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-HT1A and dopamine D2 & D3 receptors
- acts as an antagonist at serotonin 5-HT2B (high affinity) and 5-HT2A receptors (moderate affinity)
- also binds to histamine H1 receptors

**Dosage and administration**

<table>
<thead>
<tr>
<th></th>
<th>Starting Dose</th>
<th>Recommended Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bipolar I</strong></td>
<td>1.5 mg Qday</td>
<td>3 to 6 mg Qday</td>
<td>6 mg daily</td>
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<tr>
<td><strong>Schizophrenia</strong></td>
<td>1.5 mg Qday</td>
<td>1.5 to 6 mg Qday</td>
<td>6 mg daily</td>
</tr>
</tbody>
</table>

- 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**

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

**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