Dosing Guide

Caripraxine is an atypical antipsychotic indicated for:

- Treatment of schizophrenia in adult and pediatric patients 13 years of age and older
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adult and pediatric patients 13 years of age and older
- Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adult patients
- Adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adult patients

The US Food and Drug Administration (FDA) approval for the pediatric indications is supported by evidence from adequate and well-controlled studies in adults with manic and mixed episodes associated with bipolar I disorder or schizophrenia, pharmacokinetic data from adults and pediatric patients, and safety data in pediatric patients.

IMPORTANT SAFETY INFORMATION

Black Box Warnings

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

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

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

Suicidal Thoughts and Behaviors

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.

See below for additional Important Safety information.

Pharmacokinetics

Pharmacokinetics of caripraxine and its active metabolites, desmethyl-caripraxine (DCAR) and didesmethyl-caripraxine (DDCAR), were evaluated in pediatric patients (10–17 years) who received doses of caripraxine ranging from 0.5 mg to 6 mg.

Population pharmacokinetic results showed the following dose-adjusted steady state systemic exposures (maximum concentration (C_{max}) and area under the curve (AUC)) of total caripraxine compared with adult patients receiving the same dose:

- Pediatric patients 10 to 12 years of age had up to a 32% and 33% higher, respectively.
- Pediatric patients 13 to 17 years of age had up to a 10% and 11% higher, respectively.

Pediatric Safety

Safety was assessed in a long-term, open-label study in pediatric patients (N=164) with schizophrenia or bipolar I disorder, of whom 72 received caripraxine for at least 6 months. Adverse reactions reported in clinical studies for this age group were generally similar to those observed in adult patients.

	Schizophrenia (13–17 Years)	Bipolar I Disorder (10–17 Years)
Dyslipidemia		
TC shift,[a] % (n/N)	0	1.2% (1/81)
HDL-C shift,[b] % (n/N)	9.1% (1/11)	10.6% (10/94)
TG (fasting) shift,[c] % (n/N)	25% (2/8)	20% (12/60)
Hyperglycemia		
Serum glucose (fasting) shift,[d] % (n/N)	0	4.6% (4/87)
Weight gain		
Mean change in body weight,[e] kg	+2.4	+3.1
Mean change in body score[e]	+0.1 SD	+0.2 SD
Proportion of patients with an increase in body weight z-score ≥ 0.5 SD[e,f]	0%	14.6%

[a]Normal baseline (<170 mg/dL) to high (≥200 mg/dL)
[b]Normal baseline (>45 mg/dL) to low (<40 mg/dL)
Normal baseline (<90 mg/dL; fasting) to high (>130 mg/dL)
[c]Normal baseline (<150 mg/dL; fasting) to high (≥500 mg/dL)
[d]From baseline to last evaluation
[e]To adjust for normal growth, z-scores were derived (measured in standard deviations [SD]) using the World Health Organization charts of children and adolescents by gender and height to age and gender-matched population standards.
[f]Z-score change <0.5 SD is considered not clinically significant

HDL-C, high-density lipoprotein cholesterol; SD, standard deviation; TC, total cholesterol; TG, triglycerides

Denominator of percentages is N=number of subjects meeting the baseline criteria, and with at least one non-missing postbaseline value during the open label treatment period.

The safety and effectiveness of caripraxine for the treatment of schizophrenia have not been established in pediatric patients <13 years of age.

The safety and effectiveness of caripraxine for the treatment of manic and mixed episodes associated with bipolar I disorder have not been established in pediatric patients <10 years of age.

General Dosing Information

Caripraxine is given orally once daily and can be taken with or without food.

Because of the long half-life of caripraxine and its active metabolites, changes in dose will not be fully reflected in plasma for several weeks. Prescribers should monitor patients for adverse reactions and treatment response for several weeks after starting caripraxine and after each dosage change.

Pediatric-Specific Dosing

PEDIATRIC INDICATIONS

	Schizophrenia (13–17 Years)	Manic or Mixed Episodes Associated With Bipolar I Disorder (10–17 Years)
Starting dose	1.5 mg daily	0.5 mg daily
Day 2 dose	Increase to 1.5 mg daily	Increase to 1.5 mg daily
Day 5 dose	May increase to 3 mg*	May increase to 3 mg*
Day 8 dose	May increase to 4.5 mg**	May increase to 4.5 mg**
Recommended dosage	1.5 mg to 4.5 mg daily	3 mg or 4.5 mg daily

*Based on clinical response/tolerability
**Maximum recommended daily dose

Adult Dosing

ADULT INDICATIONS

	Schizophrenia	Manic or Mixed Episodes Associated With Bipolar I Disorder	Depressive Episodes Associated With Bipolar I Disorder	Adjunctive Therapy to Antidepressants for MDD
Starting dose	1.5 mg daily	1.5 mg daily	1.5 mg daily	1.5 mg daily
Day 2 dose	Can be increased to 3 mg daily	Increase to 3 mg daily	NA	NA
Dosing adjustments	1.5 mg or 3 mg incremental[a]	1.5 mg or 3 mg incremental[a]	Can increase to 3 mg starting on Day 15[b]	Can increase to 3 mg starting on Day 15[b]
Recommended dosage	1.5 mg to 6 mg daily[c]	3 mg to 6 mg daily[c]	1.5 mg or 3 mg daily	1.5 mg or 3 mg daily
Maximum recommended dosage	6 mg daily	6 mg daily	3 mg daily	3 mg daily

MDD, major depressive disorder.
[a]Depending upon clinical response and tolerability.
[b]In clinical trials, dosage titration at intervals <14 days resulted in a higher incidence of adverse reactions.
[c]In short-term controlled trials, dosages >6 mg daily did not confer increased effectiveness sufficient to outweigh dose-related adverse reactions.

Dosage Modifications for CYP3A4 Inhibitors

Dosage Modifications for the Starting Dosage of Caripraxine in Adult Patients Taking a Strong or Moderate CYP3A4 Inhibitor

Condition	When Taking a Strong CYP3A4 Inhibitor	When Taking a Moderate CYP3A4 Inhibitor
Schizophrenia	**Start at 0.5 mg daily;** increase to 0.75 mg daily, if needed*	**Start at 0.75 mg daily;** increase to 1.5 mg daily, if needed*
Manic or Mixed Episodes Associated With Bipolar I Disorder	**Start at 0.5 mg daily;** increase to 0.75 mg daily, if needed*	**Start at 0.75 mg daily;** increase to 1.5 mg daily, if needed*
Depressive Episodes Associated With Bipolar I Disorder	0.5 mg daily	0.75 mg daily
Adjunctive Therapy for Treatment of MDD	0.5 mg daily	0.75 mg daily

MDD, major depressive disorder.
*Depending upon clinical response and tolerability.

Initiating caripraxine is not recommended in pediatric patients while taking a strong CYP3A4 inhibitor.

Dosage Modifications for Caripraxine When Initiating a Strong or Moderate CYP3A4 Inhibitor and While Taking a Stable Dosage of Caripraxine in Adult and Pediatric Patients

Currently on Caripraxine Dosage	Caripraxine Dosage When Initiating a Strong CYP3A4 Inhibitor	Caripraxine Dosage When Initiating a Moderate CYP3A4 Inhibitor
1.5 mg or 3 mg daily	0.5 mg daily	0.75 mg daily
4.5 mg or 6 mg daily	0.75 mg daily	1.5 mg daily

When the strong or moderate CYP3A4 inhibitor is discontinued, the caripraxine dosage may need to be increased based on clinical response and tolerability.

DOSAGE MODIFICATIONS FOR PATIENTS CONCOMITANTLY TAKING CARIPRAXINE WITH CYP3A4 INDUCERS

Concomitant use of caripraxine and a CYP3A4 inducer has not been evaluated and is not recommended.

Important Safety Information

WARNINGS: 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. Caripraxine is not approved for 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 antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors.**

Contraindication: Caripraxine is contraindicated in patients with known hypersensitivity. Reactions have included rash, pruritus, urticaria, and reactions suggestive of angioedema.

Cerebrovascular Adverse Reactions, Including Stroke: In clinical trials with antipsychotic drugs, elderly patients with dementia had a higher incidence of cerebrovascular adverse reactions, including fatalities, vs. placebo. Caripraxine is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported with antipsychotic drugs. NMS may cause hyperpyrexia, muscle rigidity, delirium, and autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Manage with immediate discontinuation, intensive symptomatic treatment, and monitoring.

Tardive Dyskinesia (TD): Risk of developing TD (a syndrome of potentially irreversible, involuntary, dyskinetic movements) and the likelihood it will become irreversible may increase with the duration of treatment and the cumulative dose. The syndrome can develop after a relatively brief treatment period, even at low doses, or after treatment discontinuation. If signs and symptoms of TD appear, drug discontinuation should be considered.

Late-Occurring Adverse Reactions: Adverse reactions may first appear several weeks after initiation of caripraxine, possibly because plasma levels of caripraxine and its major metabolites accumulate over time. As a result, the incidence of adverse reactions in short-term trials may not reflect the rate after chronic long-term exposures. Monitor for adverse reactions, including extrapyramidal symptoms (EPS) or akathisia, and patient response for several weeks after starting caripraxine and after each dosage increase. Consider reducing the dose or discontinuing the drug.

Metabolic Changes: Atypical antipsychotics, including caripraxine, have caused metabolic changes, such as:

- **Hyperglycemia and Diabetes Mellitus:** Hyperglycemia, in some cases associated with ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics. Assess fasting glucose before or soon after initiation of treatment, and monitor periodically during long-term therapy.
- **Dyslipidemia:** Atypical antipsychotics cause adverse alterations in lipids. Before or soon after starting an antipsychotic, obtain baseline fasting lipid profile and monitor periodically during treatment.
- **Weight Gain:** Weight gain has been observed with caripraxine. Monitor weight at baseline and frequently thereafter.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia/neutropenia have been reported with antipsychotics, including caripraxine. Agranulocytosis (including fatal cases) has been reported with other antipsychotics. Monitor complete blood count in patients with pre-existing low white blood cell count (WBC)/absolute neutrophil count or history of drug-induced leukopenia/neutropenia. Discontinue caripraxine at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

Orthostatic Hypotension and Syncope: Atypical antipsychotics cause orthostatic hypotension and syncope, with the greatest risk during initial titration and with dose increases. Monitor orthostatic vital signs in patients predisposed to hypotension and in those with cardiovascular/cerebrovascular disease.

Falls: Caripraxine may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls and, consequently, fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating antipsychotic treatment and repeat for patients on long-term therapy.

Seizures: Use caripraxine with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: Somnolence was reported with caripraxine. Caution patients about performing activities requiring mental alertness (eg, operating hazardous machinery or a motor vehicle).

Body Temperature Dysregulation: Use caripraxine with caution in patients who may experience conditions that lower body temperature (eg, strenuous exercise, extreme heat, dehydration, or concomitant anticholinergics).

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotics. Antipsychotic drugs, including caripraxine, should be used cautiously in patients at risk for aspiration.

Drug Interactions: Strong and moderate CYP3A4 inhibitors increase caripraxine concentrations, so caripraxine dose reduction is recommended. Concomitant use with CYP3A4 inducers is not recommended.

Adverse Reactions: The most common adverse reactions in adult clinical trials (≥5% and at least twice the rate of placebo) are listed below:

- **Adjunctive Treatment of Major Depressive Disorder:**
  - In 6-week, fixed-dose trials the incidences within the recommended doses (caripraxine 1.5 mg/day + antidepressant therapy [ADT] or 3 mg/day + ADT vs placebo + ADT) were akathisia (7%, 10% vs 2%), insomnia (7%, 6% vs 3%), and insomnia (9%, 10% vs 5%).
  - In one 8-week flexible-dose trial, incidences within the doses (caripraxine 1-2 mg/day + antidepressant therapy [ADT] or 2-6 mg/day + ADT vs placebo + ADT) were akathisia (8%, 23% vs 3%), restlessness (8%, 8% vs 3%), fatigue (7%, 10% vs 4%), constipation (2%, 5% vs 2%), nausea (7%, 13% vs 5%), increased appetite (2%, 5% vs 2%), dizziness (4%, 5% vs 2%), insomnia (14%, 16% vs 8%), and extrapyramidal symptoms (12%, 18% vs 5%).
- **Bipolar Mania:** The incidences within the recommended dose range (caripraxine 3-6 mg/day vs placebo) were EPS (26% vs 20%), akathisia (20% vs 10%), constipation (10% vs 4%), dyspepsia (7% vs 4%), somnolence (7% vs 4%), and restlessness (7% vs 2%).
- **Bipolar Depression:** The incidences within the recommended doses (caripraxine 1.5 mg/day or 3 mg/day vs placebo) were nausea (7%, 7% vs 3%), akathisia (6%, 10% vs 2%), restlessness (2%, 7% vs 3%), and EPS (4%, 6% vs 2%).
- **Schizophrenia:** The incidences within the recommended dose range (caripraxine 1.5–3 mg/day and 4.5–6 mg/day vs placebo) were EPS (15%, 19% vs 8%) and akathisia (9%, 13% vs 4%).

Caripraxine is available in 0.5 mg, 0.75 mg, 1.5 mg, 3 mg, 4.5 mg, and 6 mg capsules.

Please also see full Prescribing Information, including Boxed Warnings.
Visit www.rxabbvie.com or contact AbbVie Medical Information at www.abbviemedinfo.com or 1-800-633-9110.

Reference

Caripraxine. Package insert. AbbVie; 2025.