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October 2018 ~ Resource #341007

Comparison of Atypical Antipsychotics

Second generation or "atypical" antipsychotics have a lower propensity than the first generation agents to cause extrapyramidal side effects and tardive dyskinesia, but are by no means devoid of these adverse effects.⁴ Clozapine may be the most effective atypical for schizophrenia, but its use is limited due to the risk of agranulocytosis.^{1,2,13} All carry "black box" warnings regarding mortality risk in dementia-related psychosis, and suicidality if indicated for depression. Atypicals pose varying risks of QT prolongation, drug interactions, and metabolic adverse effects. **Extrapyramidal side effects** are low with quetiapine, brexpiprazole, and olanzapine, and high with lurasidone, paliperidone, cariprazine, and risperidone.^{8,3-5,9,13} **Hyperprolactinemia**, associated with sexual dysfunction, gynecomastia, and irregular periods, seems most common with risperidone and paliperidone.^{4,6,13} These factors, plus cost and dosing frequency, are all considerations in choice of agent. The chart below compares atypicals in regard to **adult** indications and dosing, metabolic side effects, sedation, QT prolongation, CYP metabolism, and cost. Prescribers can bill for IM antipsychotic injections under their supervision using CPT code 96372, and add the medication code.

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) is not included. Maximum doses of oral aripiprazole, brexpiprazole, cariprazine, lurasidone, olanzapine, paliperidone, quetiapine XR, and risperidone are approved for once-daily administration. Divide asenapine, iloperidone, quetiapine IR (except for bipolar depression), and ziprasidone twice daily. Clozapine doses above 12.5 mg should be divided.

Generic (Brand)/ Cost ^b	FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day) ^{*a}	Metabolic Adverse Effects ^{a,1,2,4,7,10-13,16}			QT Prolonging ^c	CYP450 Metabolism ^a	Sedation ^{a,8,13}
		Weight Gain	Diabetes Risk	Dyslipidemia			
Aripiprazole (Abilify, generics) 10 mg tablet ~\$45 Oral solution and orally disintegrating tabs available.	Schizophrenia: 10-15 mg Bipolar I disorder (manic or mixed episodes and maintenance): 15 mg (monotherapy or with lithium or valproate) Major depression (adjunct): 5-10 mg	Low	Low	Low	Yes See footnotes e and h.	CYP2D6, CYP3A4 Specific dosing may be advised for CYP450 interactions.	Low

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Generic (Brand)/ Cost ^b	FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day) ^{*.a}	Metabolic Adverse Effects ^{c*.1,2,4,7,10-13,16}			QT Prolonging ^e	CYP450 Metabolism ^g	Sedation ^{h,8,13}
		Weight Gain	Diabetes Risk	Dyslipidemia			
Aripiprazole (Abilify Maintena long-acting injection) 400 mg \$2,166.41	Schizophrenia: 400 mg IM (gluteal or deltoid) once monthly. Continue oral agent for 14 days after first dose, then stop. Reduce dose if CYP2D6 poor metabolizer. Avoid with CYP3A4 inducers for more than 14 days. 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	Yes See footnotes e and h.	CYP2D6, CYP3A4 Specific dosing may be advised for CYP450 interactions.	Low
Aripiprazole lauroxil Aristada long-acting injection 662 mg \$1,833.55 Aristada Initio (for loading) 675 mg x 1 \$1,869.56	Schizophrenia: 441 mg IM (gluteal or deltoid), 662 mg (gluteal), or 882 mg (gluteal) once monthly; 882 mg (gluteal) once every 6 weeks; or 1,064 mg every 2 months (gluteal). Continue corresponding oral aripiprazole dose for 21 days after first dose, then stop. Alternatively, load with <i>Aristada Initio</i> 675 mg IM plus oral aripiprazole 30 mg x 1. Can start <i>Aristada</i> on same day or up to 10 days later. Missed dose: If >6 to ≤7 weeks (441 mg), >8 to ≤12 weeks (662 mg and 882 mg), or >10 to ≤12 weeks (1,064 mg) since last dose, restart oral aripiprazole x 7 days with next dose, or give with <i>Aristada Initio</i> x1. If >7 weeks (441 mg) or >12 weeks (662 mg, 882 mg, and 1,064 mg) since last dose, restart oral aripiprazole x 21 days with next dose, or give with <i>Aristada Initio</i> 675 mg x 1 plus oral aripiprazole 30 mg x 1.	Low	Low	Low	Yes See footnotes e and h.	CYP2D6, CYP3A4 Specific dosing may be advised for CYP450 interactions.	Low

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Generic (Brand)/ Cost ^b	FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day) ^{*.a}	Metabolic Adverse Effects ^{c#.1,2,4,7,10-13,16}			QT Prolonging ^e	CYP450 Metabolism ^g	Sedation ^{h,8,13}
		Weight Gain	Diabetes Risk	Dyslipidemia			
Asenapine (Saphris) 10 mg sublingual tablet \$1,200.81	Schizophrenia: 10 mg (acute), 10-20 mg (after one week) Bipolar I disorder (manic or mixed episodes): 10-20 mg (monotherapy or with lithium or valproate) • For sublingual use. Avoid food/drink for 10 min afterward.	Low to moderate	Low	Low	Yes See footnote d.	CYP1A2, CYP3A4 (minor), CYP2D6 (minor) (Weak CYP2D6 inhibitor.) Specific dosing may be advised for CYP450 interactions.	Low to Moderate
Brexpiprazole (Rexulti) 2 mg tablet \$1,109.42	Schizophrenia: 2-4 mg Major depressive disorder (adjunct to antidepressants): 2 mg Reduce dose if CYP2D6 poor metabolizer.	Moderate	Low to moderate	Low to moderate	No	CYP2D6, CYP3A4 Specific dosing may be advised for CYP450 interactions.	Low
Cariprazine (Vraylar) 3 mg capsule \$1,200.81	Schizophrenia: 1.5-6 mg Bipolar I disorder (manic or mixed episodes): 3-6 mg	Low	Low	Low	No	CYP2D6, CYP3A4 Specific dosing may be advised for CYP450 interactions. Avoid with CYP3A4 inducers.	Low to moderate

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Generic (Brand)/ Cost ^b	FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day) ^{*.a}	Metabolic Adverse Effects ^{c#.1,2,4,7,10-13,16}			QT Prolonging ^e	CYP450 Metabolism ^g	Sedation ^{h,8,13}
		Weight Gain	Diabetes Risk	Dyslipidemia			
Clozapine ^f (<i>Clozaril</i> , etc, generics) 300 mg tablet ~\$190 Oral suspension and generic orally disintegrating tablet available.	Schizophrenia (treatment-resistant): 300-450 mg Reducing suicidal behavior in schizophrenia & schizoaffective disorder: 300-450 mg NOTE: initial dose is 12.5 mg once or twice daily (for both indications).	High	High	High	Yes See footnote h.	CYP1A2, CYP3A4, CYP2D6 Specific dosing may be advised for CYP450 interactions.	High
Haloperidone (<i>Fanapt</i>) 12 mg tablet \$1,341.06	Schizophrenia: 12-24 mg	Moderate	Low	Low	Yes See footnote g.	CYP3A4, CYP2D6 Specific dosing may be advised for CYP450 interactions.	Low
Lurasidone (<i>Latuda</i>) 40 mg tablet \$1,223.40	Schizophrenia: 40-160 mg Bipolar I depression (monotherapy or with lithium or valproate): 20-120 mg • Take with food (at least 350 kcal).	Low	Low	Low	No ¹² See footnote e.	Contraindicated with strong CYP3A4 inhibitors or inducers. Specific dose decrease may be advised with moderate inhibitors.	Low to Moderate

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Generic (Brand)/ Cost ^b	FDA-Approved Indication(s) for ADULTS and Usual or Target Adult Daily Dosage Range (mg/day) ^{*.a}	Metabolic Adverse Effects ^{c*.1,2,4,7,10-13,16}			QT Prolonging ^e	CYP450 Metabolism ^g	Sedation ^{h,8,13}
		Weight Gain	Diabetes Risk	Dyslipidemia			
Olanzapine (Zyprexa, generics) 10 mg tablet <\$30 Injection: \$43.92/10 mg Generic orally disintegrating tablet available.	Schizophrenia: 10 mg Bipolar I disorder (manic or mixed episodes and maintenance): 5-20 mg (monotherapy or with lithium or valproate) Bipolar depression, with fluoxetine: 5-12.5 mg Depression (treatment-resistant), with fluoxetine: 5-20 mg Injection: <i>Zyprexa IntraMuscular</i> , agitation associated with psychosis or bipolar I mania: 10 mg (lower dose [5 mg, 7.5 mg] may be given). May repeat dose in two hours. A third dose may be given no sooner than four hours after the second dose.	High	High	High	Yes See footnotes e and h.	CYP1A2, CYP2D6	Moderate
Olanzapine pamoate (Zyprexa Relprevv long-acting injection) 300 mg \$842.40	Schizophrenia: Establish tolerability and target dose with oral olanzapine first. Patients can be switched directly to <i>Zyprexa Relprevv</i> with or without tapering. ¹⁷ <i>Zyprexa Relprevv</i> is initiated with an 8-week loading regimen, and is dosed every 2 or 4 weeks IM (gluteal). Available only through a restricted distribution program requiring prescriber, facility, patient, and pharmacy enrollment. Missed dose: see footnote i.	High	High	High	Yes See footnotes e and h.	CYP1A2, CYP2D6	Moderate Rare risk of post-injection delirium/sedation syndrome. Monitor for at least 3 hours post-dose.

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