

- **Iloperidone (Fanapt)**

- FDA-approval for schizophrenia in adults, 2009
- Structurally similar to Risperdal
- Pharmacokinetics
 - can be taken with or without food
 - peak in 2-4 hours (goes down to 90 minutes over time)
 - half life is 18 hours (and 23-26 hours for metabolites); in slow metabolizers it's 33 hours and 31-37 hours for metabolites
 - Comes in 1, 2, 4, 6, 8, 10, and 12 mg tabs
 - twice-daily dosing, at least at first; to minimize orthostatic hypotension:
 - start at 1 mg twice-a-day
 - increase no more than 4 mg each day to get to 6 mg twice-a-day
 - 12-24 mg/day, twice-daily with the possibility of once daily over time
 - 3A4/2D6 metabolism
 - Metabolites: P88 (crosses BBB) and P95 (doesn't)
- MUST get pre- and post med ECG (affects K⁺ channels and ECG rhythm.
- Pharmacodynamics; blocks, in decreasing order of magnitude
 - **NE alpha 1 (0.36) and alpha 2c block**
 - **5HT_{2a} (5.6) block**
 - **D₂ (6.3) block**
 - **D₃ (7.1) block**
 - **5HT₇ (22)**
 - **D₄ (25)**
 - **5HT₆ (43)**
 - **5HT_{1a} (168) block**
 - D₁ (216)
 - H₁ (473)
 - Muscarinic (>1000)
 - Potent blocker of hERG voltage gated, delayed, inwardly directed K⁺ rectifying channel, and, as such, may be associated with QTc prolongation and cardiac arrhythmias
- Common side effects:

▪ Dizziness:	7% placebo, 10% at 10-16 mg/day, 20% at 20-24 mg/day
▪ Dry mouth:	1% placebo, 8% at 10-16 mg/day, 10% at 20-24 mg/day
▪ Fatigue/Somnolence/Lethargy:	6% placebo, 17% at 10-16 mg/day, 22% at 20-24 mg/day
▪ Nasal congestion:	2% placebo, 5% at 10-16 mg/day, 8% at 20-24 mg/day
▪ Orthostatic hypotension:	1% placebo, 3% at 10-16 mg/day, 5% at 20-24 mg/day
• Mostly in the first week	
▪ Tachycardia:	1% placebo, 3% at 10-16 mg/day, 12% at 20-24 mg/day
▪ Weight increase:	1% placebo, 1% at 10-16 mg/day, 9% at 20-24 mg/day
• 2-4.5 pounds	
▪ Muscle stiffness:	1% placebo, 1% at 10-16 mg/day, 3% at 20-24 mg/day
• basically no muscle side effects	
▪ Diarrhea:	4% placebo, 5% at 10-16 mg/day, 7% at 20-24 mg/day
▪ Abdominal discomfort:	1% placebo, 1% at 10-16 mg/day, 3% at 20-24 mg/day
▪ Tremor:	1.9% placebo, 2.5% at 10-16 mg/day, 3.1% at 20-24 mg/day
▪ Prolactin: increased slightly in 26% vs. 12% placebo	
▪ QTc: 9 ms; comparable to Geodon, Haldol; prolongation up to 19 msec if metabolic inhibition	
▪ Glucose: ~no effects	
▪ Lipid levels: ~no effects	
- Side effects in long term studies
 - Insomnia 18.1%

- Anxiety 10.8%
- Headache
- Weight gain
- Nausea/vomiting
- Dry mouth
- Stomach discomfort
- Glucose, lipids, prolactin did NOT increase over the study period
- Efficacy
 - Psychosis (increasing efficacy through 24 mg/day)
 - Schizophrenia
 - Short term
 - Four randomized, placebo controlled studies (Potkin et al (for three); Cutler et al)
 - Efficacy at doses of 110-24 mg/day
 - Long term/relapse prevention
 - 52-week double blind study Fanapt vs. Haldol
 - Relapse rates
 - 43.5% for Fanapt
 - 41.2% for Haldol