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

Dosing and Administration Guide

How to get patients started with COBENFY

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.

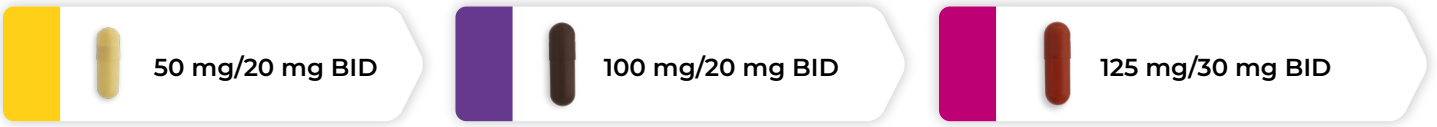
COBENFY is contraindicated in patients with pre-existing urinary retention and is not recommended in patients with moderate or severe renal impairment.

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

COBENFY offers flexible titration[1]

Starting dosage[1]

Recommended dosages[1]



Capsules not shown at actual size.

At least 2 days → At least 5 days → Based on tolerability and response

Start at 50 mg/20 mg orally BID for at least 2 days. Increase to 100 mg/20 mg BID for at least 5 days. Dosage may be increased to 125 mg/30 mg BID based on patient tolerability and response. Maximum recommended dosage is 125 mg/30 mg BID.[1]

COBENFY is taken orally and dose is expressed as mg xanomeline/mg trospium chloride.[1]

Geriatric dosing[1]

- Recommended starting dosage is 50 mg/20 mg orally BID
- Consider a slower titration
- Maximum recommended dosage is 100 mg/20 mg BID

Your patients can start and end their day with COBENFY

1 capsule when waking up[1]

1 capsule before going to bed[1]

COBENFY should be dosed BID on an empty stomach **at least 1 hour before or at least 2 hours after a meal**. Not following dosing recommendations may result in increased side effects.[1]

Recommended testing and monitoring prior to initiation and during treatment[1]

- Recommended to assess heart rate at baseline and as clinically indicated during treatment
- Recommended to assess liver enzymes and bilirubin prior to initiating COBENFY and as clinically indicated during treatment

BID=twice daily.

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS (Cont'd)

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

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Options to start and stay on COBENFY

Starter titration pack (28-day supply)[1]

In this starter pack:

1 Mixed Blister Wallet (Titration):
Four (4) 50 mg/20 mg capsules (2 days) and ten (10) 100 mg/20 mg capsules (5 days)
3 Wallets (Maintenance):
Fourteen (14) 100 mg/20 mg capsules (7 days)
NDC 0003-5200-56

Maintenance bottles (30-day supply)[1]

60-count bottles

50 mg/20 mg
NDC 0003-0050-60

100 mg/20 mg
NDC 0003-1100-60

125 mg/30 mg
NDC 0003-0125-60

Start COBENFY with available samples

Titration Sample Pack: Four (4) 50 mg/20 mg capsules (2 days) and ten (10) 100 mg/20 mg capsules (5 days)

14-count wallets (7 days) available, containing: 50 mg/20 mg capsules; 100 mg/20 mg capsules; 125 mg/30 mg capsules

Sample packs are not for sale or reimbursement.

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS (Cont'd)

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.

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Your guide to prescribing COBENFY

Studied titration[1]

COBENFY titration pack
100 mg/20 mg maintenance dose

Rx

Quantity: One (1) 28-day titration pack

Directions:

- **50 mg/20 mg** PO BID for 2 days
- **100 mg/20 mg** PO BID for 5 days
- **100 mg/20 mg** PO BID for 21 days

Dispense: One (1) pack (28-day supply)

Refill: 0

Example of slower titration[1]

Based on HCP assessment of patient response and tolerability

Optional titration example to 100 mg/20 mg

Rx

COBENFY

Rx 1

50 mg/20 mg
PO BID x 7 days
Disp #14
Refill: 0

Rx 2

100 mg/20 mg
PO BID x 30 days
Disp #60
Refill:
Per HCP direction

BID=twice daily; PO=by mouth.

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS (Cont'd)

Risk of Use in Patients with Biliary Disease (Cont'd): 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.

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.

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Clinical considerations with COBENFY

Understanding drug interactions

Monitor your patients for increased frequency and/or severity of adverse reactions[1-7]

Drug categories	Considerations
Strong Inhibitors of CYP2D6 *(e.g., fluoxetine, paroxetine, bupropion, terbinafine)**	May increase plasma concentrations of xanomeline, which may increase the frequency and/or severity of adverse reactions from COBENFY
Sensitive Substrates of CYP3A4 *(e.g., buspirone, eletriptan)**	May result in increased plasma concentrations of these medications, which may increase the frequency and/or severity of adverse reactions from such substrates
Narrow Therapeutic Index Substrates of P-glycoprotein *(e.g., digoxin, colchicine, apixaban)*	
Drugs Eliminated by Active Tubular Secretion	May increase plasma concentrations of trospium, a component of COBENFY, and/or these types of medications, which may increase the frequency and/or severity of adverse reactions from COBENFY and/or these medications
Antimuscarinic Drugs *(e.g., diphenhydramine, benztropine, oxybutynin)**	Use of COBENFY with other antimuscarinic drugs that produce anticholinergic adverse reactions (e.g., dry mouth, constipation) may increase the frequency and/or severity of such effects

COBENFY may potentially alter the absorption of some concomitantly administered drugs due to anticholinergic effects on gastrointestinal motility[1]

Dosage adjustment of concomitant medications may be necessary based on clinical response and tolerability

Anticholinergics (muscarinic antagonists) and muscarinic agonists may affect the pharmacological activity of one another.

*This is not an exhaustive list and is only used to show clinically relevant examples of medications. For a full list, visit FDA.gov.[2]
CYP2D6=cytochrome P450 2D6; CYP3A4=cytochrome P450 3A4.

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS (Cont'd)

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.

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One chat away...
Request your COBENFY Representative through our chatbot

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS (Cont'd)

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

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References: 1. COBENFY. Prescribing Information. Bristol Myers Squibb Company; 2024. **2.** For healthcare professionals | FDA's examples of drugs that interact with CYP enzymes and transporter systems. U.S. Food & Drug Administration. Accessed October 1, 2024. https://www.fda.gov/drugs/drug-interactions-labeling/healthcare-professionals-fdas-examples-drugs-interact-cyp-enzymes-and-transporter-systems#table%201 **3.** Muscarinic antagonists. DrugBank Online. Accessed October 1, 2024. https://go.drugbank.com/categories/DBCAT000534 **4.** Hansten PD, Tan MS, Horn JR, et al. Colchicine drug interaction errors and misunderstandings: recommendations for improved evidence-based management. *Drug Saf.* 2023;46(3):223-242. **5.** Ammar H, Govindu RR. A dangerous and unrecognized interaction of apixaban. *Cureus.* 2021;13(11):e19688. **6.** P-glycoprotein substrates with a narrow therapeutic index. DrugBank Online. Accessed October 1, 2024. https://go.drugbank.com/categories/DBCAT004027 **7.** Xu Y, Zhang L, Dou X, Dong Y, Guo X. Physiologically based pharmacokinetic modeling of apixaban to predict exposure in populations with hepatic and renal impairment and elderly populations. *Eur J Clin Pharmacol.* 2024;80(2):261-271.

1629-US-2400700 10/24

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