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

INDICATIONS AND USAGE
VRAYLAR (cariprazine) is indicated for the
- Treatment of schizophrenia in adults
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults
- Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults
- Adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adults

DOSAGE AND ADMINISTRATION
Administer VRAYLAR (cariprazine) once daily with or without food.

Indication	Starting Dose	Recommended Dose
Schizophrenia	1.5 mg daily	1.5 mg to 6 mg daily
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
Adjunctive therapy to antidepressants for MDD	1.5 mg daily	1.5 mg or 3 mg daily

- Schizophrenia and Bipolar Mania: Dosages above 6 mg daily do not confer significant benefit but increase the risk of dose-related adverse reactions
- Bipolar Depression: The maximum recommended daily dosage is 3 mg
- aMDD: The maximum recommended daily dosage is 3 mg

IMPORTANT SAFETY CONSIDERATIONS AND BOXED WARNING

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 (cariprazine) 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. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. Safety and effectiveness of VRAYLAR (cariprazine) have not been established in pediatric patients**

Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)

Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)

Neuroleptic Malignant Syndrome: Manage with immediate discontinuation and close monitoring

Tardive Dyskinesia: Discontinue if appropriate

Late-Occurring Adverse Reactions: Because of cariprazine's long half-life, monitor for adverse reactions and patient response for several weeks after starting VRAYLAR (cariprazine) 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 (cariprazine) if a clinically significant decline in WBC occurs in absence of other causative factors

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

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

Most common adverse reactions (incidence ≥ 5% and at least twice the rate of placebo) were

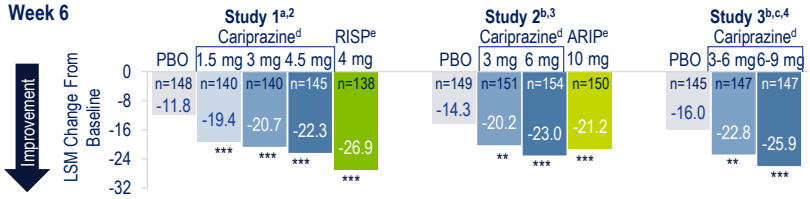
- **Schizophrenia:** extrapyramidal symptoms and akathisia
- **Bipolar mania:** extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, and restlessness
- **Bipolar depression:** nausea, akathisia, restlessness, and extrapyramidal symptoms
- **Adjunctive Treatment of MDD:** akathisia, restlessness, fatigue, constipation, nausea, insomnia, increased appetite, dizziness, and extrapyramidal symptoms

Review accompanying cariprazine full Prescribing Information for additional information or visit www.rxabbvie.com or contact AbbVie Medical Information at www.abbviemedinfo.com or 1-800-633-9110.

VRAYLAR (CARIPRAZINE) CLINICAL PROGRAM

SCHIZOPHRENIA
The efficacy and safety of cariprazine for the treatment of schizophrenia was established in three, 6-week, randomized, double-blind, placebo-controlled trials in which carprazine was superior to placebo on the primary outcome, the change from baseline to endpoint in PANSS (Positive and Negative Syndrome Scale) total score.

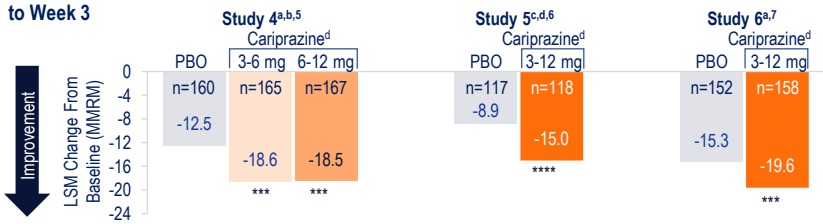
Primary Efficacy Endpoint in Schizophrenia Studies: PANSS Total Score Change from Baseline to Week 6



**P≤.01, ***P ≤.001, statistically significant versus placebo. [a]LOCF analysis. [b]MMRM analysis. [c]Adjusted p-values given. [d]Maximum recommended dosage is 6 mg daily. Dosages above 6 mg daily do not confer increased effectiveness to outweigh dose-related adverse reactions. All doses given once daily. [e]Risperidone and aripiprazole were used as active controls to determine assay sensitivity; further, these trials were not powered to directly compare efficacy between Vraylar (cariprazine) and the active controls. ARIP, aripiprazole; LOCF, last observation carried forward; LSM, least squares mean; MMRM, mixed-effects model for repeated measures; PANSS, Positive and Negative Syndrome Scale; PBO, placebo; RISP, risperidone.

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

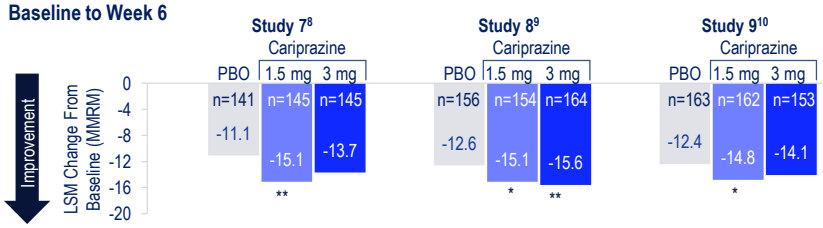
Primary Efficacy Endpoint in Bipolar I Mania Studies: YMRS Total Score Change from Baseline to Week 3



***P<.001, ****P<.0001, statistically significant versus placebo. [a]MMRM analysis. [b]Adjusted for multiple comparisons. [c]LOCF analysis. [d]The maximum recommended dose is 6 mg. Doses above 6 mg daily do not confer increased effectiveness sufficient to outweigh dose-related adverse reactions. All doses given once daily. LOCF, last observation carried forward; LSM, least squares mean; MMRM, mixed-effects model for repeated measures; PBO, placebo; YMRS, Young Mania Rating Scale.

BIPOLAR DEPRESSION
The efficacy and safety of cariprazine in the acute treatment of bipolar depression was established in one 8-week and two 6-week placebo-controlled trials in which cariprazine 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 cariprazine 3 mg was statistically superior to placebo in one 6-week trial.

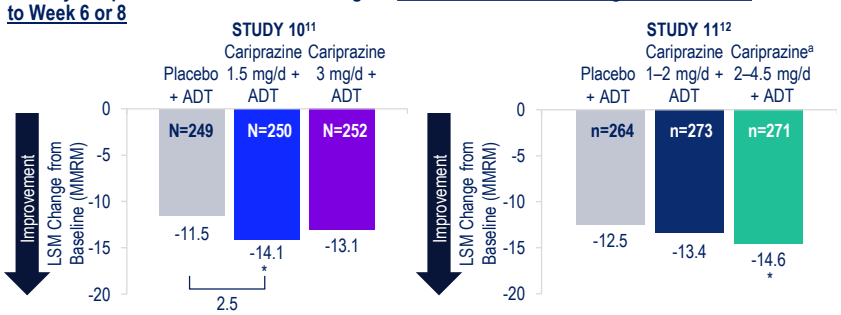
Primary Efficacy Endpoint in Bipolar I Depression Studies: MADRS Total Score Change from Baseline to Week 6



*P<.05, **P≤.01, ***P<.001 (adjusted p-values via MMRM analysis), statistically significant versus placebo. LSM, least squares mean; MADRS, Montgomery-Åsberg Depression Rating Scale; MMRM, mixed-effects model for repeated measures; PBO, placebo.

ADJUNCTIVE TREATMENT OF MAJOR DEPRESSIVE DISORDER
The efficacy of cariprazine as adjunctive therapy to antidepressants for the treatment of MDD was evaluated in 2 trials in adult patients with MDD, with or without symptoms of anxiety, who had an inadequate response to 1 to 3 courses of prior antidepressant (ADT) therapy. In each study, the primary endpoint was change from baseline to Week 6 or Week 8 in the Montgomery-Asberg Depression Rating Scale (MADRS) total score. In a 6-week, placebo-controlled trial involving two fixed doses of cariprazine (1.5 mg/day or 3 mg/day) + ADT, cariprazine 1.5 mg + ADT was superior to placebo + ADT at end of Week 6 on the MADRS total score. In an 8-week, placebo-controlled trial involving flexible doses of cariprazine (1-2 mg/day or 2-4.5 mg/day + ADT), cariprazine 2-4.5 mg + ADT was superior to placebo + ADT at end of Week 8 on the MADRS total score.

Primary Endpoint in aMDD Studies: Change in MADRS Total Score Change from Baseline to Week 6 or 8



*P<.05, ADT, antidepressant therapy. LSM, least squares means. MADRS, Montgomery-Åsberg Depression Rating Scale. MMRM, Mixed-Effects Model for Repeated Measures.

a. Study 11: Cariprazine 2–4.5 mg/d mean dose dose = 2.6 mg.

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References

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12. Sachs et al. Cariprazine for the Adjunctive Treatment of Major Depressive Disorder: Results from a Randomized Phase 3 Placebo-Controlled Study. Poster presented at APA 2022. New Orleans, LA.