Acentra HEALTH

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2025 Quarter 1 Newsletter

FDA APPROVAL SPOTLIGHT

In September of 2024, the Food and Drug Administration (FDA) approved a first-in-class therapy for the treatment of schizophrenia. This marks the first drug approval for schizophrenia in 35 years. While other schizophrenia treatments fall neatly into the first- or second-generation antipsychotic categories, Cobenfy (xanomeline/trospium chloride) has a unique mechanism of action.

Neither of its components act on dopaminergic or serotonergic receptors, as is proposed for previous antipsychotic therapies. Instead, its main effect on the schizophrenia pathophysiology is through the xanomeline component. Xanomeline crosses the blood-brain barrier and acts as an agonist at the M1 and M4 muscarinic acetylcholine receptors. The full pathophysiology of schizophrenia has not been fully elucidated. However, there are multiple theories that muscarinic receptors M1 and M4 may play a role in positive and cognitive symptoms, while M5 receptor may play a role in negative symptoms. The trospium chloride component is a muscarinic antagonist. It does not cross the blood-brain barrier and, therefore, exists only to mitigate peripheral cholinergic effects.

The clinical trials researching the efficacy and safety of Cobenfy (EMERGENT-2 and EMERGENT-3) were randomized, double-blind, and placebo-controlled. These trials follow adults aged 18-65 years with a diagnosis of schizophrenia with active psychosis through a 5-week trial of Cobenfy or placebo. The primary outcome was assessed with the Positive and Negative Syndrome Scale (PANSS). To be included in the studies, participants were required to have a PANSS score of ≥80 and a Clinical Global Impression-Severity (CGIS) score of ≥4 .In Emergent-2, the least squares mean difference in PANSS score was significantly higher with Cobenfy compared to placebo (-9.6; 95% CI -13.9 to -5.2; $p<0.0001$). In Emergent-3, the least squares mean difference in PANSS score was also significantly higher with Cobenfy compared to placebo (--8.4; 95% CI -12.4 to –4.3; $p<0.001$). Nausea/vomiting, dyspepsia, and constipation were some of the more common adverse drug reactions (ADRs) in both of the studies. Notably, symptoms of movement disorders and metabolic syndrome were not significant ADRs of Cobenfy as with current first- and second-generation antipsychotics.

In 2020, the American Psychiatric Association (APA) released its most recent treatment guidelines for the management of schizophrenia. In these guidelines, the APA recommends antipsychotic therapy as the first-line treatment for schizophrenia. The only specific antipsychotic mentioned is in the case of treatment-resistant resistant depression, in which clozapine is the preferred treatment. It is well-known that long-term use of antipsychotics comes with a host

of potential ADRs, which often require further medication therapy to treat. It is likely that the unique mechanism of Cobenfy and lower risk for movement disorders and metabolic syndrome will be attractive to both prescribers and patients. However, further research must be performed to compare efficacy of Cobenfy to antipsychotics to determine its best place in therapy for the treatment of schizophrenia.

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GUIDELINE UPDATES

IDSA
Infectious Diseases Society of America

On December 30, 2024, an updated guideline on the treatment of tuberculosis (TB) was published by a joint effort of the American Thoracic Society (ATS), Center for Disease Control and Prevention (CDC), European Respiratory Society (ERS), and Infectious Diseases Society of America (IDSA). These guidelines consisted of four major updates to the previous guidelines published by the World Health Organization (WHO) in 2023. The categories of the updates are as follows: treatment of isoniazid-susceptible, rifampin-susceptible TB in adults; treatment of non-severe, presumed isoniazid-susceptible and rifampin-susceptible TB in children; treatment of rifampin-resistant, fluoroquinolone-resistant TB; treatment of rifampin-resistant, fluoroquinolone-susceptible TB. The following are the summarized recommendations:

- For the treatment of isoniazid-susceptible and rifampin-susceptible TB in patients ≥12 years of age, the conditionally recommended regimen is isoniazid, rifapentine, moxifloxacin, and pyrazinamide at standard doses for 4 months.
    - This is a change from the previously recommended ≥6 month standard regimen.

- For the treatment of non-severe, presumed isoniazid-susceptible and rifampin-susceptible TB in patients 3 months to 16 years, the strongly recommended regimen is isoniazid, rifampin, pyrazinamide, with or without ethambutol at standard doses for 2 months, followed by only isoniazid and rifampin at standard doses for 2 months.
    - This is a change from the previously recommended regimen which required the last set of isoniazid and rifampin therapies for an additional 2 months for a total of 6 months of therapy.
- For the treatment of rifampin-resistant, fluoroquinolone-resistant TB in patients ≥14 years of age, the strongly recommended regimen is bedaquiline, pretomanid, and linezolid at standard doses for 6 months, as long as the patient has been exposed to these therapies for ≤1 month.
    - This is a change from multiple ≥15-month regimens with varying degrees of success.
- For the treatment of rifampin-resistant, fluoroquinolone-susceptible TB in patients ≥14 years of age, the strongly recommended regimen is bedaquiline, pretomanid, linezolid, and moxifloxacin at standard doses for 6 months.
    - This is also a change from multiple ≥15-month regimens with varying degrees of success.

Overall, these guidelines focused on shortening therapy duration when possible. They emphasized that this has the potential to improve adherence, decrease the risk of adverse drug reactions, and minimize cost both to patients and to healthcare providers. They also noted the updated medication regimens for drug-resistant TB with the emphasis on better and more reliable efficacy. Although tuberculosis is rare in the United States (2.9 cases per 100,000 population in 2023 per the CDC), it can still have significant morbidity and mortality, as well as high rates of transfer, if not appropriately treated. Utilizing these updated guidelines will hopefully both improve outcomes for patients and minimize the spread of tuberculosis.

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LEGISLATIVE NEWS

On September 20, 2023, the Medicaid Third Party Liability Act was introduced in the House at the 118th Congress. This proposed legislation sought to update requirements for legally liable third-party insurers of Medicaid members. It sought to repeat the exception of claims for preventative pediatric care and individuals requiring child support enforcement. In these cases, Medicaid was required to pay before the third party if billed first and seek reimbursement later. This bill also sought to strengthen current requirements for Medicaid to identify third parties prior to payment by prohibiting all payments to members whose third-party liability was not officially confirmed.

These changes were introduced to modify previous rulings on third-party liability for Medicaid members by the Centers for Medicare and Medicaid Services on March 8, 2023. The Medicaid Third Party Liability Act was subsequently referred to the House Committee on Energy and Commerce on September 20, 2023 and then to the Subcommittee on Health on September 22, 2023 with no official decision made during that congressional year. On January 16, 2025, the act was brought before the House for a second time and subsequently referred again to the House Committee on Energy and Commerce that same day.

While the fate of this act is unclear, it is likely that there will be upcoming changes surrounding claims payments for Medicaid members with third-party liability coverage. It will be imperative in the coming months to closely monitor passed legislation to ensure full compliance with all Medicaid-related rulings.

References:

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