COBENFY™
(xanomeline and trospium chloride) capsules
50mg/20mg, 100mg/20mg, 125mg/30mg

INPATIENT

PRODUCT OVERVIEW

First-in-Class M_1/M_4 Muscarinic Agonist[1-3*]

For the treatment of adults with schizophrenia

Indication and Usage

COBENFY is a combination of xanomeline, a muscarinic agonist, and trospium chloride, a muscarinic antagonist, indicated for the treatment of schizophrenia in adults.

*COBENFY is the first antipsychotic drug approved to treat schizophrenia that targets muscarinic receptors. COBENFY does not bind to dopamine receptors.[1,4]

Capsules not shown at actual size.

INDICATION

COBENFY™ (xanomeline and trospium chloride) is indicated for the treatment of schizophrenia in adults.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

COBENFY is contraindicated in patients with:

- urinary retention
- moderate (Child-Pugh Class B) or severe (Child-Pugh Class C) hepatic impairment
- gastric retention
- history of hypersensitivity to COBENFY or trospium chloride. Angioedema has been reported with COBENFY and trospium chloride.
- untreated narrow-angle glaucoma

WARNINGS AND PRECAUTIONS

Risk of Urinary Retention: COBENFY can cause urinary retention. Geriatric patients and patients with clinically significant bladder outlet obstruction and incomplete bladder emptying (e.g., patients with benign prostatic hyperplasia (BPH), diabetic cystopathy) may be at increased risk of urinary retention.

COBENFY is contraindicated in patients with pre-existing urinary retention and is not recommended in patients with moderate or severe renal impairment.

In patients taking COBENFY, monitor for symptoms of urinary retention, including urinary hesitancy, weak stream, incomplete bladder emptying, and dysuria. Instruct patients to be aware of the risk and promptly report symptoms of urinary retention to their healthcare provider. Urinary retention is a known risk factor for urinary tract infections.

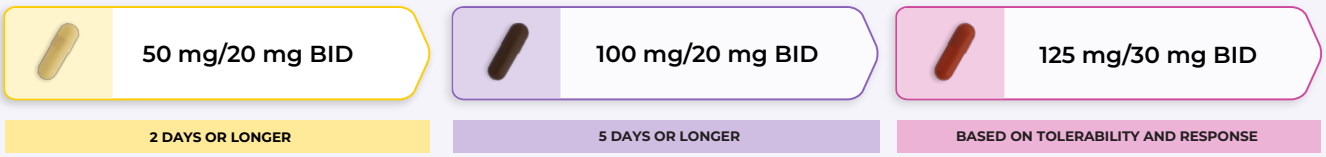
Please see additional Important Safety Information throughout and U.S. Full Prescribing Information, including Patient Information here.

COBENFY Dosage and Titration Schedule[1]

Starting dosage

- 50 mg/20 mg is not a therapeutic dose.

Maintenance dosages



- COBENFY is taken orally and dose is expressed as mg xanomeline/mg trospium chloride.
- Capsules not shown at actual size.

BID=twice daily

Titration considerations:

Only 100 mg/20 mg and 125 mg/30 mg are therapeutic doses

Initial onset of nausea and vomiting generally declined with **continued titration to 125 mg/30 mg[5a]**

91% of patients who completed the 5-week EMERGENT trials **were on 125 mg/30 mg[6b]**

[a]Percent of patients with first occurrence of nausea or vomiting by week, respectively: Week 1: 11.2% and 8.0%; Week 2: 3.6% and 4.0%; Week 3: 1.6% and 1.6%; Week 4: 2.0% and 0.4%; Week 5: 0.8% and 1.2%.[7]
[b]In EMERGENT-1, -2, & -3, 245 of 314 COBENFY patients finished the trials; 222 patients completed the trials at 125 mg/30 mg. Among those who increased to 125 mg/30 mg BID, 5% reduced their dosage back down to 100 mg/20 mg BID[5,8,9]

Dosing in geriatric patients: The recommended starting dosage of COBENFY is 50 mg/20 mg orally BID. Consider a slower titration for geriatric patients. The maximum recommended dosage in geriatric patients is 100 mg/20 mg BID.[1]

Recommended testing and monitoring: Assess liver enzymes, bilirubin, and heart rate before starting COBENFY and as clinically indicated.

Oral Administration[1]

1 capsule when waking up
1 capsule before going to bed

- Do not open capsules
- BID dosing important due to half-life of components (5-6 hours)
- Taking COBENFY with food could increase the likelihood of procholinergic side effect [1]

COBENFY should be taken orally on an empty stomach at least one hour before meals or at least two hours after meals. Do not open the capsules.

IMPORTANT SAFETY INFORMATION (CONT.)

WARNINGS AND PRECAUTIONS (CONT.)

Risk of Urinary Retention: (CONT.) In patients with symptoms of urinary retention, consider reducing the dose of COBENFY, discontinuing COBENFY, or referring patients for urologic evaluation as clinically indicated.

Risk of Use in Patients with Hepatic Impairment: Patients with hepatic impairment have higher systemic exposures of xanomeline, a component of COBENFY, compared to patients with normal hepatic function, which may result in increased incidence of COBENFY-related adverse reactions.

COBENFY is contraindicated in patients with moderate or severe hepatic impairment. COBENFY is not recommended in patients with mild hepatic impairment.

Assess liver enzymes prior to initiating COBENFY and as clinically indicated during treatment.

Risk of Use in Patients with Biliary Disease: In clinical studies with COBENFY, transient increases in liver enzymes with rapid decline occurred, consistent with transient biliary obstruction due to biliary contraction and possible gallstone passage.

COBENFY is not recommended for patients with active biliary disease such as symptomatic gallstones. Assess liver enzymes and bilirubin prior to initiating COBENFY and as clinically indicated during treatment. The occurrence of symptoms such as dyspepsia, nausea, vomiting, or upper abdominal pain should prompt assessment for gallbladder disorders, biliary disorders, and pancreatitis, as clinically indicated.

Please see additional Important Safety Information throughout and U.S. Full Prescribing Information, including Patient Information here.

Distribution

COBENFY is readily available for anyone who is prescribed it, supplied via an open distribution network through hospitals, mail-order pharmacies, specialty pharmacies, office-based physicians, and retail pharmacies including Genoa Healthcare for on-site service in care facilities.

Pharmacies can access COBENFY through Bristol Myers Squibb (BMS) authorized distributors by scanning the QR Code.

Return Goods Policy

COBENFY is eligible for return goods credit under the BMS U.S. Pharmaceuticals Return Goods Policy, which applies to the U.S. and U.S. territories.

For hospitals, BMS offers a dedicated return goods program that provides credit for all COBENFY returns, regardless of expiry date or whether the product is in its original manufacturer container. No enrollment is required to request a return; simply follow the steps outlined in the BMS U.S. Pharmaceuticals Return Goods Policy. Eligibility is limited to hospital in-patient pharmacy class of trade only.

For complete details on terms, conditions, and return procedures, please contact your primary distributor.

Storage[1]

Store at 68°F to 77°F (20°C to 25°C); excursions permitted to 59°F to 86°F (15°C to 30°C).

Supply Formats of COBENFY Capsules[1]

Designed for the hospital setting—from packaging through returns

Strength	Capsules Per Package	Package Configuration	NDC
Hospital Unit-Dose 10 x 10 Blister Packs			
50 mg/20 mg	100	10 Blister Cards with 10 Capsules Each	0003-0050-98
100 mg/20 mg	100	10 Blister Cards with 10 Capsules Each	0003-1100-98
125 mg/30 mg	100	10 Blister Cards with 10 Capsules Each	0003-0125-98
30-Day Bottles			
50 mg/20 mg	60	Bottle	0003-0050-60
100 mg/20 mg	60	Bottle	0003-1100-60
125 mg/30 mg	60	Bottle	0003-0125-60
Starter Pack for 100 mg/20 mg Dose			
Starting Dose: 50 mg/20 mg (4) **Therapeutic Dose:** 100 mg/20 mg (52)	56	**1 Mixed Blister Wallet:** four (4) 50 mg/20 mg capsules and ten (10) 100 mg/20 mg capsules **3 Wallets:** fourteen (14) 100 mg/20 mg capsules in each wallet	0003-5200-56

NDC=National Drug Code.

IMPORTANT SAFETY INFORMATION (CONT.)

WARNINGS AND PRECAUTIONS (CONT.)

Risk of Use in Patients with Biliary Disease (CONT.) Discontinue COBENFY in the presence of signs or symptoms of substantial liver injury such as jaundice, pruritus, or alanine aminotransferase levels more than five times the upper limit of normal or five times baseline values.

Please see additional Important Safety Information throughout and U.S. Full Prescribing Information, including Patient Information here.

To learn more about patient support resources for COBENFY, contact your Bristol Meyers Squibb representative.

IMPORTANT SAFETY INFORMATION (CONT.)

WARNINGS AND PRECAUTIONS (CONT.)

Decreased Gastrointestinal Motility: COBENFY contains trospium chloride. Trospium chloride, like other antimuscarinic agents, may decrease gastrointestinal motility. Administer COBENFY with caution in patients with gastrointestinal obstructive disorders because of the risk of gastric retention. Use COBENFY with caution in patients with conditions such as ulcerative colitis, intestinal atony, and myasthenia gravis.

Risk of Angioedema: Angioedema of the face, lips, tongue, and/or larynx has been reported with COBENFY and trospium chloride, a component of COBENFY. In one case, angioedema occurred after the first dose of trospium chloride. Angioedema associated with upper airway swelling may be life-threatening. If involvement of the tongue, hypopharynx, or larynx occurs, discontinue COBENFY and initiate appropriate therapy and/or measures necessary to ensure a patent airway. COBENFY is contraindicated in patients with a history of hypersensitivity to trospium chloride.

Risk of Use in Patients with Narrow-angle Glaucoma: Pupillary dilation may occur due to the anticholinergic effects of COBENFY. This may trigger an acute angle closure attack in patients with anatomically narrow angles. In patients known to have anatomically narrow angles, COBENFY should only be used if the potential benefits outweigh the risks and with careful monitoring.

Increases in Heart Rate: COBENFY can increase heart rate. Assess heart rate at baseline and as clinically indicated during treatment with COBENFY.

Anticholinergic Adverse Reactions in Patients with Renal Impairment: Trospium chloride, a component of COBENFY, is substantially excreted by the kidney. COBENFY is not recommended in patients with moderate or severe renal impairment (estimated glomerular filtration rate (eGFR) <60 mL/min). Systemic exposure of trospium chloride is higher in patients with moderate and severe renal impairment. Therefore, anticholinergic adverse reactions (including dry mouth, constipation, dyspepsia, urinary tract infection, and urinary retention) are expected to be greater in patients with moderate and severe renal impairment.

Central Nervous System Effects: Trospium chloride, a component of COBENFY, is associated with anticholinergic central nervous system (CNS) effects. A variety of CNS anticholinergic effects have been reported with trospium chloride, including dizziness, confusion, hallucinations, and somnolence. Monitor patients for signs of anticholinergic CNS effects, particularly after beginning treatment or increasing the dose. Advise patients not to drive or operate heavy machinery until they know how COBENFY affects them. If a patient experiences anticholinergic CNS effects, consider dose reduction or drug discontinuation.

Most Common Adverse Reactions (≥5% and at least twice placebo): nausea, dyspepsia, constipation, vomiting, hypertension, abdominal pain, diarrhea, tachycardia, dizziness, and gastroesophageal reflux disease.

Use in Specific Populations:

- Moderate or Severe Renal Impairment: Not recommended
- Mild Hepatic Impairment: Not recommended

Pregnancy and Lactation: There is a pregnancy exposure registry that monitors outcomes in women exposed to psychiatric medications, including COBENFY, during pregnancy. Healthcare providers are encouraged to advise patients to register by calling 1-866-961-2388 or visiting **https://womensmentalhealth.org/research/pregnancyregistry/atypicalantipsychotic/**.

There are no available data on COBENFY use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Additionally, there are no data on the presence of xanomeline or trospium in human milk, the effects on the breastfed infant, or the effects on milk production. However, xanomeline and trospium are present in animal milk, suggesting they may also be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COBENFY and any potential adverse effects on the breastfed infant from COBENFY or the underlying maternal condition.

COBENFY (xanomeline and trospium chloride) is available in 50mg/20mg, 100mg/20mg, and 125mg/30mg capsules.

Please see U.S. Full Prescribing Information, including Patient Information here.

References: 1. COBENFY [package insert]. Princeton, NJ: Bristol Myers Squibb Company; 2026. **2.** Kaul I, Sawchak S, Walling DP, et al. Efficacy and safety of xanomeline-trospium chloride in schizophrenia: a randomized clinical trial. *JAMA Psychiatry*. 2024;81(8):749-756. **3.** Paul SM, Yohn SE, Popiolek M, Miller AC, Felder CC. Muscarinic acetylcholine receptor agonists as novel treatments for schizophrenia. *Am J Psychiatry.* 2022;179(9):611-627. doi: 10.1176/appi.ajp.21101083 **4.** FDA Press Release. Published September 26, 2024. Accessed January 28, 2026. https://www.fda.gov/news-events/press-announcements/fda-approves-drug-new-mechanism-action-treatment-schizophrenia **5.** Dyme R, et al. Presented at: Psych Congress; September 17-21, 2025; San Diego, CA. **6.** Data on file, REF-03512-1629. Karuna Therapeutics, Inc., a Bristol Myers Squibb company; Boston, MA. **7.** Data on file, REF-02364-1629. Karuna Therapeutics, Inc., a Bristol Myers Squibb company; Boston, MA. **8.** Data on file, REF-02460-1629. Karuna Therapeutics, Inc., a Bristol Myers Squibb company; Boston, MA. **9.** Data on file, REF-00441-1629. Karuna Therapeutics, Inc., a Bristol Myers Squibb company; Boston, MA.

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