

Name: Generic/TRADE (& receptor activity) <small>g=generic</small>	GROUP	Clinical Equivalency (mg)	SIDE EFFECTS -SE (%)				ANTI-EMETIC	DOSE: INITIAL; MAX; <i>{elderly}</i>	USUAL DOSE RANGE	\$ /Month
			Anticholinergic	Sedation	Hypotension	EPS				
Chlorpromazine LARGACTIL g (25 ⁵ ,50 ⁵ ,100 ⁵ mg tab)(liquid made by some pharmacies) 50mg/2ml amp; (100mg supp ^{xv})	Aliphatic	100	>30	>30	>30	>10	Pregnancy category → ++++	25mg 1200mg	50mg po bid 100mg po bid	21 30
Cholestatic jaundice <1%, Weight gain ~3-5kg, Seizures <1%, Photosensitivity <3%										
Methotrimeprazine NOZINAN g (2.5,25.50mg tab) (25mg/ml amp ^{xv})	Phenothiazine	70	>30	>30	>30	>10	+	5mg 1000mg	25mg po bid 50mg po bid	15 19
Pericyazine NEULEPTIL (5,10,20mg cap; 10mg/ml liquid)	Piperidine	15	>30	>30	>10	>2	++++	5mg; (max 60mg)	10mg po bid	27
Pipotiazine PIPOTIL (DEPOT) 25mg/ml,50mg/ml,100mg/2ml ^x Amp			20mg IM q4week	>10	>10	>2	10-30	+	25-250mg IM q4w	25mg IM q10d 50-75mg IM q2-4w
Less akathisia & dystonic reactions than other DEPOT medications										
Thioridazine MELLARIL g (10,25,50,100mg tab; 30mg/ml liquid) Discontinued -Canada Sept/05	Phenothiazine	100	>30	>30	>30	>2	+	25mg 800mg →Retinal pigmentosa	50mg po bid 100mg po bid	Available in USA
ECG: ↑QT interval (sertindole >thioridazine >ziprasidone), T wave Δ's, priapism, retrograde ejaculation; FDA: kids >2 approved										
Fluphenazine MODECATE,MODITEN g (DEPOT) with preservative 125mg/5ml Vial & 100mg/1ml Amp; 1, 2, 5mg tab	Piperazine	5 15mg IM q4week	>2	>2	>2	>30	+	1-40mg PO 12.5-75mgIM/SCq2w	2-5mg po bid 25-50mg IMq2-4w	22-20 15
Perphenazine TRILAFON g (2,4,8,16mg tab); (5mg/ml amp ^{xv})			8	>2	>10	>2	>30	++++	2mg 64mg	4mg po bid 8mg po bid ~20mg/d CATIE
Trifluoperazine STELAZINE g (1,2,5,10, 20 ^{xv} mg tab; 10mg/ml soln)	Thioxanthenes	6	>2	>2	>10	>30	++++	2mg 40mg	2mg po bid 5mg po bid	17 20
Flupenthixol FLUANXOL (DEPOT) 20mg/1ml amp, 100mg/1ml amp; 0.5,3mg tab			10 24mg IM q4week	>10	>2	>2	>30	++	2-12mg po 10-80mg IM q2-3w	3mg po bid 20-40mg Imq2-3w
Zuclopenthixol CLOPIXOL (10,25mg tabs), Accuphase (50mg/1 ml amp) DEPOT 200mg/1 ml amp)	50 120mg IM q4week	>10	>30	>2	>30	++	20-100mg po 50-400mg IM q2w	10mg po bid 25mg po bid 100-200mgIMq2-3w	34 74 35	
LESS with DEPOT										
Clozapine CLOZARIL g (25 ⁵ , 50 ⁵ , 100 ⁵ , 200 ⁵ mg tab) D1-5,HT1&2,α1,α2,H1,M1-5 cardiomyopathy; TALT≤37%, diabetes, ↑lipids, akathisia ~10%, Dis: ↓clozapine level, carbamazepine (& ↑neutropenia) & smoking; Fluvoxamine & erythromycin ↑clozapine level; benzodiazepines-rare resp. arrest. ↔prolactin effect	Dibenzodiazepine	50	>30	>30	>30	>2	+	6.25-25mg (↑25-50mg/d) 900mg	100mg po tid 200mg po bid	285 _g , 394 371 _g , 516
SE: Dizzy, constipation, N/V, fever, ↑sweat, ↑HR, ↓BP, ↑salivation; Atropine eye drops/Alveret nasal spray, enuresis nocturnal, seizure (≤5%-dose related), agranulocytosis ^{15%} →CBC qweek (q2week if stable), weight ↑↑↑, ECG Δ's, ↓BPAD: acute Tx of manic & mixed episodes; maintenance										
Haloperidol HALDOL g (0.5 ⁵ ,1 ⁵ ,2 ⁵ ,5 ⁵ ,10 ⁵ mg tab; 2mg/ml soln; DEPOT with preservative 250mg/5ml, 500mg/5ml Vial, 100mg/1ml Amp ^{xv} ; 5mg/ml amp) D2-D1	Butyrophenone	2 - 6 40mg IM q4week	>2	>2	>2	>30	+++	1-100mg PO 25-300mg IM q4w (0.25-2mg/d)	2mg po bid 5mg po bid 50-100mgIMq2-4w	15 18 20
↑QT interval esp. with IV dosing, ↑ALT ≤16%, Weight gain ≤1 kg; FDA: kids >3 approved										
Loxapine LOXAPAC g (5 ⁵ ,10 ⁵ ,25 ⁵ ,50 ⁵ mg tab); (2.5 ⁵ mg tab ^{xv}) (25mg/ml soln ^{xv} ; 50mg/ml amp ^{xv})	Dibenzoxapine	15	>10	>30	>10	10-30	+	5mg 250mg	5mg po bid 25mg po bid	18 35
Weight gain minimal										
Olanzapine ZYPREXA g Reg + Zydys (2.5,5,7.5,10,15mg tab) (ZYDIS 5,10,15mg tab ¹⁵) 10mg IM ^{xv} ; D1-4, 5HT1&2,α1,H1,M1-3&5 (approved 1996)	Thienobenzodiazepine	2.5 - 5	>10	>30	>2	>2	+	2.5-5mg (1.25-7.5mg/d) 20-30mg	10mg od (generic: 1, 5 soon) 15-20mg CATIE po od	250 360-475
SE: somnolence, dry mouth, dizzy, headache, asthenia, constipation, blurred vision, urinary incontinence, dyspepsia, ↑ALT ≤6%, diabetes, weight ↑↑, ↑BP, ↑akathisia >10%, postural hypotension, seizures 0.9%, ?↑stroke/death, ↑↑triglycerides, ↑↑cholesterol. Dis: ↓olanzapine by smoking, ↑ by fluvoxamine ↔↑prolactin										
Pimozide ORAP g (2,4mg tab)	Diphenylbutyl piperidine	2 ↑QTc with >8mg/d or azole antifungals, diltiazem, fluvoxamine, macrolides, sertraline, paroxetine, P1 ^s IV & verapamil. FDA: kids >12 approved	>2	>10	>2	>10	+	2mg 8-20mg	2mg po bid 4mg po bid	24 37
Quetiapine SEROQUEL g (25,100,200,300mg tab); (XR: 50,200,300,400mg) ^o	Dibenzothiazepine	60 - 75	>2-10	>10-30	>10	>2	+	12.5mg (12.5-150mg/d) 800mg	200mg po tid ac 600mg hs ~540mg/d CATIE 300mg po bid ac 300mg po tid ac	190 _g , 285 185 _g , 277 185 _g , 277 270 _g , 400
SE: somnolence, dizzy, drowsy, constipation, dry mouth, lens changes in beagles-annual slit lamp exam, ↓BP, weight ↑, seizures ≤0.8%, dyspepsia, headache, urinary incontinence, diabetes, ↑ALT ≤9%, akathisia >2%, ?↑stroke/death, ↑triglyceride ^{17%} , ↑cholesterol ^{11%} , hypothyroidism ^{0.4%} , ?pancreatitis/↓platelet, low EPS effect. ↔prolactin effect										
BPAD: acute Tx of manic, depressive & mixed episodes 600mg XR od \$275, 800mg XR od \$370										
Risperidone RISPERDAL g (0.25,0.5 ⁵ ,1,2 ⁵ ,3 ⁵ ,4 ⁵ mg tab) (DEPOT) 12.5,25,37.5,50mg vial ^o M-TAB melts 0.5,1,2,3,4 mg tab; 1mg/ml soln D1-4, 5HT1&2,α1,α2,H1 - little M1 (approved 1993)	Benzisoxazole	2	>2	>2-10	>10-30	>10	+	0.25-1mg (0.25-2mg/d) 6-10mg Max:50mg IM q2w \$750	1mg po bid 2mg bid CATIE 25-50mg IM q2w CONSTA	50 93 350-670
SE: sedation, headache, dry mouth, constipation, blurred vision, urinary incontinence, insomnia, agitation, asthenia, ↓BP, akathisia >10%, ↓appetite, TTP, seizures ≤0.3%, photosensitive, ↑↑stroke/death, weight ↑. Oral liquid not mix with cola or tea. DI: furosemide. ↑EPS at doses >2-4mg/day & ↑prolactin										
BPAD: acute Tx of manic & mixed episodes ≥10yr ^{15%} ; Autism: irritability Age 5-16yr ^{15%} ; Schizophrenia Age ≥13yr ^{15%}										

General: Onset 7days; a good trial is 4-6 wks. 25% of pts. respond poorly to Tx, yet 30% of these respond to clozapine. **Positive S/Sx:** hallucinations, delusions, thought disorders; **Negative S/Sx:** social withdrawal, isolation & apathy. **↓** = ↓ dose for renal/dysf c = scored Neuroleptic Malignant Syndrome. **↑** = ↑ dose. **pto** 1%, often within 30days; esp. younger males. high potency depot; mortality of 10%. S/Sx: >39°C, muscle rigidity, delirium, autonomic instability (ie. ↑BP, ↑CPK, ↑HR, arrhythmias, tremors, seizures & coma, TX: D/C neuroleptic, cooling blanket, hydrate, dantrolene, bromocriptine & benzodiazepines). **Tardive dyskinesia** - after months to yrs of neuroleptics, ↑ in elderly. S/Sx: fly catching/protruding motions of tongue, tics of the face, chewing motions or excessive blinking. TX: D/C/change/↓ neuroleptic, ↓anticholinergics, tetrabenazine, donepezil, Vit E 400-1600IU/d. **Depot Medications** - after 3-6 months many accumulate; thereby, requiring ↓ dose, onset of action for most are 2-3 days (Peak 4-7day), except Clopixol Accuphase with onset: 2-4hr, duration: 2-3days and max. sedation at 8hr. **Pregnancy:** Consider the risk versus benefit! -use lowest possible dose, high potency agent preferred (ie. haloperidol FDA Category C), if possible try to D/C before delivery. Avoid if possible especially during first trimester. **Level ↓ by:** antacid, cholestyramine, carbamazepine, phenobarbital, phenytoin, rifampin, & smoking. **Level ↑ by:** amitriptyline, amiodarone, cimetidine, ciprofloxacin, diltiazem, erythromycin, fluoxetine, fluvoxamine, grapefruit juice, isoniazid, ketoconazole, nefazodone, paroxetine, propranolol, quinidine & ritonavir. **EPS** Acute dystonia - spasm of face, neck & back-like seizure (Onset 1-5day esp. young male, Tx: **benztropine**) Akathisia - motor restless-not verbal, pacing, fidgety (Onset 5-60day, esp. old female; Tx: ↓dose/Δ low potency, lorazepam, propranolol, diphenhydramine) **Parkinsonism** - rigid, bradykinesia, shuffling gait, tremor (Onset 5-30day esp. old female; Tx: **benztropine**, amantadine) **Rabbit Syndrome** - rapid chewing movements (Onset after months esp. old females; Tx: **benztropine**). **EDS** = Non-formulary Sask **New:** Aripiprazole **ABILIFY** (USA: 10,15,20,30mg tab) 10-15mg od. Max 30mg/d; FDA: adult & kid ≥13yr; minimal ↑weight, ↑anxiety; DI: fluoxetine, erythromycin & carbamazepine. **Ziprasidone ZELDOX**, **GEODON** (Canada: 20,40,60,80mg cap) ^o 40-80mg bid ¹⁵⁰; CATIE 110mg/d with meal; ↑QT interval^{15%}; Dis⁵; EPS -5%; minimal ↑wt. **Paliperidone INVEGA** (Canada: 3,6,9mg XR tabs) ^{xv} 3-6-9mg od ¹²⁰⁻¹⁷⁰⁻²³⁰. Max 12mg ^o; active metabolite of risperidone; ↑absorption ~50% with high fat meal; ↑QT; limited short trials to date; DI: carbamazepine, paroxetine, & ↑QT interval meds.

ANTIPSYCHOTICS: Frequently asked Questions.

1. What is the difference in WEIGHT GAIN among the different antipsychotics?¹

Estimated weight change at 10 weeks:^{1,2}
using a Fixed effects Model:

	kg
loxapine	minimal
haloperidol	0.48
risperidone	2.0
chlorpromazine	2.1
quetiapine	~2.5
thioridazine	3.49
olanzapine	3.51
clozapine	3.9

Allison, David
 Am J Psyc Nov 99, JCP 2001

The following statements from the CPS or specific studies state:

Risperidone RISPERDAL	-can ↑ weight by 2 kg at 10 weeks, then 2.3kg after long term treatment -18% of pts vs 9% of placebo pts ↑ by >7% from baseline (Catie ^{18months} ; 14% ↑ by >7%; Mean change 0.8 lbs)
quetiapine SEROQUEL	-can ↑ weight by 2 kg at 4-8 weeks, 3.5kg at 18-26 week & 5.6kg at 1year -25% of pts vs 4% of placebo pts ↑ by >7% from baseline (Catie ^{18months} ; 16% ↑ by >7%; Mean change 1.1 lbs)
olanzapine ZYPREXA	-can ↑ weight by ~3.5kg at 10 weeks, then 5.4kg at 6-8months -29% of pts vs 3% of placebo pts ↑ by >7% from baseline (Catie ^{18months} ; 30% ↑ by >7%; Mean change 9.4 lbs)
clozapine CLOZARIL	-can ↑ weight by 4 kg at 10 weeks

2. What are the different EXTRAPYRAMIDAL SIDE EFFECTS (EPS) and COSTS?

Atypical agent	EPS effect	Prolactin levels	Younger patients (Dose & Cost/month)	Geriatric patients (Dose & Cost/month)
haloperidol	High	↑↑	5mg po bid \$18	1mg po hs \$10
risperidone RISPERDAL	Low ⁺	↑	1mg po bid \$50 2mg po bid \$93	0.5mg po hs \$23 1mg po hs \$29 <small>New generics cheaper</small>
olanzapine ZYPREXA	Lower ⁺	↑ ↔	10mg po od \$250 15mg po od \$360	2.5mg po od \$71 <small>(generics: 1, \$ soon)</small> 5mg po od \$136
quetiapine SEROQUEL	Even lower	↔	100mg po tid \$ 98 200mg po bid \$129	25mg po hs \$19 <small>(generics: 1, \$ now)</small> 50mg po hs \$30
clozapine	Lowest*	↔	100mg po tid \$285	100mg po hs \$102

⁺ dose dependent *even some anti- tremor effect

3. Are there any SPECIAL SITUATIONS where one agent differs from the other agents?

Atypical agent	Liver Enzymes (↑ ALT 2-3x)	Seizure Risk	Neutropenia	Special differences
risperidone RISPERDAL	Rare	≤ 0.3%	NO	Approved→behavioral disturbances in severe dementia & for acute treatment of mania; Liquid formulation, M tab & depot forms available; Parkinson's motor function worse esp. if >2mg/d
olanzapine ZYPREXA	↑ ≤ 6%	≤ 0.9%	Rare	Approved for acute treatment of mania, ↑ diabetes, ↑ weight, anticholinergic & ↑lipid. Zydys wafer avail.
quetiapine SEROQUEL	↑ ≤ 9%	≤ 0.8%	NO	Approved: acute mania. Better for Parkinson's psychosis ↑ cholesterol (11%), ↑ triglycerides (17%), TSH changes (ie hypothyroidism ~0.4%) Eye lens changes→ cataracts in beagle dogs
clozapine CLOZARIL	↑ ≤ 37% <small>Most effective agent but TSE, withdrawal/delirium possible if stop med abruptly.</small>	≤ 5% dose dependent	YES 1%	Anti-tremor effects, Useful for Parkinson's induced psychosis but ADR's & weekly q 2weeks if stable blood tests discourage its use. Approved to ↓suicide risk in schizophrenics CSAN: 1-800-267-2726 Gen: 1-866-501-3338 Apo: 1-877-276-2569
haloperidol	↑ ≤ 16%	<1%	NO	Available in IV/IM & depot formulations, Useful option for acute treatment of delirium

1. Allison DB et al. Antipsychotic Induced Weight Gain: A comprehensive Research Synthesis. Am J Psychiatry 1999;156(11):1686-96.
 2. Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. J Clin Psychiatry. 2001;62 Suppl 7:22-31.
 3. Expert Consensus Guideline Series- Treatment of Schizophrenia 1999. J Clin Psychiatry 1999;60 (Suppl 11)
 4. Switching Antipsychotics- Canadian Expert Consensus Panel July 2000
 5. Canadian Clinical Practice Guidelines for the Treatment of Schizophrenia, Nov 1998, Vol 43, Supp 2; Can J Psyc Vol 50 Suppl 1 Nov 2005
http://www.cpa-apc.org/Publications/Clinical_Guidelines/schizophrenia/november2005/cjp-cpg-suppl1-05_full_spread.pdf
 6. Lehman AF, et al. APA:Practice guideline for the treatment of patients with schizophrenia, 2nd Ed. Am J Psychiatry. 2004 Feb;161(2 Supp):1-56.

4. What DEPOT MEDICATIONS are available?

MEDICATION	DEPOT SOLUTION
flupenthixol - FLUANXOL	fluphenazine-MODECATE (preserv. benzyl alc.)
haloperidol - HALDOL LA (preserv. benzyl alcohol)	pipotiazine -PIPORTIL
zuclopenthixol - CLOPIXOL Depot	coconut oil
risperidone - RISPERDAL CONSTA Depot	microspheres ^{in diluent}

5. Selecting Medications for SPECIFIC COMPLICATING PROBLEMS^{3,4,5,6}

	Recommended antipsychotic medication choices	Recommended adjunctive medication
Aggression/violence Agitation/excitement	haloperidol 2-5mg IM/1-2mg IV q1h prn Max 20mg/d (with promethazine 25-50mg IM prn useful) lorazepam 1-4mg IV/IM/ q1h prn Max 8mg/d zuclopenthixol accuphase 50-150mg IM q2d prn Max total cumulative dose ≤ 400mg & ≤ 4 inj Olanzapine 10mg IM prn (but ↑\$) inj ziprasidone & aripiprazole in USA High potency CAP or AAP (ie. risperidone)	valproic acid Possibly lithium, carbamazepine, propranolol, BZ (if no hx of substance abuse)
Insomnia	AAP (quetiapine, olanzapine) or low potency CAP preferred	Bz -short term use of Tema-/ lora-/ oxa-zepam
♦ if history of abuse consider trazodone, diphenhydramine, hydroxyzine & methotrimeprazine		
Dysphoria	AAP strongly preferred over CAP	SSRI
Suicidal behavior	AAP strongly preferred over CAP	SSRI-if in the context of postpsychotic depression
Comorbid substance abuse	AAP preferred over CAP Depot meds may be helpful for non-compliance	
Cognitive problems	AAP strongly preferred over CAP	
Compulsive water drinking (psychogenic polydipsia)	AAP preferred over CAP clozapine (but not for initial treatment)	

6. Selecting Medications to Avoid SIDE EFFECTS^{3,4,5,6}

	LEAST likely to cause	MOST likely to cause
Sedation	risperidone high potency CAP	Low potency CAP clozapine, quetiapine, olanzapine
Weight Gain	haloperidol, perphenazine, risperidone (aripiprazole & ziprasidone seem less)	clozapine most, then olanzapine, then quetiapine
Extrapyramidal effects (EPS side effects)	clozapine quetiapine olanzapine risperidone ↓ More EPS	Mid & high potency CAP
Anticholinergic side effects & Cognitive side effects	risperidone quetiapine, high potency CAP	Low potency CAP clozapine
Sexual side effects	quetiapine, olanzapine, clozapine	CAP
Cardiovascular SE (eg. QT effect), concern if cardiac risk/DIs/elderly, consider ECG testing in select pts	risperidone olanzapine, high potency CAP, quetiapine	Low potency CAP (eg. thioridazine), clozapine, pimoizide & ziprasidone
Tardive dyskinesia (TD) -Vitamin B6 1200mg/d may help -Levetiracetam may help Woods 08	clozapine quetiapine olanzapine risperidone ↓ Likely More TD	CAP
Recurrence of neuroleptic malignant syndrome	olanzapine clozapine quetiapine, risperidone ↓ More	CAP
Prolactin Elevation	cloz- olanz- & queti -apine; aripiprazole	Risperidone, CAP

AAP -atypical antipsychotics (clozapine, olanzapine, quetiapine & risperidone); BZ -benzodiazepines;
 CAP -conventional antipsychotics (chlorpromazine, haloperidol, zuclopenthixol etc...);
 Low potency CAP - chlorpromazine, methotrimeprazine, & thioridazine etc.;
 Mid potency CAP - perphenazine; High potency CAP - flupenthixol, fluphenazine, haloperidol, loxapine, trifluoperazine etc.

Drug induced psychosis: ACEI, acetazolamide, acyclovir, amantadine, amphetamine & cocaine withdrawal, anticholinergics, anticonvulsants, antidepressants, baclofen, barbiturates, benzodiazepines, beta-blockers, bromocriptine, bupropion, caffeine, calcium channel blockers, cephalosporins, chemo some, chloroquine, cimetidine, clonidine, cyclobenzaprine, dapsone, DEET, digoxin, diphenhydramine, disopyramide, disulfiram, DM, dopamine agonists, dronabinol, efavirenz, EPO, ethanol, fluoroquinolones, ganciclovir, ifosfamide, interleukin-2, interferon, isoniazid, isotretinoin, ketamine, levodopa, lidocaine, mefloquine, methylodopa, methylphenidate, methysergide, metronidazole, nevirapine, nitrofurantoin, NSAIDs, opiates, procainamide, propafenone, pseudoephedrine, quinidine, selegiline, sildenafil, steroids, sulfas, tizanidine & zaleplon.