Clinical Policy: Cariprazine (Vraylar)

Reference Number: CP.PMN.91
Effective Date: 11.16.16
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Cariprazine (Vraylar®) is an atypical antipsychotic.

FDA Approved Indication(s)

Vraylar is indicated for:

- Treatment of schizophrenia in adults and pediatric patients 13 years of age and older
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults and pediatric patients 10 years of age and older
- 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

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Vraylar is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Bipolar Disorder and Schizophrenia (must meet all)**:**

1. Diagnosis of bipolar disorder or schizophrenia;
2. Age is one of the following (a, b, or c):
   a. Schizophrenia: ≥ 13 years;
   b. Bipolar disorder: ≥ 10 years;
   c. Depressive episodes of bipolar disorder: ≥ 18 years;
3. Member meets one of the following (a or b):*
   ** For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of two preferred atypical antipsychotics (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, olanzapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless clinically significant adverse effects are experienced or all are contraindicated;
4. Dose does not exceed one of the following (a or b):

a. Schizophrenia or manic or mixed episodes of bipolar disorder (i and ii):
   i. One of the following (1 or 2):
      1) Adults: 6 mg per day;
      2) Pediatrics: 4.5 mg per day;
   ii. 1 capsule per day;
b. Depressive episodes of bipolar disorder (i and ii):
   i. 3 mg per day;
   ii. 1 capsule per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Major Depressive Disorder (must meet all)**:**
1. Diagnosis of MDD;
2. Age ≥ 18 years;
3. Member meets one of the following (a or b):*
   ** For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of THREE antidepressants from at least TWO different classes (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless member is unable to satisfy this requirement due to clinically significant adverse effects experienced, member's age ≥ 65 years, or contraindication(s) to multiple antidepressants;
4. Member meets one of the following (a or b):*
   ** For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of a ≥ 4-week trial of aripiprazole at up to maximally indicated doses, used concurrently with an antidepressant, unless contraindicated or clinically significant adverse effects are experienced;
5. Vraylar is prescribed concurrently with an antidepressant;
6. Dose does not exceed both of the following (a and b):
   a. 3 mg per day;
   b. 1 capsule per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Vraylar for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Schizophrenia or manic or mixed episodes of bipolar disorder (i and ii):
      i. One of the following (1 or 2):
         1) Adults: 6 mg per day;
         2) Pediatrics: 4.5 mg per day;
      ii. 1 capsule per day;
   b. Depressive episodes of bipolar disorder or MDD (i and ii):
      i. 3 mg per day;
      ii. 1 capsule per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. Dementia-related psychosis.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MDD: major depressive disorder
SNRI: serotonin/norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
TCA: tricyclic antidepressant

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Antipsychotics		
aripiprazole (Abilify®)	**Bipolar Disorder and Schizophrenia** 10 to 15 mg PO QD	30 mg/day
olanzapine (Zyprexa®)	**Schizophrenia** Initial: 5 to 10 mg PO QD; target: 10 mg PO QD **Bipolar Disorder** Monotherapy: 10 to 15 mg PO QD; adjunct to lithium or valproate: 10 mg PO QD	20 mg/day
quetiapine (Seroquel®)	**Schizophrenia** Initial: 25 mg PO BID; target: 400 to 800 mg/day **Bipolar Disorder** Initial: 50 mg PO BID; target: 400 to 800 mg/day	800 mg/day
risperidone (Risperdal®)	**Schizophrenia**	Schizophrenia: 16 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Initial: 1 mg PO BID or 2 mg PO QD; target: 4 to 8 mg PO QD **Bipolar Disorder** 2 to 3 mg PO QD	Bipolar Disorder: 6 mg/day
ziprasidone (Geodon®)	**Schizophrenia** Adults: 20 mg PO BID **Bipolar Disorder** Adults: Initial: 40 mg PO BID; target: 40 to 80 mg PO BID	160 mg/day
Selective Serotonin Reuptake Inhibitors (SSRIs)		
citalopram (Celexa®)	**Major Depressive Disorder** Refer to prescribing information	40 mg/day
escitalopram (Lexapro®)		20 mg/day
fluoxetine (Prozac®)		Immediate-release: 80 mg/day (20 mg/day if pediatric) Delayed-release: 90 mg/week
fluvoxamine* (immediate-release) (Luvox®)		150 mg/day
paroxetine (Paxil®, Paxil CR®, Pexeva®)		Immediate-release: 50 mg/day (40 mg/day if geriatric) Extended-release: 62.5 mg/day (50 mg/day if geriatric)
sertraline (Zoloft®)		200 mg/day (20 mg/day if age 6-11 years)
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)		
desvenlafaxine (Pristiq®)	**Major Depressive Disorder** Refer to prescribing information	400 mg/day
duloxetine (Cymbalta®)		120 mg/day
Fetzima® (levomilnacipran)		120 mg/day
venlafaxine (Effexor®, Effexor XR®)		Extended-release: 225 mg/day
Tricyclic Antidepressant (TCAs)		
amitriptyline (Elavil®)	**Major Depressive Disorder**	150 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
amoxapine	Refer to prescribing information	400 mg/day (300 mg/day if geriatric)
clomipramine* (Anafranil®)		250 mg/day (200 mg/day if pediatric)
desipramine (Norpramin®)		300 mg/day (100 mg/day if pediatric)
doxepin (Sinequan®)		300 mg/day
imipramine HCl (Tofranil®)		200 mg/day (150 mg/day if geriatric or pediatric)
imipramine pamoate (Tofranil PM®)		200 mg/day (100 mg/day if geriatric or pediatric)
nortriptyline (Pamelor®)		150 mg/day
protriptyline (Vivactil®)		60 mg/day (30 mg/day if geriatric or pediatric)
trimipramine (Surmontil®)		200 mg/day (100 mg/day if geriatric or pediatric)
Monoamine Oxidase Inhibitors		
isocarboxazid (Marplan®)	**Major Depressive Disorder** Refer to prescribing information	60 mg/day
phenelzine (Nardil®)		90 mg/day
selegiline (EMSAM® transdermal; Eldepryl®, Zelapar®, Carbex®)		Transdermal: 12 mg/24 hr Oral: 30 mg/day
tranylcypromine (Parnate®)		60 mg/day
Other Antidepressants		
bupropion (Aplenzin®, Budeprion SR® , Budeprion XL®, Forfivo XL®, Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	**Major Depressive Disorder** Refer to prescribing information	Immediate-release: 450 mg/day (300 mg/day if pediatric) Sustained-release: 400 mg/day Extended-release (HCl): 450 mg/day Extended-release (HBr): 522 mg/day
mirtazapine (Remeron®)		45 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
perphenazine/ amitriptyline (Triavil®)		16 mg/day perphenazine and 200 mg/day amitriptyline
maprotiline (Ludiomil®)		150 mg/day
nefazodone (Serzone®)		600 mg/day
trazodone (Desyrel®, Oleptro®)		Immediate-release: 400 mg/day Extended-release: 375 mg/day
vortioxetine (Trintellix®)		20 mg/day
vilazodone (Viibryd®)		40 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to Vraylar
- Boxed warning(s): 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. Safety and effectiveness of Vraylar have not been established in pediatric patients.

Appendix D: States with Limitations against Redirections in Certain Mental Health Settings

State	Step Therapy Prohibited?	Notes
AR	Yes	**Applies to HIM requests only** For the treatment of psychosis and serious mental illness through antipsychotic prescription drugs, no step therapies allowed.
NV	No	**Applies to Medicaid requests only** • **MDD**: Failure of aripiprazole or an antidepressant (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) at up to maximally indicated doses, used for ≥ 4 weeks, unless member is unable to satisfy this requirement due to clinically significant adverse effects experienced, member's age ≥ 65 years, or contraindication(s) to multiple antidepressants. • **Bipolar Disorder** and **Schizophrenia**: Failure of ONE preferred atypical antipsychotic (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, olanzapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless clinically significant adverse effects are experienced or all are contraindicated.

State	Step Therapy Prohibited?	Notes
TX	No	**Applies to HIM requests only** • **MDD**: Failure of aripiprazole or an antidepressant (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) at up to maximally indicated doses, used for ≥ 4 weeks, unless member is unable to satisfy this requirement due to clinically significant adverse effects experienced, member's age ≥ 65 years, or contraindication(s) to multiple antidepressants. • **Bipolar Disorder** and **Schizophrenia**: Failure of ONE preferred atypical antipsychotic (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, olanzapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless clinically significant adverse effects are experienced or all are contraindicated.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Schizophrenia	Adults: 1.5 mg to 6 mg PO QD Pediatric patients age 13-17 years: 1.5 mg to 4.5 mg PO QD	Adults: 6 mg/day Pediatrics: 4.5 mg/day
Bipolar I disorder	Manic or mixed episodes: • Adults: 3 mg to 6 mg PO QD • Pediatric patients age 10-17 years: 3 mg or 4.5 mg PO QD Depressive episodes: 1.5 mg or 3 mg PO QD	Manic or mixed episodes: 6 mg/day (adults), 4.5 mg/day (pediatrics) Depressive episodes: 3 mg/day
MDD	As adjunct to antidepressants: 1.5 mg or 3 mg PO QD	3 mg/day

VI. Product Availability

Capsules: 0.5 mg, 0.75 mg, 1.5 mg, 3 mg, 4.5 mg, 6 mg

VII. References

1. Vraylar Prescribing Information. Irvine, CA: Allergan USA, Inc.; December 2025. Available at: http://www.vraylar.com/. Accessed December 26, 2025.
2. Hirschfeld RMA, Bowden CL, Gitlin MJ, et al. Practice guideline for the treatment of patients with bipolar disorder, second edition. Arlington, VA: American Psychiatric Association; April 2002. Available online at http://www.psychiatryonline.org/guidelines. Accessed April 23, 2025.
3. Moore TA, Buchanan RW, Buckley PF, et al. The Texas medication algorithm project antipsychotic algorithm for schizophrenia: 2006 Update. J Clin Psychiatry. 2007; 68:1751-1762.

4. Suppes T, Swann AC, Dennehy EB, et al. Texas medication algorithm project: development and feasibility testing of a treatment algorithm for patients with bipolar disorder. J Clin Psychiatry. 2021;62(2):429-447/.
5. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed April 23, 2025.
6. Keepers G, Fochtmann L, Anzia J, et al. APA Practice guideline for the treatment of patients with schizophrenia, third edition. Am J Psychiatry. 2020 Sept;177(9):868-872.
7. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder, third edition. Arlington, VA: American Psychiatric Association; May 2010. Available online at http://www.psychiatryonline.org/guidelines. Accessed April 23, 2025.
8. Qaseeem A, Owens DK, Etxeandia-Ikobaltzeta I, et al. Nonpharmacological and pharmacologic treatments of adults in the acute phase of major depressive disorder: A living clinical guideline from the American College of Physicians. Annals of Internal Medicine. February 2023; 172(2):239-253.
9. Management of bipolar disorder work group. Clinical practice guideline for management of bipolar disorder Version 2.0 - 2023. Veterans Affairs/Department of Defense. Available at: https://www.healthquality.va.gov/guidelines/MH/bd/VA-DoD-CPG-BD-Full-CPGFinal508.pdf. Accessed April 23, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: no significant changes; revised Commercial auth limit from Length of Benefit to 12 months or duration of request whichever is less; references reviewed and updated.	11.13.21	02.22
Per September SDC added HIM line of business to policy.	09.26.22	11.22
1Q 2023 annual review: no significant changes; addition of dementia-related psychosis to section III for diagnoses/indications for which coverage is not authorized; references reviewed and updated. RT4: added new indication for use as adjunctive treatment in MDD per PI. Template changes applied to other diagnoses/indications and continued therapy section.	01.09.23	02.23
Added redirection bypass for members in a State with limitations on step therapy in certain mental health settings along with Appendix D, which includes Arkansas.	07.05.23	
3Q 2023 annual review: no significant changes; references reviewed and updated. Added Texas to Appendix D with requirements for single drug redirection for HIM requests.	07.13.23	08.23
Added Nevada to Appendix D with requirements for single drug redirection for Medicaid requests.	08.31.23	
3Q 2024 annual review: no significant changes; revised continued therapy criteria to allow continuity of care for all indications; references reviewed and updated.	05.09.24	08.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2025 annual review: added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	06.27.25	08.25
RT4: updated criteria with pediatric extension to include age 10 years and older for bipolar disorder and age 13 years and older for schizophrenia (both previously approved only in adults) per PI; added new 0.5 mg and 0.75 mg capsule strengths per PI.	12.26.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.