Cobenfy™ (xanomeline and trospium hydrochloride) – New drug approval

- On September 26, 2024, the FDA announced the approval of Bristol-Myers Squibb's Cobenfy (xanomeline and trospium hydrochloride capsules) or the treatment of schizophrenia in adults.

- Cobenfy is the first antipsychotic drug approved to treat schizophrenia that targets cholinergic receptors. It is a combination of xanomeline, a muscarinic agonist, and trospium chloride, a muscarinic antagonist. The current standard of care treatments target dopamine receptors.

- Schizophrenia is a mental disorder characterized by disruptions in thought processes, perceptions, emotional responsiveness, and social interactions. Symptoms of schizophrenia include psychotic symptoms such as hallucinations, delusions, and thought disorder, as well as reduced expression of emotions, reduced motivation to accomplish goals, difficulty in social relationships, motor impairment, and cognitive impairment.

    - In the US approximately 2.8 million people are living with schizophrenia. Approximately half of individuals with schizophrenia have co-occurring mental and/or behavioral health disorders.

- The safety and efficacy of Cobenfy were based on two placebo-controlled studies with identical design. Both were 5-week, randomized, double-blind, placebo-controlled, multi-center clinical trials in adults with a diagnosis of schizophrenia according to DSM-5 criteria. The primary efficacy measure was the change from baseline in the Positive and Negative Syndrome Scale (PANSS) total score at Week 5.

    - The PANSS is a 30-item scale that measures symptoms of schizophrenia. Each item is rated by a clinician on a seven-point scale.
    - In EMERGENT-2, Cobenfy demonstrated a 9.6-point reduction (-21.2 Cobenfy vs. -11.6 placebo, $p<0.0001$) in PANSS total score compared to placebo at week five.

    - In EMERGENT-3, Cobenfy demonstrated an 8.4-point reduction (-20.6 Cobenfy vs. -12.2 placebo; $p<0.0001$) in PANSS total score compared to placebo at week five.

- Warnings and precautions for Cobenfy include increased risk for urinary retention, hepatic impairment, decreased gastrointestinal motility, angioedema, glaucoma, increased heart rate, anticholinergic adverse reactions, and central nervous system effects.

- Cobenfy is contraindicated in:
    - urinary retention
    - moderate or severe hepatic impairment
    - gastric retention
    - history of hypersensitivity to COBENFY or trospium chloride
    - untreated narrow-angle glaucoma

- The most adverse reactions (incidence ≥ 5% and at least twice placebo) were nausea, dyspepsia, constipation, vomiting, hypertension, abdominal pain, diarrhea, tachycardia, dizziness, and gastrointestinal reflux disease.

- The recommended starting dosage of COBENFY is 50 mg/20 mg orally twice daily for at least two days, then increase the dosage to 100 mg/20 mg twice daily for at least five days.

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  - Dosage may be increased to 125 mg/30 mg orally twice daily based on patient tolerability and response.
  - In geriatric patients, the recommended dose is 50 mg/20 mg orally twice daily. Consider a slower titration. The maximum recommended dosage is 100 mg/20 mg twice daily.
  - Cobenfy should be taken at least 1 hour before a meal or at least 2 hours after a meal.
- Cobenfy will be available in three different strength capsules containing xanomeline/trospium chloride 50 mg/20 mg, 100 mg/20 mg, and 125 mg/30 mg.
  - Cobenfy will also be available in a Starter Pack with 4 blister wallets containing the 50 mg/20 mg and 100 mg/20 mg doses.
  - BMS plans to launch Cobenfy in mid-October.
- The WAC price is expected to be $1,850 for a 30-day supply, or $22,500 annually.

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