Clinical Policy: Olanzapine/Samidorphan (Lybalvi)

Reference Number: CP.PMN.265
Effective Date: 09.01.21
Last Review Date: 08.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Olanzapine/samidorphan (Lybalvi®) is combination of olanzapine, an atypical antipsychotic, and samidorphan, an opioid antagonist.

FDA Approved Indication(s)

Lybalvi is indicated for the treatment of:

- Schizophrenia in adults
- Bipolar I disorder in adults
  - Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate
  - Maintenance monotherapy treatment

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 Lybalvi 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 ≥ 18 years;
3. Member meets one of the following (a, b, or c):
   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. Member must use olanzapine at up to maximally indicated doses, unless contraindicated to excipients, clinically significant adverse effects are experienced;
   c. Member has diabetes mellitus or body mass index (BMI) > 30 kg/m^2;
4. Member meets one of the following (a or b):
   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 one additional preferred atypical antipsychotic (e.g., aripiprazole, ziprasidone, quetiapine, risperidone) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;

5. Dose does not exceed 20 mg olanzapine/10 mg samidorphan (1 tablet) per day.

Approval duration: 12 months

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.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Lybalvi for bipolar disorder or schizophrenia 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 20 mg olanzapine/10 mg samidorphan (1 tablet) per day.

Approval duration: 12 months

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

BMI: body mass index
FDA: Food and Drug Administration

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
aripiprazole (Abilify®)	**Bipolar Disorder and Schizophrenia** Adults: 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** 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	Schizophrenia: 16 mg/day Bipolar Disorder: 6 mg/day
ziprasidone (Geodon®)	**Schizophrenia** 20 mg PO BID **Bipolar Disorder** Initial: 40 mg PO BID; target: 40 to 80 mg PO BID	160 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): patients using opioids; patients undergoing acute opioid withdrawal; if Lybalvi is administered with lithium or valproate, refer to the lithium or valproate prescribing information for the contraindications for those products
- Boxed warning(s): increased mortality in elderly patients with dementia-related psychosis

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** Failure of a 4-week trial of olanzapine or one preferred atypical antipsychotic (e.g., aripiprazole, ziprasidone, quetiapine, risperidone) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated.
TX	No	**Applies to HIM requests only** Failure of a 4-week trial of olanzapine or one preferred atypical antipsychotic (e.g., aripiprazole, ziprasidone, quetiapine, risperidone) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Schizophrenia	Initiate at 5 mg/10 mg or 10 mg/10 mg PO QD. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg. Dosage may be adjusted at weekly intervals of 5 mg (based on the olanzapine component) depending upon clinical response and tolerability.	20 mg/10 mg/day
Bipolar I disorder	Monotherapy: Initiate at 10 mg/10 mg or 15 mg/10 mg PO QD. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg PO QD. Dosage adjustments should occur at intervals of not less than 24 hours. When dosage adjustments are necessary, dose increments/decrements of 5 mg (based on the olanzapine component) are recommended.	20 mg/10 mg/day

Indication	Dosing Regimen	Maximum Dose
	Maintenance monotherapy: Administer at 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg PO QD. Adjunctive to lithium or valproate: Initiate at 10 mg/10 mg PO QD. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg or 20 mg/10 mg PO QD. Dosage may be adjusted at weekly intervals of 5 mg (based on the olanzapine component), depending upon clinical response and tolerability.	

VI. Product Availability

Tablets (olanzapine/samidorphan): 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg, 20 mg/10 mg

VII. References

1. Lybalvi Prescribing Information. Waltham, MA: Alkermes, Inc.; January 2024. Available at: https://www.lybalvi.com/. Accessed May 10, 2024.
2. Keepers G, Fochtmann L, Anzia J, et al. American Psychiatric Association practice guideline for the treatment of patients with schizophrenia, third edition (2020). Available at: https://psychiatryonline.org/doi/10.1176/appi.books.9780890424841. Accessed May 17, 2024.
3. McDonagh MS, Dana T, Selph S, Devine EB, et al. Treatments for schizophrenia in adults: A systematic review. Comparative Effectiveness Review No. 198. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 17(18)-EHC031-EF. Rockville, MD: Agency for Healthcare Research and Quality; October 2017.
4. Hirschfield RMA, Bowden CL, Gitlin MJ, et al. American Psychiatric Association practice guideline for the treatment of patients with bipolar disorder, second edition (2010). Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bipolar.pdf . Accessed May 17, 2024.
5. Butler M, Urosevic S, Desai P, et al. Treatment for bipolar disorder in adults: A systematic review. Comparative Effectiveness Review No. 208. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-2012-00016-I.) AHRQ Publication No. 18-EHC012-EF. Rockville, MD: Agency for Healthcare Research and Quality; August 2018.
6. 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 May 17, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	06.03.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.12.22	08.22
Template changes applied to other diagnoses/indications.	10.07.22	
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; addition of dementia-related psychosis to Section III; added Texas to Appendix D with requirements for single drug redirection for HIM requests; references reviewed and updated.	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; references reviewed and updated.	05.10.24	08.24

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.