VRAYLAR® (cariprazine) capsules, for oral use
Medicaid Clinical Summary

Schizophrenia and bipolar disorder are serious mental health disorders that are among the leading causes of disability worldwide, particularly in young adults.[1,2] Approximately 50% of patients with bipolar disorder work below qualifications, part-time, in a limited capacity, or are unable to work.[3] Patients with schizophrenia and bipolar disorder are many-fold more likely to die by suicide than the general population.[4,5]

INDICATIONS AND USAGE[6]

Vraylar (cariprazine) is an atypical antipsychotic indicated for: (1) Treatment of schizophrenia in adults, (2) Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults, (3) Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults.

DOSAGE AND ADMINISTRATION[6]

Indication	Starting Dose	Recommended Dose	Maximum Recommended Dosage
Schizophrenia	1.5 mg daily	1.5 mg to 6 mg daily	6 mg once daily Dosages above 6 mg daily do not confer significant benefit but increase the risk of dose-related adverse reactions
Bipolar Mania	1.5 mg daily	3 mg to 6 mg daily	
Bipolar Depression	1.5 mg daily	1.5 mg or 3 mg daily	3 mg once daily

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS; and SUICIDAL THOUGHTS AND BEHAVIORS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. VRAYLAR is not approved for the treatment of patients with dementia-related psychosis.

Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and for the emergence of suicidal thoughts and behaviors. The safety and effectiveness of VRAYLAR have not been established in pediatric patients.

CONTRAINDICATIONS[6]

Vraylar is contraindicated in patients with known hypersensitivity. Reactions have included rash, pruritus, urticaria, and events suggestive of angioedema.

ADVERSE EVENTS[6]

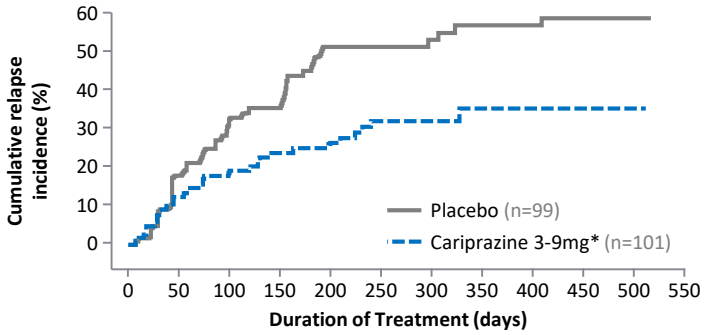
The most common adverse reactions (≥ 5% and at least twice the rate of placebo): Schizophrenia: extrapyramidal symptoms (EPS) and akathisia. Bipolar mania: EPS, akathisia, vomiting, dyspepsia, somnolence, and restlessness. Bipolar depression: nausea, akathisia, restlessness, and EPS.

VRAYLAR CLINICAL PROGRAM[6]

Schizophrenia

- The efficacy of Vraylar for the treatment of schizophrenia was established in three, 6-week, randomized, double-blind, placebo-controlled trials in which Vraylar was superior to placebo on the primary outcome, the change from baseline to endpoint in PANSS (Positive and Negative Syndrome Scale) total score.
- The safety and efficacy of Vraylar as maintenance treatment in adults with schizophrenia were demonstrated in a randomized withdrawal trial that included patients who were clinically stable following 20 weeks of open-label Vraylar. Patients were randomized to receive either placebo or Vraylar at the same dose for up to 72 weeks for observation of relapse. Time to relapse was statistically significantly longer in the Vraylar-treated group compared to the placebo group.

Kaplan-Meier Curves of Cumulative Rate of Relapse During the Double-Blind Treatment Period



*The maximum recommended daily dose is 6 mg. Doses above 6 mg daily do not confer increased effectiveness sufficient to outweigh dose-related adverse reactions.

Bipolar Mania

- The efficacy of Vraylar in the acute treatment of bipolar mania was established in three, 3-week placebo-controlled trials in which Vraylar was statistically superior to placebo in the change from baseline to endpoint on the primary outcome, Young Mania Rating Scale (YMRS) total score.

Bipolar Depression

- The efficacy of Vraylar in the acute treatment of bipolar depression was established in one 8-week and two 6-week placebo-controlled trials in which Vraylar 1.5 mg was statistically superior to placebo in the change from baseline to endpoint on the primary outcome, Montgomery-Asberg Depression Rating Scale (MADRS) total score at the end of Week 6 for all three studies and Vraylar 3 mg was statistically superior to placebo in one 6-week trial.

WARNINGS AND PRECAUTIONS[6]

- Increased Mortality in Elderly Patients with Dementia-Related Psychosis
- Suicidal Thoughts and Behaviors in Children, Adolescents and Young Adults
- Cerebrovascular Adverse Reactions, Including Stroke, in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)
- Neuroleptic Malignant Syndrome (NMS): Manage with immediate discontinuation and close monitoring
- Tardive Dyskinesia: Discontinue if appropriate
- Late-Occurring Adverse Reactions: Because of VRAYLAR's long halflife, monitor for adverse reactions and patient response for several weeks after starting VRAYLAR and with each dosage change
- Metabolic Changes: Monitor for hyperglycemia/diabetes mellitus, dyslipidemia and weight gain
- Leukopenia, Neutropenia, and Agranulocytosis: Perform complete blood counts (CBC) in patients with pre-existing low white blood cell counts (WBC) or history of leukopenia or neutropenia. Consider discontinuing VRAYLAR if a clinically significant decline in WBC occurs in absence of other causative factor
- Orthostatic Hypotension and Syncope: Monitor heart rate and blood pressure and warn patients with known cardiovascular or cerebrovascular disease, and risk of dehydration or syncope
- Falls: Complete fall risk assessments in appropriate patients
- Seizures: Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold
- Potential for Cognitive and Motor Impairment: Use caution when operating machinery
- Body Temperature Dysregulation: May disrupt the body's ability to reduce core body temperature
- Dysphagia: Use cautiously in patients at risk for aspiration

Please contact your Medical Outcomes Science Liaison with any questions. For full prescribing information, visit www.rxabbvie.com.

REFERENCES

1. Vos T et al. Lancet. 2016;388:1545-1602.
2. Gore FM et al. Lancet. 2011;377:2093-2102.
3. Suppes T et al. J Affect Disord. 2001;67:45-59.
4. Palmer BA et al. Arch Gen Psychiatry. 2005;62:247-253.
5. Shastry BS. Neurochem Int. 2005;46:273-279.
6. VRAYLAR® [prescribing information]. Madison, NJ: Allergan USA, Inc.; May 2019.