Oscar Clinical Guideline: Cobenfy (xanomeline and trospium) (PG253, Ver. 1)

Cobenfy (xanomeline and trospium)

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.

Summary

Schizophrenia is a chronic and severe mental disorder affecting approximately 1% of the population. It is characterized by positive symptoms (hallucinations, delusions), negative symptoms (diminished emotional expression, avolition), and cognitive impairment that can significantly impact social and occupational functioning. Current first-line treatment consists of second-generation (atypical) antipsychotics, which primarily work through dopamine receptor blockade. While effective for many patients, existing antipsychotics are associated with significant adverse effects including extrapyramidal symptoms, metabolic complications, and weight gain that can impact adherence and long-term health outcomes.

Cobenfy (xanomeline and trospium) is a FDA-approved non-dopaminergic antipsychotic. It combines xanomeline (a muscarinic agonist) with trospium (a peripheral muscarinic antagonist added to reduce side effects). Clinical trials demonstrated efficacy in reducing schizophrenia symptoms without the metabolic and movement disorder adverse effects typically associated with current antipsychotics.

Definitions

"**Atypical Antipsychotic**" is a class of medications, also known as second-generation antipsychotics, that are primarily used to treat psychiatric conditions. Unlike the first-generation antipsychotics, these drugs are less likely to produce extrapyramidal side effects but more likely to cause weight gain and metabolic abnormalities.

"**Child-Pugh Score**" is a scoring system used to assess the prognosis of chronic liver disease and cirrhosis. Classes are:

- Class A (5-6 points): Mild liver disease (well-compensated disease).
- Class B (7-9 points): Moderate liver disease (significant functional compromise).
- Class C (10-15 points): Severe liver disease (decompensated disease).

"Schizophrenia" is a psychiatric disorder involving chronic or recurrent psychosis and is commonly associated with impairments in social and occupational functioning.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Cobenfy (xanomeline and trospium)** medically necessary when **ALL** of the following criteria are met:

1. The medication is prescribed by or in consultation with a psychiatrist; ***AND***
2. The member is 18 years of age or older; ***AND***
3. The member has a diagnosis of schizophrenia; ***AND***
4. Clinical documentation is provided demonstrating at least **ONE** of the following:
    a. Documented trial and failure of at least **TWO** different antipsychotics, each tried for at least 4 weeks at adequate doses, where at least one trial must be a second-generation (atypical) antipsychotic, such as:
        i. aripiprazole; ***and/or***
        ii. asenapine; ***and/or***
        iii. lurasidone; ***and/or***
        iv. olanzapine; ***and/or***
        v. paliperidone; ***and/or***
        vi. quetiapine; ***and/or***
        vii. risperidone; ***and/or***
        viii. ziprasidone; ***and/or***
    b. Documentation of significant adverse effects with other antipsychotics, such as:

i. Demonstrated history of significant metabolic complications (e.g., diabetes, significant weight gain, dyslipidemia) with other antipsychotic medications; ***and/or***
ii. Severe extrapyramidal symptoms; ***and/or***
iii. Tardive dyskinesia; ***and/or***

c. Clinical rationale for why **ALL** other Formulary antipsychotics are not appropriate; ***AND***

5. The member does **NOT** have **ANY** of the following:
   a. Current urinary retention; ***or***
   b. Moderate to severe hepatic impairment (Child-Pugh Class B or C); ***or***
   c. Untreated narrow-angle glaucoma; ***or***
   d. Known hypersensitivity to either active component (xanomeline or trospium chloride); ***or***
   e. Moderate to severe renal impairment (eGFR <60 mL/min); ***AND***
6. The member is not currently using and will not use Cobenfy (xanomeline and trospium) concurrently with other antipsychotic medications, except:
   a. During cross-titration period when switching from another antipsychotic, which should not exceed 30 days; ***and***
   b. Documentation of cross-titration plan is provided; ***AND***
7. Cobenfy (xanomeline and trospium) 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 12-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12-months will be granted if the member has recent (within the last 3 months) documentation from the prescriber indicating **BOTH** of the following:

1. The member has experienced a documented clinical benefit from therapy as evidenced by:
   a. Reduction in psychotic symptoms (e.g., hallucinations, delusions, disorganized thinking); ***or***
   b. Maintenance of psychiatric stability (i.e., stability or improvement in functional status); ***or***
   c. Reduction in hospitalizations or acute episodes; ***or***
   d. Member/caregiver report of symptomatic improvement; ***or***
   e. Improved ability to function; ***or***

2. The member is not currently using and will not use Cobenfy (xanomeline and trospium) concurrently with other antipsychotic medications.
   NOTE: If claims history shows concurrent antipsychotic fills, prescriber must provide clinical rationale or documentation of active cross-titration.

Experimental or Investigational / Not Medically Necessary

Cobenfy (xanomeline and trospium) 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:

- Treatment of conditions other than schizophrenia, including:
  - Schizoaffective disorder.
  - Bipolar disorder.
  - Major depressive disorder.
  - Alzheimer's disease.
  - Other psychiatric or neurological conditions.
- Use in combination with other antipsychotic medications outside of short-term cross-titration periods.
- Use in pediatric members (under age 18).
- Use for primary treatment of negative symptoms of schizophrenia.

References

1. By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023 Jul;71(7):2052-2081. doi: 10.1111/jgs.18372. Epub 2023 May 4. PMID: 37139824.
2. Cobenfy (xanomeline and trospium) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; September 2024.
3. Keepers GA, Fochtmann LJ, Anzia JM, Benjamin S, Lyness JM, Mojtabai R, Servis M, Walaszek A, Buckley P, Lenzenweger MF, Young AS, Degenhardt A, Hong SH; (Systematic Review). The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia. Am J Psychiatry. 2020 Sep 1;177(9):868-872. doi: 10.1176/appi.ajp.2020.177901. PMID: 32867516.
4. Kidambi N, Elsayed OH, El-Mallakh RS. Xanomeline-Trospium and Muscarinic Involvement in Schizophrenia. Neuropsychiatr Dis Treat. 2023 May 10;19:1145-1151. doi: 10.2147/NDT.S406371. PMID: 37193547; PMCID: PMC10183173.

Clinical Guideline Revision / History Information

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