

Lybalvi (olanzapine/samidorphan)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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Summary

Bipolar depression and schizophrenia require comprehensive treatment approaches. Treatment plans usually include both medication and non-medication approaches. Tolerance and response to antipsychotic agents vary, and those who do not tolerate or respond to a specific agent may be treated with a different agent and expect a different response or adverse effect(s). The choice of an antipsychotic agent depends on a multitude of factors, including but not limited to response (or lack thereof) to previously used medications, safety and tolerability of each agent, and patient-specific considerations.

Antipsychotic-induced weight gain (AIWG) is a metabolic side effect of antipsychotic medications and contributes to metabolic complications such as obesity. Among second generation antipsychotics, Clozaril (clozapine) and Zyprexa (olanzapine) have the highest likelihood of causing weight gain. Low risk or weight neutral antipsychotics include Abilify (aripiprazole), Caplyta (lumateperone), Geodon (ziprasidone), Latuda (lurasidone), and Vraylar (cariprazine). Moderate risk antipsychotics include Invega (paliperidone), Risperdal (risperidone), Saphris (asenapine), and Seroquel (quetiapine).

Other ways to manage AIWG include nonpharmacologic strategies (e.g., cognitive and behavioral interventions, diet and exercise, and pharmacologic interventions, including switching to another antipsychotic medication with a lower risk of AIWG, or using metformin.

Definitions

“Adjunctive therapy” is treatment with an additional medication added to the main therapy.

“Atypical antipsychotics” are second generation antipsychotic medications used to treat conditions like schizophrenia and bipolar disorder. Examples include aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone.

“Bipolar depression” refers to depressive episodes associated with bipolar disorder.

“Bipolar disorder” is a mental health condition characterized by extreme mood swings between manic and depressive episodes.

“Documentation” refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

“Monotherapy” means treatment with a single medication.

“No evidence of” indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

“Schizophrenia” is a chronic mental health condition characterized by hallucinations, delusions, disorganized thinking and behavior.

“[s]” indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Bipolar I Disorder or Schizophrenia

The Plan considers Lybalvi (olanzapine/samidorphan) medically necessary when ALL of the following criteria are met:

1. The medication is prescribed by or in consultation with a with a psychiatrist or a physician who specializes in mental health care; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has a diagnosis of ONE of the following:
 - a. bipolar I disorder; *or*
 - b. schizophrenia; *AND*
4. The member is unable to use, or has tried and failed TWO the following^[s]:
 - a. aripiprazole; *and/or*
 - b. Caplyta (lumateperone); *and/or*
 - c. lurasidone; *and/or*
 - d. ziprasidone; *AND*
5. The member has tried and failed generic olanzapine and meets ALL of the following^[s]:
 - a. Improvement or positive response; *and*
 - b. unacceptable weight gain (e.g., $\geq 5\%$ from baseline); *AND*
6. The member meets ALL of the following:
 - a. No evidence of using opioids; *and*
 - b. No evidence of undergoing acute opioid withdrawal; *AND*
7. Lybalvi (olanzapine/samidorphan) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-months.^[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Bipolar I Disorder or Schizophrenia

The Plan considers Lybalvi (olanzapine/samidorphan) medically necessary when ALL of the following criteria are met:

1. The member has experienced a documented improvement (e.g., signs or symptoms) of bipolar I disorder or schizophrenia; *AND*
2. The member meets ALL of the following:
 - a. No evidence of using opioids; *and*
 - b. No evidence of undergoing acute opioid withdrawal.
3. Lybalvi (olanzapine/samidorphan) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.^[s]

Experimental or Investigational / Not Medically Necessary^[s]

Lybalvi (olanzapine/samidorphan) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Attention Deficit Hyperactivity Disorder (ADHD)
- Anorexia nervosa
- Borderline Personality Disorder (BPD)
- Cancer cachexia
- Chemotherapy-induced nausea and vomiting
- Delirium
- Irritability Associated With Autism Spectrum Disorder (ASD)
- Major depressive disorder (MDD)
- Postoperative nausea and vomiting
- Post Traumatic Stress Disorder (PTSD)
- Schizoaffective disorder.

References

1. Cooper SJ, Reynolds GP; With expert co-authors. BAP guidelines on the management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment. *J Psychopharmacol*. 2016 Aug;30(8):717-48.
2. Dayabandara M, Hanwella R, Ratnatunga S, Seneviratne S, Suraweera C, de Silva VA. Antipsychotic-associated weight gain: management strategies and impact on treatment adherence. *Neuropsychiatr Dis Treat*. 2017 Aug 22;13:2231-2241.
3. Lybalvi (olanzapine and samidorphan) [prescribing information]. Waltham, MA: Alkermes Inc; December 2025.
4. Pillinger T, McCutcheon RA, Vano L, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. *Lancet Psychiatry*. 2020 Jan;7(1):64-77.

Clinical Guideline Revision / History Information

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