STEP THERAPY POLICY

POLICY: Antipsychotics Step Therapy

Product	Manufacturer
First-Generation (Typical) Antipsychotics	
chlorpromazine tablets and oral concentrate	Generic only
fluphenazine tablets and elixir	Generic only
haloperidol tablets and oral concentrate	Generic only
loxapine capsules	Generic only
molindone tablets	Generic only
perphenazine tablets	Generic only
pimozide tablets	Generic only
prochlorperazine tablets	Generic only
thioridazine tablets	Generic only
thiothixene capsules	Generic only
trifluoperazine tablets	Generic only
Second-Generation (Atypical) Antipsychotics	
Aripiprazole Products • Abilify® (aripiprazole tablets, orally disintegrating tablets, and oral solution; generic) • Abilify Mycite® (aripiprazole tablets with sensor) • Mezofy™ (aripiprazole oral film) • Opipza (aripiprazole oral film)	 Otsuka, generic Otsuka/Proteus CMG Xiamen
Bysanti™ (milsaperidone tablets)	Vanda
Clozapine Products • Clozaril® (clozapine tablets, generic)	 HLS Therapeutic, generic
Lurasidone Products • Latuda® (lurasidone tablets, generic)	 Sunovion, generic
Olanzapine Products • Zyprexa® (olanzapine tablets, generic) • Zyprexa Zydis® (olanzapine orally disintegrating tablets, generic)	 Eli Lilly, generic Eli Lilly, generic
Quetiapine Products • Seroquel® (quetiapine tablets, generic) • Seroquel XR® (quetiapine extended-release tablets, generic)	 AstraZeneca, generic AstraZeneca, generic
Risperidone Products • Risperdal® (risperidone tablets and oral solution, generic) • Risperdal M-TAB® (risperidone orally disintegrating tablets, generic)	 Janssen, generic Janssen, generic
Ziprasidone Products • Geodon® (ziprasidone capsules, generic)	 Pfizer, generic

REVIEW DATE: 08/12/2026

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a

Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna National Formulary Coverage:

OVERVIEW

Bysanti is an atypical antipsychotic indicated for the following uses:[1]

- Treatment of schizophrenia in adults;
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults.

Many other antipsychotic medications are commercially available which have overlapping indications with Bysanti. Most of the products in this policy (Step 1 and Step 2) carry indications for schizophrenia and/or psychotic disorders.[1-19] Of note, pimozide is not indicated specifically for schizophrenia, although it has been used in this manner.[15,20,21] In addition, the following Step 1 Products have overlapping indications with Bysanti regarding manic or mixed episodes of bipolar I disorder: aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone. Some of the products have additional indications which are not further detailed in this document.

Guidelines

Bysanti is not addressed in guidelines. In the American Psychiatric Association (APA) Practice Guideline for Treatment of Patients with Schizophrenia (2020), APA recommends that patients with schizophrenia be treated with an antipsychotic medication and monitored for effectiveness and adverse events (AEs).[21] An evidence-based ranking of first- and second-generation antipsychotics or an algorithmic approach to antipsychotic selection is not possible because of significant heterogeneity in trial designs, sparse data, and limited head-to-head comparisons. Although there may be clinically meaningful distinctions in response to and tolerability of different antipsychotic medications in an individual patient, there is no definitive evidence that one antipsychotic will have consistently superior efficacy compared with another, with the possible exception of clozapine. Furthermore, there is no reliable strategy to predict response or risk of AEs with one agent compared with another. Consequently, the choice of a particular agent will typically occur in context of discussion with the patient about likely benefits and possible AEs of medication options and will incorporate patient preferences; past responses to

treatment (including symptom response and tolerability); AE profile; physical health conditions that may be affected by medication AEs; and other factors, such as available formulations, potential for drug-drug interactions, receptor binding profiles, and pharmacokinetic considerations.

POLICY STATEMENT

This program has been developed to encourage the use of Step 1 Products prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Step 1: aripiprazole, clozapine, lurasidone, olanzapine, quetiapine, risperidone, ziprasidone, first-generation antipsychotics (e.g., chlorpromazine, fluphenazine, haloperidol, loxapine, molindone, perphenazine, pimozide, prochlorperazine, thioridazine, thiothixene, trifluoperazine)

Step 2: Bysanti

***Antipsychotics Step Therapy Policy* product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.**

CRITERIA

1. If the patient has tried three Step 1 Products, approve.
Note: Any oral or injectable product containing a Step 1 chemical would count as a trial of the respective Step 1 Product.

2. If the patient has bipolar disorder, approve if the patient has tried two Step 1 Products.
Note: Any oral or injectable product containing a Step 1 chemical would count as a trial of the respective Step 1 Product.

3. If the patient has metabolic syndrome, approve if the patient has tried one of aripiprazole or ziprasidone.
Note: Any oral or injectable product containing a Step 1 chemical would count as a trial of the respective Step 1 Product.

4. If the patient is currently taking Bysanti or has taken Bysanti at any time in the past, approve.

REFERENCES

1. Bysanti™ tablets [prescribing information]. Washington, DC: Vanda; February 2026.

2. Abilify® tablets [prescribing information]. Rockville, MD: Otsuka; January 2025.
3. Clozaril® tablets [prescribing information]. Rosemont, PA: HLS Therapeutics; June 2025.
4. Geodon® capsules and intramuscular injection [prescribing information]. Morgantown, WV: Viatris; January 2025.
5. Latuda® tablets [prescribing information]. Marlborough, MA: Sunovion; January 2025.
6. Risperdal® (tablets/oral solution) and Risperdal® M-Tab® [prescribing information]. Titusville, NJ: Janssen; January 2025.
7. Seroquel® tablets [prescribing information]. Wilmington, DE: AstraZeneca; January 2025.
8. Zyprexa®, Zyprexa® Zydis® and Zyprexa® IntraMuscular [prescribing information]. Indianapolis, IN: Lilly; January 2026.
9. Chlorpromazine tablets [prescribing information]. Cranbury, NJ: Sun Pharmaceuticals; June 2026.
10. Fluphenazine tablets [prescribing information]. Bridgewater, NJ: Ajanta Pharma; November 2025.
11. Haloperidol tablets [prescribing information]. Hauppauge, NY: AiPing Pharmaceutical; January 2026.
12. Loxapine capsules [prescribing information]. Parsippany, NJ: Teva; March 2025.
13. Molindone tablets [prescribing information]. Laurelton, NY: Epic Pharma; November 2024.
14. Perphenazine tablets [prescribing information]. Congers, NY: Chartwell Rx; November 2023.
15. Pimozide tablets [prescribing information]. Malvern, PA: Endo USA; August 2024.
16. Prochlorperazine tablets [prescribing information]. Bridgewater, NJ: Ajanta Pharma; November 2025.
17. Trifluoperazine tablets [prescribing information]. Morgantown, WV: Mylan; January 2025.
18. Thioridazine tablets [prescribing information]. Congers, NY: Chartwell Rx; February 2025.
19. Thiothixene capsules [prescribing information]. Bridgewater, NJ: Amneal; November 2024.
20. Mothi M, Sampson S. Pimozide for schizophrenia or related psychoses. *Cochrane Database Syst Rev*. 2013 Nov 5;2013(11):CD001949.
21. Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. *Am J Psychiatry*. 2020;177(9):868-872.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	08/12/2026