



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES  
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/18/2021  
LAST REVIEW DATE:  
LAST CRITERIA REVISION DATE:  
ARCHIVE DATE:

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## LYBALVI™ (olanzapine and samidorphan)

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Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com). **Incomplete forms or forms without the chart notes will be returned.**

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### Criteria:

- **Criteria for initial therapy:** Lybalvi (olanzapine and samidorphan) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Psychiatrist
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of **ONE** of the following:
    - a. Individual meets most current version Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for Schizophrenia
    - b. Individual meets most current version Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for Bipolar I disorder for:
      - i. Acute treatment of manic or mixed episode as monotherapy and as adjunct to lithium or valproate
      - ii. Maintenance monotherapy
  4. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
    - a. Fasting blood glucose
    - b. Fasting lipid profile
    - c. Weight
    - d. **For Schizophrenia:**
      - i. Positive and Negative Syndrome Scale (PANSS) total score of at least 50 or more
      - ii. Body weight has increased by 5% or more or has gain at least 5 kg or more over the last 3 months while on olanzapine
    - e. **For Bipolar I Disorder:**
      - i. Young Mania Rating Scale (Y-MRS) total score of 16 or more
  5. **ONE** of the following:
    - a. **For Schizophrenia:**
      - i. Documented failure, contraindication per FDA label, intolerance, or not a candidate for Olanzapine and **ONE** of the following:
        1. Aripiprazole
        2. Quetiapine
        3. Risperidone
    - b. **For Bipolar I Disorder:**
      - i. Documented failure, contraindication per FDA label, intolerance, or not a candidate for Olanzapine and **ONE** of the following:
        1. Lithium or valproate
        2. Aripiprazole
        3. Quetiapine
        4. Risperidone
        5. Ziprasidone

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6. There are **NO** FDA-label contraindications, such as:
  - a. Individual using opioids
  - b. Individual undergoing opioid withdrawal
7. Individual does not have dementia-related psychosis
8. Individual does not have a recent history of myocardial infarction or unstable cardiovascular disease
9. Individual has not had a short-acting opioid in the last 7-days or a long-acting opioid in the last 14-days
10. Individual does not have end-stage renal disease (estimated glomerular filtration rate less than 15 mL/min/1.73 m<sup>2</sup>)
11. There are no significant interacting drugs

**Initial approval duration:** 6 months

➤ **Criteria for continuation of coverage (renewal request):** Lybalvi (olanzapine and samidorphan) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Psychiatrist
2. Individual's condition has responded while on therapy
  - a. Response defined as:
    - i. **For Schizophrenia:**
      1. Has not gained weight or weight gain is not more than 2 kg
      2. There is at least a 20% improvement in the Positive and Negative Syndrome Scale (PANSS) total score over baseline
      3. Clinical Global Impression of Severity (CGI-S) or Clinical Global Impression of Improvement (CGI-I) score of 2 or less
    - ii. **For Bipolar I Disorder:**
      1. There is a decrease in the Young Mania Rating Scale (Y-MRS) total score to 12 or less
3. Individual has been adherent with the medication
4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
  - a. Contraindications as listed in the criteria for initial therapy section
  - b. Significant adverse effect such as:
    - i. Neuroleptic malignant syndrome (NMS)
    - ii. Drug reaction with eosinophilia and systemic symptoms (DRESS)
    - iii. Tardive dyskinesia
    - iv. Leukopenia, neutropenia, agranulocytosis



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### v. Seizures

5. Individual does not have dementia-related psychosis
6. Individual does not have a recent history of myocardial infarction or unstable cardiovascular disease
7. Individual has not had a short-acting opioid in the last 7-days or a long-acting opioid in the last 14-days
8. Individual does not have end-stage renal disease (estimated glomerular filtration rate less than 15 mL/min/1.73 m<sup>2</sup>)
9. There are no significant interacting drugs

**Renewal duration:** 12 months

➤ Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of a Non-Cancer Medications**
2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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### **Description:**

Lybalvi is a combination of olanzapine, an atypical antipsychotic, and samidorphan, a mu-opioid receptor antagonist, indicated for the treatment of schizophrenia in adults and bipolar I disorder in adults for the acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate and as maintenance monotherapy treatment. Lybalvi (olanzapine and samidorphan) **is not approved** for the treatment of patients with dementia-related psychosis.

The mechanism of action of olanzapine is unclear; however, its efficacy in the treatment of schizophrenia or bipolar I disorder could be mediated through a combination of dopamine and serotonin type 2 (5HT<sub>2</sub>) antagonism. The mechanism of action of samidorphan could be mediated through opioid receptor antagonism; it has partial agonist activity at kappa- and delta-opioid receptors. Samidorphan is 3-carboxamido-4-hydroxynaltrexone.

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### **Definitions:**

#### **Positive and Negative Syndrome Scale (PANSS):**

The PANSS is a 30-item scale that measures positive symptoms of schizophrenia (7 items), negative symptoms of schizophrenia (7 items), and general psychopathology (16 items), each rated on a scale of 1 (absent) to 7 (extreme). Total PANSS scores range from 30 to 210, with a higher score reflecting greater symptom severity.

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### **Positive scale:**

7 Items, (minimum score = 7, maximum score = 49)

- Delusions
- Conceptual disorganization
- Hallucinations
- Excitement
- Grandiosity
- Suspiciousness/persecution
- Hostility

### **Negative scale:**

7 Items, (minimum score = 7, maximum score = 49)

- Blunted affect
- Emotional withdrawal
- Poor rapport
- Passive/apathetic social withdrawal
- Difficulty in abstract thinking
- Lack of spontaneity and flow of conversation
- Stereotyped thinking

### **General Psychopathology scale:**

16 Items, (minimum score = 16, maximum score = 112)

- Somatic concern
- Anxiety
- Guilt feelings
- Tension
- Mannerisms and posturing
- Depression
- Motor retardation
- Uncooperativeness
- Unusual thought content
- Disorientation
- Poor attention
- Lack of judgment and insight
- Disturbance of volition
- Poor impulse control
- Preoccupation
- Active social avoidance

PANSS Total score minimum = 30, maximum = 210

### **Clinical Global Impression (CGI):**

CGI is a 3-item observer-rated scale that measures illness severity (CGI-S), global improvement or change (CGI-C) and therapeutic response. The illness severity and improvement sections of the instrument are used more frequently than the therapeutic response section in both clinical and research settings

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CGI-Severity is a validated scale that requires clinicians to rate a patient's current illness severity and overall clinical state based on experience with the illness population. Scores range from 1 (normal, not at all ill) to 7 (extremely ill).

Clinical Global Impression – Severity (CGI-S)	
Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?	
0 = Not assessed	4 = Moderately ill
1 = Normal, not at all ill	5 = Markedly ill
2 = Borderline mentally ill	6 = Severely ill
3 = Mildly ill	7 = Among the most extremely ill patients

Clinical Global Impression – Improvement (CGI-I)	
Rate total improvement whether or not, in your judgement, it is due entirely to drug treatment. Compared to the patient's condition at baseline, how much has changed?	
0 = Not assessed	4 = No changes
1 = Very much improved	5 = Minimally worse
2 = Much improved	6 = Much worse
3 = Minimally improved	7 = Very much worse

**Young Mania Rating Scale (Y-MRS):**

Y-MRS, is an 11-item clinician-rated scale traditionally used to assess the degree of manic symptomatology in a range from 0 (no manic features) to 60 (maximum score) where higher scores indicate more severe mania, thus, a negative change (or decrease) from baseline indicates a reduction (or improvement) in manic symptoms. Total score ≤ 12 indicates remission; 13-19 = minimal symptoms; 20-25 = mild mania, 26-37 = moderate mania, 38-60 = severe mania.

Specify <b>ONE</b> of the reasons listed by indicating the number that describes severity	
1	Elevated Mood 0 = Absent 1 = Mildly or possibly increased on questioning 2 = Definite subjective elevation; optimistic, self-confident, cheerful; appropriate to content 3 = Elevated, inappropriate to content; humorous 4 = Euphoric; inappropriate laughter; singing
2	Increased Motor Activity Energy 0 = Absent 1 = Subjectively increased 2 = Animated; gestures increased 3 = Excessive energy; hyperactive at times; restless (can be calmed) 4 = Motor excitement; continuous hyperactivity (cannot be calmed)
3	Sexual Interest 0 = Normal; not increased 1 = Mildly or possibly increased 2 = Definite subjective increase on questioning

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	<p>3 = Spontaneous sexual content; elaborates on sexual matters; hypersexual by self report 4 = Overt sexual acts (towards patients, staff, or interviewer)</p>
4	<p>Sleep 0 = Reports no decrease in sleep 1 = Sleeping less than normal amount by up to one hour 2 = Sleeping less than normal amount by more than one hour 3 = Reports decreased need for sleep 4 = Denies need for sleep</p>
5	<p>Irritability 0 = Absent 2 = Subjectively increased 4 = Irritable at times during interview; recent episodes of anger or annoyance on ward 6 = Frequently irritable during interview; short; curt throughout 8 = Hostile, uncooperative; interview impossible</p>
6	<p>Speech (rate and amount) 0 = No increase 2 = Feels talkative 4 = Increased rate or amount at times; verbose at times 6 = Push; consistently increased rate and amount; difficult to interrupt 8 = Pressured; uninterruptible; continuous speech</p>
7	<p>Language-Thought Disorder 0 = Absent 1 = Circumstantial; mildly distractibility; quick thoughts 2 = Distractible; loses goal of thought; changes topics frequently; racing thoughts 3 = Flight of ideas; tangentiality; difficult to follow; rhyming; echolalia 4 = Incoherent; communication impossible</p>
8	<p>Content 0 = Normal 2 = Questionable plans, new interests 4 = Special project(s); hyperreligious 6 = Grandiose or paranoid ideas; ideas of reference 8 = Delusions; hallucinations</p>
9	<p>Disruptive-Aggressive Behavior 0 = Absent; cooperative 2 = Sarcastic; loud at times, guarded 4 = Demanding; threats on ward 6 = Threatens interviewer; shouting; interview difficult 8 = Assaultive; destructive; interview impossible</p>
10	<p>Appearance 0 = Appropriate dress and grooming 1 = Minimally unkempt 2 = Poorly groomed; moderately disheveled; overdressed 3 = Disheveled; partly clothed; garish make-up 4 = Completely unkempt; decorated; bizarre garb</p>
11	<p>Insight 0 = Present; admits illness; agrees with need for treatment 1 = Possibly ill 2 = Admits behavior change; but denies illness 3 = Admits possible change in behavior; but denies illness 4 = Denies any behavior change</p>



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### Resources:

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