Clinical Policy: Xanomeline/Trospium Chloride (Cobenfy)

Reference Number: CP.PMN.299
Effective Date: 01.01.25
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Xanomeline/trospium chloride (Cobenfy™) is a combination of xanomeline, a muscarinic agonist, and trospium chloride, a muscarinic antagonist.

FDA Approved Indication(s)

Cobenfy is indicated for the treatment of schizophrenia in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Cobenfy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia (must meet all):

1. Diagnosis of schizophrenia;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with a psychiatrist or mental health specialist (*see Appendix E*);
4. Member meets one of the following (a, b, or c):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of a ≥ 4-week trial of one of the following generic atypical antipsychotics at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: risperidone, quetiapine, olanzapine, ziprasidone;
   c. Member has diabetes mellitus or body mass index (BMI) > 30;
5. Member meets one of the following (a or b):
   a. Request is for the treatment of a member in a State with limitations on step therapy in certain mental health settings (*see Appendix D*);
   b. Failure of a ≥ 4-week trial of aripiprazole at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed both of the following (a and b):
   a. 250 mg/60 mg per day;
   b. 2 capsules per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Schizophrenia (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Cobenfy for schizophrenia and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 250 mg/60 mg per day;
   b. 2 capsules per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BMI: body mass index

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
aripiprazole (Abilify®)	10 to 15 mg PO QD	30 mg/day
olanzapine (Zyprexa®)	Initial: 5 to 10 mg PO QD; target: 10 mg PO QD	20 mg/day
quetiapine immediate-release (Seroquel®)	Initial: 25 mg PO BID; target: 400 to 800 mg/day	800 mg/day
risperidone (Risperdal®)	Initial: 1 mg PO BID or 2 mg PO QD; target: 4 to 8 mg PO QD	16 mg/day
ziprasidone (Geodon®)	Initial: 20 mg PO BID	160 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): urinary retention, moderate or severe hepatic impairment, gastric retention, history of hypersensitivity to Cobenfy or trospium chloride, untreated narrow-angle glaucoma
- Boxed warning(s): none reported

Appendix D: States with Limitations against Redirections in Certain Mental Health Settings

State	Step Therapy Prohibited?	Notes
AR	Yes	**Applies to HIM requests only**

State	Step Therapy Prohibited?	Notes
		For the treatment of psychosis and serious mental illness through antipsychotic prescription drugs, no step therapies allowed.
NV	No	**Applies to Medicaid requests only** Failure of a ≥ 4-week trial of ONE preferred atypical antipsychotic (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, olanzapine) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated
TX	No	**Applies to HIM requests only** Failure of a ≥ 4-week trial of ONE of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: aripiprazole, risperidone, quetiapine, olanzapine, ziprasidone

Appendix E: Prescriber Restriction

- Prescriber restriction was implemented based on specialist feedback recommendation. The rationale is due to Cobenfy's unique mechanism of action as a first-in-class therapy and to ensure appropriate use while awaiting additional long-term data on the drug's safety and efficacy.
- Mental health specialists can include any of the following: clinical psychologists, psychiatric mental health nurse practitioners, psychiatric physician assistants, and therapists or counselors.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Schizophrenia	Initiate at 50 mg/20 mg PO BID for 2 days, then 100 mg/20 mg PO BID for at least 5 days. Dosage may be increased to 125 mg/30 mg PO BID based on patient tolerability and response.	250 mg/60 mg per day
	Geriatric patients: Initiate at 50 mg/20 mg PO BID. Consider a slower titration.	200 mg/40 mg per day

VI. Product Availability

Capsules: 50 mg/20 mg, 100 mg/20 mg, 125 mg/30 mg

VII. References

1. Cobenfy Prescribing Information. Princeton, NJ: Karuna Therapeutics, Inc., a Bristol Myers Squibb company; September 2024. Available at: www.cobenfy.com. Accessed October 14, 2024.
2. Keepers G, Fochtmann L, Anzia J, et al. APA Practice guideline for the treatment of patients with schizophrenia, third edition. Am J Psychiatry. 2020 Sept;177(9):868-872.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	11.05.24	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.