PHARMACY COVERAGE GUIDELINE

CAPLYTA® (lumateperone)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Caplyta (lumateperone) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** 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. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Schizophrenia with a Positive and Negative Syndrome Scale (PANSS) total score of 79 indicating moderate to extreme symptoms (see Definitions section)

b. Depressive episode associated with Bipolar I or Bipolar II (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate

4. **ONE** of the following:
   a. **For Schizophrenia**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **THREE** of the following:
      i. Aripiprazole (brand or generic)
      ii. Lurasidone (brand or generic)
      iii. Paliperidone (brand or generic)
      iv. Quetiapine (brand or generic) or Quetiapine XR (brand or generic)
      v. Risperidone (brand or generic)
      vi. Ziprasidone (brand or generic)

   b. **For Depressive episodes associated with Bipolar I or Bipolar II**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **TWO** of the following:
      i. Lithium (if not tried before)
      ii. Lurasidone
      iii. Valproate
      iv. Quetiapine
      v. Lamotrigine
      vi. Olanzapine

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual does not have dementia-related psychosis

7. Individual does not have a recent history of myocardial infarction or unstable cardiovascular disease

8. Individual is not using CYP3A4 inducers (e.g., armodafinil, bexarotene, bosentan, rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, others)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Caplyta (lumateperone) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

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 with response defined as the following:
   a. **For Schizophrenia:**
      i. Documented evidence of efficacy, disease stability and/or improvement demonstrated by an improvement in the Positive and Negative Syndrome Scale (PANSS) total score

ii. Less hallucinations, delusions, disorganized thoughts and behaviors, improved affect, improved socialization, improved energy, fewer to no hospitalizations over baseline

b. **For Depressive episodes associated with Bipolar I or Bipolar II:** At least a 50% improvement in the number, intensity, and frequency of symptoms

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
   a. Neuroleptic malignant syndrome
   b. Tardive dyskinesia (unless alternatives are not effective, harmful, or not appropriate)
   c. Significant leukopenia, neutropenia, agranulocytosis or absolute neutrophil count (ANC) < 1,000/mm^3

6. Individual does not have dementia-related psychosis

7. Individual whose depression is persistently worse, or is experiencing suicidal thoughts or behaviors

8. Individual does not have a recent history of myocardial infarction or unstable cardiovascular disease

9. Individual is not using CYP3A4 inducers (e.g., armodafinil, bexarotene, bosentan, rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, others)

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 Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Caplyta (lumateperone) is indicated for the treatment of schizophrenia in adults. It is not approved for the treatment of patients with dementia-related psychosis. It is also indicated for the treatment of depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults, as monotherapy and as adjunctive therapy with lithium or valproate.

Caplyta (lumateperone) is a second-generation antipsychotic with antagonist activity at central serotonin 5-HT_{2A} receptors and postsynaptic antagonist activity at central dopamine D_2 receptors. Lumateperone has high binding

affinity for serotonin 5-HT_{2A} receptors and moderate binding affinity for dopamine D_2 receptors. Lumateperone also has moderate binding affinity for dopamine D_1 and D_4 and adrenergic $alpha_{1A}$ and $alpha_{1B}$ receptors but has low binding affinity for muscarinic and histaminergic receptors.

Metabolic syndrome is characterized by elevated lipid profile, hypertension, hyperglycemia, and obesity (especially abdominal weight gain). Antipsychotic agents with greatest risk for metabolic syndrome are clozapine, olanzapine, and quetiapine. Aripiprazole, asenapine, lurasidone, and ziprasidone have the least risk.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Positive and Negative Syndrome Scale (PANSS):

Please rate each item on the PANSS using the following scale		
1 - absent, **2** - minimal, **3** - mild, **4** - moderate, **5** - moderate severe, **6** - severe, **7** - extreme		
		Indicate score: 1 2 3 4 5 6 7
P1	Delusions	
P2	Conceptual disorganization	
P3	Hallucinatory behavior	
P4	Excitement	
P5	Grandiosity	
P6	Suspiciousness/persecution	
P7	Hostility	
N1	Blunted affect	
N2	Emotional withdrawal	
N3	Poor rapport	
N4	Passive/apathetic social withdrawal	
N5	Difficulty in abstract thinking	
N6	Lack of spontaneity and flow of conversation	
N7	Stereotyped thinking	
G1	Somatic concern	
G2	Anxiety	
G3	Guilt feelings	
G4	Tension	
G5	Mannerisms and posturing	
G6	Depression	
G7	Motor retardation	
G8	Uncooperativeness	

G9	Unusual thought content	
G10	Disorientation	
G11	Poor attention	
G12	Lack of judgment and insight	
G13	Disturbance of volition	
G14	Poor impulse control	
G15	Preoccupation	
G16	Active social avoidance	
Scoring:		
Positive (P) scale score:		
Negative (N) scale score:		
General (G) psychopathology scale score:		
Total score:		
PANSS score ranges: • Normal: Less than 48 • Borderline mentally ill: 48–60 • Mildly ill: 61–78 • Moderately ill: 79–95 • Markedly ill: 96–118 • Severely ill: 118 or higher		
Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin, 13*(2), 261‑276. https://doi.org/10.1093/schbul/13.2.261		

Atypical (second generation) antipsychotics:

Generic agents*	Brand agents*
- aripiprazole (generic for Abilify) - clozapine (generic for Clozaril) - olanzapine (generic for Zyprexa) - palperidone ER (generic for Invega) - quetiapine (generic for Seroquel) - quetiapine XR (generic Seroquel XR) - risperidone (generic for Risperdal) - ziprasidone (generic for Geodon)	- aripiprazole lauroxil (Aristada) injection - asenapine (Saphris) - brexpiprazole (Rexulti) - cariprazine (Vraylar) - iloperidone (Fanapt) - lumateperone (Caplyta) - lurasidone (Latuda)

Informational purposes only, listing does not imply formulary status or whether or not prior authorization is required

Resources:

Caplyta (lumateperone) product information, revised by Intra-Cellular Therapies, Inc. 06-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Marder S. Psychosis in adults: Epidemiology, clinical manifestations, and diagnostic evaluation. In: UpToDate, Stein MB, Friedman M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated April 15, 2024. Accessed March 03, 2025.

Marder S. Psychosis in adults: Initial management. In: UpToDate, Stein MB, Friedman M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated November 13, 2024. Accessed March 03, 2025.

Stroup TS, Marder S. Schizophrenia in adults: Maintenance therapy and side effect management. In: UpToDate, Stein MB, Friedman M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated June 27, 2024. Accessed March 03, 2025.

Kane J, Rubio JM, Kishimoto T, Correll CU. Treatment-resistant schizophrenia. In: UpToDate, Marder S, Friedman M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated August 15, 2024. Accessed March 03, 2025.

Siris SG, Braga RJ. Depression in schizophrenia. In: UpToDate, Marder S, Friedman M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated September 30, 2024. Accessed March 03, 2025.

Shelton RC, Bobo WV. Bipolar major depression in adults: Choosing treatment. In: UpToDate, Keck P, Solomon D (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated May 21, 2024. Accessed March 03, 2025.

Sajatovic M, Chen P. Geriatric bipolar disorder: Maintenance treatment. In: UpToDate, Keck P, Schmader KE, Solomon D (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated September 10, 2024. Accessed March 03, 2025.

Post RM. Bipolar mania in adults: Choosing maintenance treatment. In: UpToDate, Keck P, Solomon D (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated April 19, 2023. Accessed March 03, 2025.

Stovall J. Bipolar mania and hypomania in adults: Choosing pharmacotherapy. In: UpToDate, Keck P, Solomon D (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated June 21, 2024. Accessed March 03, 2025.