

<b>Clinical Policy Title:</b>	olanzapine and samidorphan
<b>Policy Number:</b>	RxA.697
<b>Drug(s) Applied:</b>	Lybalvi™
<b>Original Policy Date:</b>	08/16/2021
<b>Last Review Date:</b>	09/14/2021
<b>Line of Business Policy Applies to:</b>	All line of business

## Background

Lybalvi™ is a combination of olanzapine, an atypical antipsychotic, and samidorphan, an opioid antagonist, 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.

## Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
olanzapine and samidorphan (Lybalvi™)	Schizophrenia	<p><u>Initial dose:</u> Initiate Lybalvi™ at 5 mg/10 mg olanzapine/samidorphan or 10 mg/10 mg olanzapine/samidorphan orally once daily</p> <p><u>Recommended dose:</u> 10 mg/10 mg olanzapine/samidorphan, 15 mg/10 mg olanzapine/samidorphan, or 20 mg/10 mg olanzapine/samidorphan once daily.</p>	20 mg olanzapine with 10 mg samidorphan orally once daily.
olanzapine and samidorphan (Lybalvi™)	Bipolar I disorder (manic or mixed episodes)	<p><u>Monotherapy:</u> Initial dose: Lybalvi™ at 10 mg/10 mg or 15 mg/10 mg once daily.</p> <p><u>Recommended dose:</u> olanzapine/samidorphan, 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg once daily.</p> <p><u>Maintenance Monotherapy:</u> 5 to 20 mg olanzapine with 10</p>	20 mg olanzapine with 10 mg samidorphan orally once daily.

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

Dosing Information			
Drug Name	Indication	Dosing Regimen	Maximum Dose
		mg samidorphan orally once daily.	
olanzapine and samidorphan (Lybalvi™)	Bipolar disorder I adjunctive to lithium or valproate	<p><u>Initial dose:</u> Lybalvi™ at 10 mg/10 mg once daily.</p> <p><u>Recommended dose:</u> 10 mg/10 mg, 15 mg/10 mg or 20 mg/10 mg, once daily.</p>	20 mg/10 mg orally once daily.

### Dosage Forms

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

### Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

#### I. Initial Approval Criteria

##### A. Schizophrenia (must meet all):

1. Diagnosis of schizophrenia;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with a psychiatrist;
4. Member meets DSM-5 criteria for schizophrenia;
5. Patient does not have a known opioid use disorder, undergoing acute opioid withdrawal or is dependent on opioids;
6. Trial of generic olanzapine for at least 4 weeks with documentation demonstrating positive therapeutic benefit but clinically significant weight gain (at least 3%) while on therapy;
7. Dose does not exceed 20 mg olanzapine with 10 mg samidorphan orally once daily.

##### Approval Duration

**Commercial:** 6 months

**Medicaid:** 6 months

##### B. Bipolar I Disorder (must meet all):

1. Diagnosis of Bipolar I Disorder;
2. Request is for one of the following (a or b):
  - a. Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate;
  - b. Maintenance monotherapy treatment;
3. Age ≥ 18 years;
4. Prescribed by or in consultation with a psychiatrist;
5. Member meets DSM-IV criteria for a manic or mixed episode of bipolar I disorder;
6. Patient does not have a known opioid use disorder, undergoing acute opioid withdrawal or is dependent on opioids;

7. Trial of generic olanzapine for at least 4 weeks with documentation demonstrating positive therapeutic benefit but clinically significant weight gain (at least 3%) while on therapy;
8. Dose does not exceed 20 mg olanzapine with 10 mg samidorphan orally once daily.

**Approval Duration**

**Commercial:** 6 months

**Medicaid:** 6 months

**II. Continued Therapy Approval**

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 20 mg olanzapine with 10 mg samidorphan orally once daily.

**Approval Duration**

**Commercial:** 12 months

**Medicaid:** 12 months

**III. Appendices**

**APPENDIX A: Abbreviation/Acronym Key**

DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms

DSM: Diagnostic and Statistical Manual of Mental Disorders

**APPENDIX B: Therapeutic Alternatives**

Not applicable.

**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: General Information**

- Lybalvi™ is not approved for the treatment of patients with dementia related psychosis.
- Prior to initiating treatment, there should be at least a 7-day opioid free interval from the last use of short-acting opioids and at least a 14-day window with long acting opioids.
- Attempting to overcome Lybalvi's™ opioid blockade with high or repeated doses of exogenous opioids (e.g., because of ineffective analgesia or opioid withdrawal symptoms) could lead to life-threatening or fatal opioid intoxication (e.g., respiratory arrest, circulatory collapse), particularly if Lybalvi™ therapy is interrupted or discontinued, subjecting the patient to high levels of unopposed opioid agonist as samidorphan blockade wanes.
- Discontinue Lybalvi™, if a Lybalvi™-treated patient requires opioid treatment as part of anesthesia or analgesia.

- Patients with a history of chronic opioid use prior to treatment with Lybalvi™ may have decreased opioid tolerance if Lybalvi™ therapy is interrupted or discontinued. Advise patients that this decreased tolerance may increase the risk of opioid overdose if opioids are resumed at the previously tolerated dosage.
- Neuroleptic Malignant Syndrome (NMS) is a potentially fatal symptom complex reported in association with administration of antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, delirium, and autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.
- Other warnings and precautions include metabolic changes, tardive dyskinesia, orthostatic hypotension, syncope, leukopenia, neutropenia, agranulocytosis, seizures, potential for cognitive and motor impairment, anticholinergic (antimuscarinic) effects, and hyperprolactinemia.
- The Diagnostic and Statistical Manual of Mental Disorders (DSM) is the handbook used by health care professionals in the United States and much of the world as the authoritative guide to the diagnosis of mental disorders. DSM contains descriptions, symptoms, and other criteria for diagnosing mental disorders.

**References**

1. Lybalvi™ [prescribing information]. Waltham, MA: Alkermes Inc; May 2021. Available at: <https://www.lybalvi.com/>. Accessed August 16, 2021.
2. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2021. Accessed with subscription at: <http://www.clinicalkey.com> . Updated February 10, 2021. Accessed August 16, 2021.
3. DSM. FAQ. American Psychiatric Association. Available at: <https://www.psychiatry.org/psychiatrists/practice/dsm/feedback-and-questions/frequently-asked-questions .2021> . Accessed August 17, 2021.
4. Keepers GA, et al. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia, third edition. *Am J Psychiatry*. 2020;177(9):868-872. doi:10.1176/appi.ajp.2020.177901
5. Kinon BJ, et al. Long-term olanzapine treatment: weight change and weight-related health factors in schizophrenia. *J Clin Psychiatry*. 2001;62(2):92-100.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	08/16/2021	09/14/2021