Inhibits or Induces	
Alprazolam (Xanax)	0.25 - 1 tid to qid	0.25 - 1 qhs	0.5	9 - 20	3A4	2B4 Cumulative effect with other sedatives; Caution in pregnancy In liver disease suggest lorazepam, oxazepam, temazepam Caution with Clozapine, Digoxin; Avoid in sleep apnea Abuse liability--less likely with longer onset of action Withdrawal syndromes -- most severe with short-acting agents Risk of confusion & falls in the elderly; See P450 interactions Risk of mania in elderly; Not effective on prn basis Withdrawal syndrome, Risk hypotension, leukopenia; Caution with sedatives Cumulative effect with sedatives Zolpidem only: Risk delirium & hallucinations combined with SSRIs, SNRI, Caution with other serotonergic agents, lithium; Avoid in pregnancy, diabetes Withdrawal syndrome, Avoid in pregnancy, Avoid with Ginkgo Biloba Caution with anticholinergics, serotonergics; Risk hypotension, priapism	
Lorazepam (Ativan)	0.5 - 2 tid to qid	0.5 - 2 qhs	1	8 - 24	Conjugation		
Temazepam (Restoril)	15 - 30 bid to tid	15 - 30 qhs	10	3 - 25	Conjugation		
Oxazepam (Serax)	15 - 30 bid to tid	15 - 30 qhs	15	3 - 25	Conjugation		
Clonazepam (Rivotril)	0.5 - 2 bid to tid	0.5 - 1 qhs	0.25 - 0.5	19 - 60	2B4, 2E1, 3A4		
Diazepam (Valium)	2 - 10mg od to tid	5 - 10mg qhs	5	30 - 200	3A4, 2C, 2B6		
Buspirone (Buspar)	5 - 60/day div. tid			2 - 11	3A4, 2C19, 2D6		
Gabapentin (Neurontin)	900 - 3600/day div. tid			5 - 7	Renal		
Zopiclone (Imovane)		3.75 - 15 qhs		3.5 - 6	1A2, 2C9		
Zolpidem (Ambien)		5 - 20 qhs		1.5 - 4.5	3A4		
Zaleplon (Starnoc)		5 - 20 qhs		1	3A4, ald. oxidase		
L-tryptophan (Tryptan)		1000 - 5000 qhs	15.8				
Trazodone (Desyrel)		25 - 100 qhs		4 - 9	1A2, 3A4		

CHOLINESTERASE INHIBITORS (MILD TO MOD. DEMENTIA)	Total Daily Dose Range (mg)	Dosing	t ^{1/2} (hours)	P450 Substrate of:	Special Considerations (All listed are Class Effects) (Avoid, Caution with, Risk of)
Donepezil (Aricept)	5 - 10	qhs or od	70 - 80	2D6, 3A4	Caution with cardiac or coronary artery disease, ulcers, asthma Caution with NSAIDs; Toxic in Overdose; Risk Withdrawal Syndrome Avoid with anesthesia, anticholinergics, cholinomimetics, or in Epilepsy
Rivastigmine (Exelon)	6 - 121	bid, w/ meals	1 - 2	Esterases	
Galantamine (Reminyl)	16 - 241	bid, w/ meals	5 - 7	2D6, 3A4	

MOOD STABILIZERS	Total Daily Dose Range (mg)	Dosing	Blood Level	t ^{1/2} (hours)	P450 Systems		Special Considerations (Avoid, Caution with, or Risk of) (Carefully review mood stabilizers in pregnancy & breastfeeding)
					Substrate of:	Inhibits or Induces:	
Lithium (Eskalith) Lithium SR (Durallith)	600 - 1800 600 - 1800	qhs or tid qhs	0.8 - 1.2 mEq/L	18 - 36 18 - 36	Renal Renal		Toxic > 1.5mEq/L, Avoid fluid balance shifts, Avoid with breastfeeding, Iodide salts, Caution in cerebral/cardiac/renal disease, Caution NSAIDs antihypertensives, Risk hypothyroidism, renal disease, Teratogenic
<i>Start 600 - 900mg/day & CBC, lytes, Cr, Ca, TSH, +/- ECG, up 300mg q 5 days, follow levels</i>							
Divalproex Sodium (Epival)	750 - 3000	qhs or bid	350 - 700 µmol/L	5 - 20	2C9, UGT	2C9, 2C19, UGT	Risk Liver & Pancreatic Toxicity, Blood Dyscrasias including Thrombocytopenia, Serious Rashes, Teratogenic Caution ASA, Warfarin, Lamotrigine, BDZs
<i>Start 750mg/day divided or qhs & CBC, lytes, Cr, LFT, up 250mg/week to levels</i>							
Carbamazepine (Tegretol)	300 - 1600	qhs or bid	17 - 50 µmol/L	10 - 20	3A4	3A4, 1A2, 2C9, 2B6	Risk Serious Rash, Blood Dyscrasias, SIADH, Teratogenic Caution in Liver Disease, Check CYP interactions, Induces own metab. Avoid with Clozapine, MAOIs
<i>Start 200mg bid or qhs & CBC, lytes, Cr, LFT, up 200mg q 3 - 5 days following levels</i>							
Oxcarbazepine (Trileptil)	600 - 2400	bid	Not Monitored	8 - 11	Conjugation	2C19, 3A4	Risk Arrhythmias, Serious Rash, Hyponatremia, Liver Toxicity Caution in Pregnancy, Lactation, Cardiac Disease, Renal Disease P-450 inducers & DVPX decrease level of active compound
<i>Start 300mg bid & check Sodium, 600mg bid average target dose</i>							
Lamotrigine (Lamictal)	100 - 500	bid or qhs	Not Monitored	26 - 33	Conjugation & Renal		Risk Rashes, SJ Synd., PR Prolongation, Titrate slowly Anticonvulsants affect levels, Caution with DVPX, Avoid in pregnancy and watch for rashes
<i>Start 25-50mg/day, up 25mg q week to target (300-500mg), use 1/2 these doses if added to DVPX, higher doses if added to CBZ,</i>							
Topiramate (Topamax)	50 - 500	qhs	Not Monitored	21	Renal		Avoid Carbonic Anhydrase Inhibitors Caution in Renal Disease, CBZ decreases levels
<i>Start 25mg bid, up 25mg bid/week to target (200-400mg/day)</i>							
<i>¹ Initial dose is 1/2 minimum target daily dose, divided bid, increase after 4 weeks to first target dose, can increase further after 4 week intervals</i>							

ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN	Dosing	Timing	Duration Action (hrs)	P450 Systems		Special Considerations (Class Effects Boxed) (Avoid, Caution with, Risk of)
				Substrate of:	Inhibits or Induces	
Methylphenidate (Ritalin)	0.3 to 0.6mg/kg/dose	q8am +12pm	3 - 5	Esterases ²	2D6, 2C9	Can give low dose regular methylphenidate at 4pm if needed
Methylphenidate SR (Ritalin SR) ¹	0.6 - 1.2mg/kg/day	q8am	3 - 5	Esterases ²	2D6, 2C9	Monitor height/weight; Risk anorexia, dysphoria or tolerance
Dextroamphetamine (Dexedrine)	0.15 - 0.3mg/kg/dose	q8am +12pm	4 - 5	2D6		Caution with cardiovascular disease, psychosis, tic disorder,
Dextroamphetamine SR (spansules)	0.3 - 0.6mg/kg/day	q8am	7 - 8	2D6		hyperthyroidism, seizure disorder; Caution noradrenergics
Tricyclic Antidepressants (i.e. desipramine)	25mg - 2.5mg/kg/day	qhs	Refer to Antidepressant Section			Baseline ECG recommended in children
Bupropion SR (Wellbutrin) SR	1 - 6mg/kg/day	divide >150mg	Refer to Antidepressant Section			Risk of seizures limits use for ADHD

¹ Slow time of onset, and limited duration of action

² Methylphenidate metabolism inhibited by phenytoin, phenobarbital, primidone, warfarin

SIDE EFFECT MANAGEMENT Medication	Indication	Dosing (# per dose)	COMBINATIONS FOR REFRACTORY DEPRESSION	
			Primary Agent	Augmenting Agent + Dosing
Beztoprine (Cogentin)	Extra Pyramidal Side Effects (EPS)	1 - 2mg bid or prn	Antidepressant	Lithium 0.5 - 0.8 mmol/L
Benzodiazepines	EPS	See Anxiolytics/Sedatives	Antidepressant	T3 (Cytome) 25 - 50 µg/day
Diphenhydramine (Benadryl)	EPS	25 - 50mg prn	SSRI or SNRI ¹	Bupropion (Wellbutrin) 150 - 300mg/day
Propranolol (Inderal)	Akathisia	10 - 20mg bid to tid	SSRI or SNRI ¹	Mirtazapine (Remeron) 15 - 60mg/day
Atenolol (Tenormin)	Akathisia	25 - 50mg od to bid	SSRI	Risperidone (Risperdal) 0.5 - 2mg/day
Atropine Eye Drops	Sialorrhea	1 - 2 drops SL od to bid	SSRI	Olanzapine (Zyprexa) 2.5 - 15mg/day
Dantrolene (Dantrium)	Neuroleptic Malignant Syndrome	1mg/kg IV q6h prn max 10mg/kg	Note: Before augmenting, optimize dose of primary agent & address co-morbid diagnoses, eg personality disorder or substance use	
Bromocriptine (Parlodel)	Neuroleptic Malignant Syndrome	2.5 - 5mg tid by NG tube	<i>Caution with other combinations of two antidepressants</i>	
Bromocriptine (Parlodel)	Hyperprolactinemia	1.25 - 10mg bid	<i>Combinations involving MAOIs should be monitored by a specialist</i>	
Amantadine (Symmetrel)	Hyperprolactinemia/Weight Gain	100mg od to bid	¹ SNRI = Serotonin & Norepinephrine Reuptake Inhibitor (eg Venlafaxine XR)	
Nizatidine (Axid)	Medication Induced Weight Gain	150mg bid		
Topiramate (Topamax)	Medication Induced Weight Gain	25 - 200mg bid		
Bupropion SR (Wellbutrin SR)	Sexual Side Effects	150mg od to bid		
Sildenafil (Viagra)	Sexual Side Effects	25 - 100mg before intercourse		

P450 System Information for Common Interacting Non-Psychiatric Medications
Medications Listed by P450 System, as Substrate, Inhibitor, or Inducer

1A2	2B6	2C19	2C9	2D6	3A4	
Cycloenzaprine	Cyclophosphamide	Cyclophosphamide	Celecoxib	Tamoxifen	Antiarrhythmics	Ca Channel Blockers
Caffeine	Ifosfamide	Phenobarbitone	Diclofenac	Tolbutamide	Codeine	Vincristine
Mexiletine	Orphenadrine	Phenytoin	Fluvastatin	Torsemide	Dextromethorphan	Chlorpheniramine
Naproxen	Thiotepa	Progesterone	Glipizide	Warfarin	Metoprolol	Clarithromycin
Riluzole	Phenobarbital	Proguanil	Ibuprofen	Amiodarone	Onandsetron	Cyclosporine
Theophylline	Rifampin	Proton Pump Inhibitors	Irbesartan	Fluconazole	Pindolol	Ergotamine
Zileuton		Ketoconazole	Losartan	Isoniazid	Tamoxifen	Erythromycin
Zolmitriptan		Lansoprazole	Naproxen	Ticlopidine	Timolol	Granisetron
Fluoroquinolones	2E1	Omeprazole	Phenytoin	Rifampin	Tramadol	Methadone
Ticlopidine	Acetaminophen	Oral Contraceptives	Piroxicam	Secobarbital	Amiodarone	Oral Contraceptives
Tobacco	Chlorzoxazone	Ticlopidine	Sulphonamides		Chlorpheniramine	Pimozide
	Ethanol				Methadone	Protease Inhibitors
	Propranolol				Mibefradil	Oxybutynin
	Volatile Anaesthetics				Quinidine	Phenobarbital
	Disulfiram				Ritonavir	Quinine
	Ethanol					Sildenafil
	Isoniazid					Steroids
						Statins
						Tacrolimus
						Tamoxifen
						Troglitazone

With Permission: Flockhart, DA. Jan 2002. Drugs Metabolized by Known P450's. Reference Card. Indiana University School of Medicine
Bezchlibnyk-Butler, KZ & Jeffries, JJ. 2002. Clinical Handbook of Psychotropic Drugs 12 ed. Hogrefe & Huber Publishers.

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