Pharmacy Policy Bulletin: J-1119 Lybalvi (olanzapine/samidorphan) – Commercial and Healthcare Reform	
Number: J-1119	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1119-006	**Original Date:** 08/04/2021
Effective Date: 12/20/2024	**Review Date:** 12/04/2024

Drugs Product(s):	• Lybalvi (olanzapine/samidorphan)

FDA-Approved Indication(s):	• For the treatment of schizophrenia in adults
	• For the treatment of bipolar I disorder in adults
	  ○ Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate
	  ○ Maintenance monotherapy treatment

Background:	• Lybalvi is a combination medication containing the atypical antipsychotic, olanzapine, and the opioid receptor antagonist, samidorphan. The mechanism of action of olanzapine is unknown; however, its effects are thought to be mediated through dopamine and serotonin ($5HT_2$) antagonism. Samidorphan is included to reduce the weight gain typically seen with olanzapine and is not thought to impact the clinical efficacy of olanzapine. • Schizophrenia is a severe, chronic mental health disorder, typically presenting in the third decade of life. Schizophrenia is rare, occurring in 0.6%-1.9% of the U.S. population and is characterized by various symptoms such as hallucinations, disorganized speech, and impaired cognitive behavior. • Bipolar 1 disorder is a rare, chronic mental disorder, typically diagnosed in late adolescence and early adulthood. It is associated with periods of mania that last for at least a week in which patients experience insomnia, decreased appetite, show poor judgment, and partake in risky behavior, followed by periods of depression. • Patients on stable, chronic olanzapine therapy were not specifically studied in the Lybalvi clinical trials, so the weight effect of switching from olanzapine to Lybalvi is unknown. • Antipsychotic-induced weight gain (AIWG) is a major contributory factor to obesity and related metabolic complications and results in poor medication adherence. Clozapine and olanzapine have the highest likelihood of causing weight gain, while aripiprazole, asenapine, ziprasidone, and lurasidone (Latuda)

	have the lowest risk. Quetiapine and risperidone carry a moderate risk of AIWG, but a lower risk compared to olanzapine. • Other ways to manage AIWG include nonpharmacologic strategies, such as cognitive and behavioral interventions, nutritional counseling, and exercise, and pharmacologic interventions, including switching to another antipsychotic medication with a lower risk of AIWG, or using metformin. While metformin is not FDA-approved for this indication, its off-label use is supported by pharmacy compendia. The BAP guidelines on the management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment recommend metformin as a first-line medication if lifestyle interventions are unsuccessful. • Prescribing Considerations: ○ Lybalvi should be prescribed by or in consultation with a psychologist or psychiatrist. ○ Similar to all atypical antipsychotics, Lybalvi has a black box warning for an increased risk of mortality in elderly patients with dementia-related psychosis. ○ Lybalvi may cause false positive results with urinary immunoassay methods used for detecting opioids. Use an alternative analytical technique to confirm positive opioid urine drug screen results. ○ Lybalvi contains samidorphan, an opioid antagonist, and for that reason is contraindicated in those currently taking opioids or those who are undergoing acute opioid withdrawal. ○ Lybalvi is a fixed-dose combination with each strength containing 10 mg of samidorphan, which should be taken once daily. Even when titrating the medication, patients should not receive more than one tablet daily (10 mg samidorphan).

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Lybalvi may be approved when all of the following criteria are met **(A. through D.)**:

A. The member is 18 years of age or older.

B. The member has one (1) of the following diagnoses **(1. or 2.)**:
- **1.** Schizophrenia (ICD-10: F20)
- **2.** Bipolar I disorder or Bipolar II disorder (ICD-10: F31)

C. The member meets one (1) of the following criteria **(1. or 2.)**:
- **1.** The member has experienced therapeutic failure, intolerance, or contraindication to two (2) of the following plan-preferred generic agents **(a., b., or c.)**:
  - **a.** aripiprazole
  - **b.** risperidone
  - **c.** quetiapine
- **2.** The provider attests that the member is currently stable on and responding to olanzapine but is experiencing weight gain from the medication.

D. The member has experienced therapeutic failure, intolerance, or contraindication to metformin in combination with an antipsychotic.

II. Reauthorization

When a benefit, reauthorization of Lybalvi may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Members requesting a non-preferred metformin product must meet criteria outlined in J-0600, if applicable.
II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

- None

References:

1. Lybalvi [package insert]. Waltham, MA: Alkermes Inc.; January 2024.
2. Patel KR, Cherian J, Gohil K, Atkinson D. Schizophrenia: overview and treatment options. *PT*. 2014;39(9):638-645.
3. National Institute of Mental Health. Bipolar Disorder. U.S. Department of Health and Human Services. 2020. Available at: /. Accessed October 14, 2024.
4. Dayabandara M, Hanwella R, Ratnatunga S, et al. Antipsychotic-associated weight gain: management strategies and impact on treatment adherence. *Neuropsychiatr Dis Treat*. 2017;13:2231-2241.
5. Cooper SJ, Reynolds GP, Barnes T et al. BAP guidelines on the management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment. *J Psychopharmacol*. 2016;30(8):717-48.