CARIPRAZINE (Vraylar) Fact Sheet

Bottom Line:
Cariprazine, like aripiprazole and brexpiprazole, is a partial dopamine agonist. Some preliminary data imply that it might be effective for negative symptoms, but it's too soon to tell. Beyond that, it appears similar to the other two partial dopamine agonists with regard to akathisia and minimal weight gain. It is available as a brand name only and is therefore very expensive (as opposed to aripiprazole, which has gone generic).

FDA Indications:
Schizophrenia; acute treatment of **bipolar disorder** (manic or mixed episodes); bipolar I depression; depression adjunct.

Off-Label Uses:
Negative symptoms of schizophrenia.

Dosage Forms:
Capsules: 1.5 mg, 3 mg, 4.5 mg, 6 mg.

Dosage Guidance:
- Schizophrenia and bipolar disorder: Start 1.5 mg/day, may ↑ to 3 mg/day as early as second day. Adjust by 1.5–3 mg/day increments to usual dose 1.5–6 mg/day in schizophrenia and 3–6 mg/day in bipolar disorder.
- Bipolar depression: Start 1.5 mg QD, may ↑ to 3 mg QD after two weeks or longer; max dose 3 mg/day.
- Dose timing: Either morning or night; many patients experience restlessness that can interfere with sleep, in which case morning is preferred.

Monitoring: Fasting glucose, lipids.

Cost: $$$$$

Side Effects:
- Most common: EPS, akathisia, weight gain, sedation.
- Serious but rare: See class warnings in chapter introduction.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Dopamine D2 and D3 and serotonin 5-HT1A receptor partial agonist; serotonin 5-HT2A receptor antagonist.
- Metabolized primarily by CYP3A4; t ½: 2–4 days for cariprazine (1–3 weeks for active metabolites).
- Caution with CYP3A4 inhibitors; 50% dose reduction may be necessary. Avoid use with 3A4 inducers.

Clinical Pearls:
- Most closely similar to aripiprazole with partial D2 agonism.
- Manufacturer and very early data suggest D3 activity may result in negative symptom improvement.
- While cariprazine showed enough efficacy to gain an indication for bipolar depression, this was only true in patients with bipolar type I. In trials with bipolar II patients, it was no better than placebo.
- Very long half-life may make this a good choice in patients with partial or irregular medication adherence.

Fun Fact:
Cariprazine was developed by a Hungarian pharmaceutical company, Gedeon Richter, which was founded in 1901 by a pharmacist. Gedeon Richter initially processed extracts from plants to produce herbal drugs.