MHC Toolbox: Antipsychotics

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The newer second generation antipsychotics (see table 1 on the next page) serves as a quick reference that reviews indications, dosing, adverse effects, drug interactions and administration requirements for the newer antipsychotics, as well as highlights important pharmacokinetic and pharmacodynamic properties of these agents.

REFERENCES:

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Table 1. Newer Second Generation Antipsychotics

Brand (generic)	FDA-Approved Indication(s)	Recommended Dosing	Receptor Binding Affinity	Pharmacokinetics	Side Effects	Drug Interactions	Administration	Special Considerations/Warnings	Cost[4,5]
Fanapt[1] (iloperidone)	Acute treatment of schizophrenia	Target Dose: 6-12 mg BID Titration Schedule: Day 1: 1 mg BID Day 2: 2 mg BID Day 3: 4 mg BID Day 4: 6 mg BID Day 5: 8 mg BID Day 6: 10 mg BID Day 7: 12 mg BID	High: $5\text{-}HT_{2A}>D_2>D_3$ Moderate: $D_4>5\text{-}HT_7>5\text{-}HT_6>\alpha_1$ Low: $5\text{-}HT_{1A}>D_1>H_1$	Absorption: Peak 2-4 hrs Distribution: ~95% protein bound Metabolism: CYP 2D6 and 3A4, two active metabolites Half-life: CYP2D6 extensive metabolizers- 18 hrs CYP2D6 poor metabolizers- 33 hrs Elimination: Mostly urine	Common§: dizziness, dry mouth, fatigue nasal congestion, orthostatic hypotension, somnolence, tachycardia Metabolic Profile: ≥7% increase in body weight: 13% FPG: Not reported TC:-8.8 to-26.5 mg/dL TG: + 3.9 mg/dL at doses of 20-24 mg/day	Strong 2D6 inhibitors: Must ↓ iloperidone dose by 50% Strong 3A4 inhibitors: Must ↓ iloperidone dose by 50%	Without regard to food	Must titrate slowly to avoid orthostasis If miss > 3 days, need to follow initiation titration schedule due to risk of orthostasis Iloperidone shown to prolong QT interval by 9 msec-avoid in combination with other QT prolonging agents	6 mg or 12 mg # 60 = $630.08
Saphris[2] (asenapine)	Acute treatments of schizophrenia Acute treatment (monotherapy or adjunct) of Bipolar I Disorder manic/mixed episodes	Acute treatment of schizophrenia, starting and target dose: 5 mg SL BID Schizophrenia maintenance: 5 mg SL BID for 1 week then 10 mg SL BID Bipolar mania monotherapy- acute treatment: 10 mg SL BID; mtn: 5-10 mg SL BID Bipolar mania adjunct to Lithium or Divalproex: starting 5 mg SL BID; dose range: 5-10 mg SL BID	High: 5-HT>D>α adrenergic>H_1 Moderate: H_2 No affinity: M	Absoprtion: Peak 0.5-1.5 hrs Distribution: ~ 95% protein bound Metabolism: glucuronidation, CYP 1A2 Half-life: 24 hrs Elimination: 50% urine, 40% feces	Common§: Akathisia, oral hypoesthesia, somnolence, dizziness, EPS, weight gain Metabolic Profile: ≥ 7% increase in body weight:4.9-5.8% FPG- not significant TC: + 0.4-1.1 mg/dL TG: -3.5 to 3.8 mg/dL	CYP1A2 inhibitors yield ~30% ↑ in asenapine concentration CYP1A2 inducers yield ~20% ↓ in asenapine concentration	Must dissolve under tongue and cannot eat or drink for 10 minutes	Bioavailability <2% if tablet swallowed Asenapine is a weak 2D6 inhibitor	5 mg: # 60 = $676.02 10 mg: # 60 = $665.99

Brand (generic)	FDA-Approved Indication(s)	Recommended Dosing	Receptor Binding Affinity	Pharmacokinetics	Side Effects	Drug Interactions	Administration	Special Considerations/Warnings	Cost[4,5]
Latuda[3] (lurasidone)	Treatment of schizophrenia	Initiation: 40 mg/day Max: 80 mg/day	High: D_2>$5HT_{2A}$>$5HT_7$ Moderate: α_{2C}>α_{2A} Minimal: H_1 and M_1 Partial Agonist: $5HT_{1A}$	Absorption: Peak 1-3hr Distribution: ~99% protein bound Metabolism: CYP 3A4, 2 active and 2 non-active metabolites Half-life: 18 hours Elimination: 89% feces, 9% urine	Common[§]: somnolence, akathisia, nausea, parkinsonism, agitation Metabolic Profile: ≥ 7% increase in body weight: 5.6% FPG: -0.9 to 2.5 mg/dL TC: -9.4 to -9.8 mg/dL TG:-6.2 to -14.2 mg/dL Hyperprolactinemia (>5x UNL): 3.6%	Lurasidone is contraindicated with strong CYP3A4 inhibitors and inducers Diltiazem (moderate 3A4 inhibitor): Lurasidone should not exceed 40 mg/day	Must take with food (≥ 350 calories)	Food triples Cmax and doubles AUC	80 mg: # 30= $523.24

[§]: incidence > 5% and 2-fold greater than placebo