

Comparison of Atypical Antipsychotics (Canada)

The chart below compares second-generation antipsychotics “atypicals” in regard to **adult** indications, dosing, adverse effects, metabolism, and cost.

NOTE: *Usual or target daily ADULT dosage range may not include initial and maximum doses. Use lowest effective dose. Dosing in special populations (e.g., renal impairment, geriatrics) is not included. Maximum doses of oral aripiprazole, brexpiprazole, cariprazine, lurasidone, olanzapine, paliperidone, quetiapine XR, and risperidone are approved for once-daily administration. Total daily doses of asenapine, quetiapine IR (except for bipolar depression), and ziprasidone are divided twice daily. Clozapine doses above 12.5 mg should be divided.

Generic (Brand)/ Cost ^b	Health Canada-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day) ^{*,a}	Notable Adverse Effects ^{1,a,c}				CYP450 Metabolism ^a
		Weight Gain	Diabetes Risk	Dys-lipidemia	Sedation	
Aripiprazole (<i>Abilify</i> , generics) 10 mg ~\$35	Schizophrenia and related psychotic disorders: 10-15 mg Bipolar I disorder (manic or mixed episodes and maintenance): 15-30 mg (10-30 mg with concomitant lithium or valproate) Major depression (adjunct to antidepressants): 2-15 mg	Low	Low	Low	Low (may cause insomnia ²)	CYP3A4, CYP2D6 Reduce dose by 50% with strong CYP3A4 or CYP2D6 inhibitors. Double the dose with strong CYP3A4 inducers.
Aripiprazole (<i>Abilify Maintena</i> long-acting injection) 400 mg ~\$500	Schizophrenia: 400 mg IM (gluteal or deltoid) once monthly. Continue oral agent for 14 days after first dose, then stop. Missed dose: If >6 weeks elapse since last dose (>5 weeks if 2 nd or 3 rd dose is missed), restart oral aripiprazole x 14 days with the next dose.	Low	Low	Low	Low	CYP3A4, CYP2D6 Reduce dose with strong CYP2D6 or CYP3A4 inhibitors taken for >14 days. Reduce dose in known CYP2D6 poor metabolizers. Avoid with CYP3A4 inducers for >14 days.

Generic (Brand)/ Cost ^b	Health Canada-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*.a	Notable Adverse Effects ^{1,a,c}				CYP450 Metabolism ^a
		Weight Gain	Diabetes Risk	Dys-lipidemia	Sedation	
Asenapine (Saphris) 5 mg twice daily ~\$105	Schizophrenia: 10 mg (acute) Bipolar I disorder (manic or mixed episodes): 10-20 mg (monotherapy or with lithium or valproate) For sublingual use. Avoid food/drink for 10 minutes afterward.	Moderate	Moderate	Moderate	Moderate	CYP1A2, CYP3A4 (minor), CYP2D6 (minor) Weak CYP2D6 inhibitor.
Brexpiprazole (Rexulti) 2 mg ~\$115	Schizophrenia: 2-4 mg Major depressive disorder (adjunct to antidepressants): 2 mg	Low	Low	Moderate	Moderate	CYP3A4, CYP2D6 Reduce dose by 50% with strong CYP2D6 inhibitors (schizophrenia indication), with strong CYP3A4 inhibitors, and in poor metabolizers. Reduce dose by 75% for patients taking a strong or moderate CYP2D6 inhibitor plus a strong or moderate CYP3A4 inhibitor. Reduce dose by 75% for CYP2D6 poor metabolizers taking a strong or moderate CYP3A4 inhibitor. Double the dose over 1-2 weeks with strong CYP3A4 inducers.

Generic (Brand)/ Cost ^b	Health Canada-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*.a	Notable Adverse Effects ^{1,a,c}				CYP450 Metabolism ^a
		Weight Gain	Diabetes Risk	Dys-lipidemia	Sedation	
Cariprazine (Vraylar) 1.5, 3, 4.5, and 6 mg capsules: ~\$160	Schizophrenia: 1.5-6 mg Bipolar I disorder (manic or mixed episodes): 1.5-6 mg Bipolar I disorder (depression): 1.5-3 mg Note: doses above 4.5 mg should be used with caution in patients weighing 63 kg or less.	Moderate	Low	Low	Moderate	CYP3A4, CYP2D6 (minor) Contraindicated with strong and moderate CYP3A4 inhibitors or inducers. Do not start CYP3A4 inhibitors for two weeks after stopping cariprazine.
Clozapine ^d (Clozaril, generics) 100 mg tablet 3 times daily ~\$260	Schizophrenia (treatment-resistant): 300-450 mg NOTE: initial dose is 12.5 mg once or twice the first day, increased by 25 mg to 50 mg (divided) increments, under medical supervision, with vital sign monitoring for at least six to eight hours after the first 2-3 doses.	High	High	High	High	CYP1A2, CYP3A4, CYP2D6
Lurasidone (Latuda, generics) 40 mg tablet ~\$120	Schizophrenia: 40-80 mg Bipolar I depression (monotherapy or with lithium or valproate): 20-60 mg Take with food (at least 350 kcal).	Low	Low ³	Low ³	Moderate	CYP3A4 Contraindicated with strong CYP3A4 inhibitors or inducers. Start with 20 mg/day and do not exceed 40 mg/day with moderate CYP3A4 inhibitors.

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		Weight Gain	Diabetes Risk	Dys-lipidemia	Sedation	
Olanzapine (Zyprexa, generics) 10 mg tablet ~\$25 Injection ~\$35/10 mg Orally disintegrating tablet available.	Schizophrenia and related psychotic disorders: 10 mg Bipolar I disorder (manic or mixed episodes and maintenance): 5-20 mg <i>Zyprexa IntraMuscular</i> , agitation associated with psychosis or bipolar mania: 10 mg (lower dose [5 mg, 7.5 mg] may be given). May repeat dose in 2 hours. A third dose may be given no sooner than 4 hours after the second dose (max daily dose 20 mg [oral plus IM]).	High	High	High	High	CYP1A2, CYP2D6
Paliperidone (Invega) 6 mg extended-release tablet ~\$190	Schizophrenia and related psychotic disorders: 6 mg	Moderate	Low	Moderate	Low	CYP2D6 (minor), CYP3A4 (minor) It may be necessary to increase the dose if used with a strong inducer of CYP3A4 and/or p-glycoprotein.
Paliperidone palmitate (Invega Sustenna long-acting injection) 75 mg ~\$530	Establish tolerability with oral paliperidone or risperidone before use. Taper off oral agent with first IM dose. 150 mg on day 1 IM (deltoid), 100 mg on day 8 IM (deltoid), then 75 mg (schizophrenia [25-150 mg]) or 50-150 mg (schizoaffective disorder) IM once monthly (deltoid or gluteal). Approximate dose equivalency: 75 mg IM monthly ~6 mg oral once daily. Missed maintenance dose: resume regular monthly dosing if up to 2 weeks late. Details on handling other missed dosing scenarios are provided in the product labelling.	Moderate	Low	Moderate	Low	CYP2D6 (minor), CYP3A4 (minor) It may be necessary to increase the dose if used with a strong inducer of CYP3A4 and/or p-glycoprotein.

Generic (Brand)/ Cost ^b	Health Canada-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)* ^a	Notable Adverse Effects ^{1,a,c}				CYP450 Metabolism ^a
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Paliperidone palmitate (<i>Invega Trinza</i> long-acting injection) 263 mg ~\$1,545/dose	Schizophrenia, after adequate treatment with <i>Invega Sustenna</i> for at least 4 months: IM (deltoid or gluteal) every 3 months, using only the needle provided. Dose is 3.5 times the previous <i>Invega Sustenna</i> dose. Start 7 days before or after the scheduled dose of <i>Invega Sustenna</i> . Can give up to 2 weeks early or up to 1 month late. Details on handling missed doses are provided in the product labelling.	Moderate	Low	Moderate	Low	CYP2D6 (minor), CYP3A4 (minor) It may be necessary to increase the dose if used with a strong inducer of CYP3A4 and/or p-glycoprotein.
Quetiapine (<i>Seroquel</i> , generics) 200 mg tablet twice daily ~\$20	Schizophrenia: 300 mg Bipolar mania (acute): 400-800 mg Bipolar depression (acute): 300 mg	Moderate	Moderate	High	High	CYP3A4 Reduce dose with strong CYP3A4 inhibitors. It may be necessary to increase the dose if used with CYP3A4 inducers.
Quetiapine (<i>Seroquel XR</i> , generics) 400 mg extended-release tablet ~\$45	Schizophrenia: 400-800 mg Bipolar mania (acute): 400-800 mg Bipolar depression (acute): 300 mg Major depression: 150 mg	Moderate	Moderate	High	High	CYP3A4 Reduce dose with strong CYP3A4 inhibitors. It may be necessary to increase the dose if used with CYP3A4 inducers.

Generic (Brand)/ Cost ^b	Health Canada-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*.a	Notable Adverse Effects ^{1,a,c}				CYP450 Metabolism ^a
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<p>Risperidone (<i>Risperdal</i>, generics)</p> <p>4 mg tablet ~\$30</p> <p>Oral solution available.</p>	<p>Schizophrenia and related psychotic disorder: 4-6 mg</p> <p>Bipolar mania: 1-4 mg</p> <p>Severe Alzheimer’s dementia (symptomatic control of inappropriate behavior): 1 mg (divide twice daily)</p>	Moderate	Moderate	Low	Moderate	<p>CYP2D6, CYP3A4 (minor)</p> <p>It may be necessary to reduce the dose if used with a strong CYP2D6 inhibitor or a strong inhibitor of CYP3A4 and/or p-glycoprotein.</p> <p>It may be necessary to increase the dose if used with a strong inducer of CYP3A4 and/or p-glycoprotein.</p>
<p>Risperidone (<i>Risperdal Consta</i> long-acting injection)</p> <p>25 mg ~\$210/dose</p>	<p>Schizophrenia and related psychotic disorders: 25 mg IM every 2 weeks</p> <p>Bipolar I maintenance: 25 mg IM every 2 weeks</p> <p>Continue oral agent for 3 weeks after first dose, then stop.</p>	Moderate	Moderate	Low	Moderate	<p>CYP2D6, CYP3A4 (minor)</p> <p>It may be necessary to reduce the dose if used with a strong CYP2D6 inhibitor or a strong inhibitor of CYP3A4 and/or p-glycoprotein.</p> <p>It may be necessary to increase the dose if used with a strong inducer of CYP3A4 and/or p-glycoprotein.</p>

Generic (Brand)/ Cost ^b	Health Canada-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day)*.a	Notable Adverse Effects ^{1,a,c}				CYP450 Metabolism ^a
		Weight Gain	Diabetes Risk	Dys-lipidemia	Sedation	
Risperidone (Perseris long-acting injection) 90 mg ~\$450 ⁵	Schizophrenia: 90-120 mg once monthly (subcutaneous in the abdomen or back of upper arm). Establish tolerability with oral risperidone before starting. <i>Perseris</i> 90 mg monthly equals ~3 mg oral risperidone once daily; <i>Perseris</i> 120 mg equals ~4 mg oral risperidone once daily. Missed dose: restart as soon as possible.	Moderate	Moderate	Low	Moderate	CYP2D6, CYP3A4 (minor) Consider decreasing the dose to 90 mg with strong CYP2D6 inhibitors. Consider increasing the dose to 120 mg with CYP3A4 inducers. Additional oral risperidone may be needed.
Ziprasidone (Zeldox, generics) 80 mg capsule twice daily ~\$100	Schizophrenia and related psychotic disorders: 40-160 mg Bipolar I (manic or mixed episodes): 80-160 mg Take with a meal.	Low	Low	Low	Moderate	CYP3A4, CYP1A2 (minor)

- a. **Per Canadian product monograph:** *Abilify* (February 2021), *Abilify Maintena* (March 2021), *Saphris* (April 2021), *Rexulti* (December 2020), *Vraylar* (September 2022), *Clozaril* (May 2022), *Latuda* (March 2020), *Zyprexa* (April 2020), *Invega* (December 2020), *Invega Sustenna* (December 2020), *Invega Trinza* (December 2020), *Seroquel* (November 2021), *Seroquel XR* (January 2022), *Teva-risperidone* (October 2022), *Risperdal Consta* (December 2020), *Perseris* (May 2023), *Zeldox* (December 2021).
- b. Wholesale cost per month (unless otherwise specified), for generic if available, of dose specified.
- c. **Extrapyramidal side effects** are low with aripiprazole, brexpiprazole, cariprazine, quetiapine, ziprasidone, and high with lurasidone, paliperidone, and risperidone.¹ **Hyperprolactinemia** and associated effects (e.g., sexual dysfunction, gynecomastia, irregular periods) seem most common with risperidone and paliperidone, and lowest with aripiprazole, brexpiprazole, cariprazine, clozapine, lurasidone, and quetiapine.¹ **QT prolongation** risk varies among agents. Aripiprazole and lurasidone may pose relatively lower risk versus other agents, while ziprasidone may pose the highest risk.¹ See our resource, *Drug-Induced QT Prolongation: A Stepwise Approach* for more information. **Anticholinergic effects** (e.g., dry mouth, constipation, difficult urination) may be most problematic with clozapine, cariprazine, olanzapine, and quetiapine,¹ and least problematic with brexpiprazole, asenapine, and lurasidone.⁴

- d. Clozapine is associated with severe neutropenia, seizures, and myocarditis. Hematological monitoring required. Clozapine is only available through manufacturer-specific registration and distribution systems in Canada. Prescribers may obtain details by calling the number in the manufacturer's product monograph.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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