Cariprazine (Vraylar®)
FDA approved September 2015

Indication
Cariprazine is an atypical antipsychotic indicated for the
- Treatment of schizophrenia
- Acute treatment of manic or mixed episodes associated with bipolar I disorder

Mechanism
Serotonin-dopamine activity modulator
- acts as a partial agonist (high affinity) for serotonin 5-HT_{1A} and dopamine D_2 & D_3 receptors
- acts as an antagonist at serotonin 5-HT_{2B} (high affinity) and 5-HT_{2A} receptors (moderate affinity)
- also binds to histamine H_1 receptors

Dosage and administration

	Starting Dose	Recommended Dose	Maximum Dose
Bipolar I	1.5 mg Qday	3 to 6 mg Qday	6 mg daily
Schizophrenia	1.5 mg Qday	1.5 to 6 mg Qday	6 mg daily

- dose adjustment needed in concomitant use with CYP3A4 inhibitor
- concomitant use with CYP3A4 *inducer* is not recommended
- use not recommended (not studied) in renal impairment (CrCl <30 mL/min) or severe hepatic impairment (Child-Pugh class C)
- administer once daily with or without food
- due to long half-life, dose adjustments will not be fully reflected for several weeks
- Formulation: 1.5mg, 3mg, 4.5mg, and 6mg capsules. Also available in mixed blister pack (one 1.5 mg, six 3 mg)

Pharmacokinetics

Protein binding	91% - 97%
Tmax	Cariprazine: 3 to 6 hours
Metabolism	Hepatic extensively by CYP3A4 & to a lesser extent by CYP2D6 2 major active metabolites, desmethyl cariprazine (DCAR) & didesmethyl cariprazine (DDCAR), which are pharmacologically equipotent to cariprazine
Steady-state	Mean cariprazine & DCAR: week 1 to 2, mean DDCAR: week 4 to 8
Half-life	Cariprazine: 2 to 4 days, DDCAR: 1 to 3 weeks equipotent to cariprazine
Elimination	Urine 21%

Adverse Reactions: Most common (≥5% & at least twice the rate for placebo)
- Bipolar mania: extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, and restlessness
- Schizophrenia: extrapyramidal symptoms & akathisia

Warnings and Precautions
- Black box warning regarding increased mortality in elderly patients with dementia-related psychosis as other atypical antipsychotics

References available upon request

- Monitor for adverse reactions and response for several weeks after starting Vraylar due to long half life
- Cerebrovascular adverse reactions in elderly patients with Dementia-Related Psychosis
- Neuroleptic Malignant Syndrome
- Tardive dyskinesia
- Metabolic changes
- Leukopenia, neutropenia & agranulocytosis
- Orthostatic hypotension and syncope, seizures
- Potential for cognitive and motor impairment, body temperature dysregulation, dysphagia

Use in specific populations

- Pregnancy: May cause extrapyramidal &/or withdrawal symptoms in neonates with 3rd trimester exposure
- Safety and efficacy have not been established in pediatric patients

Formulary status: PA required

Please contact BHRS Pharmacy Services for additional information

References available upon request