June 9, 2026

Mehmet Oz, MD
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244
ATTN: CMS-1849-P

Re: Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals (IPPS) and the Long-Term Care Hospital Prospective Payment System and Policy Changes and Fiscal Year (FY) 2027 Rates; Requirements for Quality Programs; and Other Policy Changes [CMS-1849-P]

Dear Administrator Oz:

On behalf of the Alliance for Patient Access, thank you for the opportunity to provide comment regarding the Fiscal Year 2027 Hospital Inpatient Prospective Payment System proposed rule, specifically the New Technology Add-On Payment application for Cobenfy, or xanomeline and trospium chloride.

About the Alliance for Patient Access

Founded in 2006, AfPA is a national network of policy-minded health care providers who advocate for patient-centered care. AfPA supports health policies that reinforce clinical decision-making, promote personalized care and protect the physician-patient relationship. Motivated by these principles, AfPA members participate in clinician working groups, advocacy initiatives, stakeholder coalitions and the creation of educational materials. AfPA's Mental Health Working Group convenes clinicians focused on ensuring patient-centered mental health policy and appropriate patient access.

Impact of Schizophrenia

Schizophrenia has profound personal and societal impacts, including difficulty maintaining employment, lost educational and economic opportunities, lower productivity, higher incarceration and homelessness rates, premature mortality and a significant strain on caregivers. Without reliable access to treatment, this burden only increases.

According to a recent study, the direct health care costs from this disease are more than $62 billion, while the total societal costs are nearly $281 billion.[1] The breakdown of these societal costs include a $112.3 billion annual burden on caregivers, $61.6 billion in unemployment and lost productivity costs, and $35 billion in law enforcement, homeless and income support costs. The higher premature mortality rates impose another $77.9 billion annually in economic burden. When considering the immense financial and societal impact, the value of effective treatment is of the utmost importance.

Unmet Need, Novel Mechanism of Action and Substantial Clinical Improvement

Many medications for the treatment of schizophrenia are older and come with significant side effects. Antipsychotic medications are known to often result in significant weight gain, metabolic disturbances, sedation and fluid retention, among others.[2] In addition to the previously listed impacts, many older, first-generation antipsychotics can result in a condition called tardive dyskinesia (TD). Tardive dyskinesia is a movement disorder that causes involuntary movements, often in the head or face, that can be uncomfortable – even painful – and further stigmatizing for those living with an already stigmatized condition.

These side effects can contribute to significant nonadherence rates, which can be as high as 65 percent in some studies.[3] Therefore, the need for new treatments and new mechanisms of action is immense. Fortunately, xanomeline and trospium chloride, approved by the FDA in 2024 for the treatment of schizophrenia in adults, provides an alternative. This approval provided an innovative treatment option so that patients, especially those who respond poorly to currently available treatments, may avoid many of these side effects. This treatment is novel in that it targets cholinergic receptors, as opposed to dopamine receptors, which have historically been the mechanism of action for antipsychotic medications. Xanomeline and trospium chloride has been effective in reducing schizophrenia symptoms with minimal adverse events.[4]

When considering the value to the community of individuals living with schizophrenia offered by xanomeline and trospium chloride, it is important to recognize the substantial clinical improvement that goes beyond a new mechanism of action. While the proposed rule questions the improvement offered by this treatment, we are concerned that the comparisons take an incomplete look at the larger treatment landscape for schizophrenia. While injectable antipsychotic medications might serve a role and aid in higher rates of adherence, these types of treatments might not be suitable for the larger patient population. As demonstrated by the provided data, the real-world evidence shows an

[1] Kadakia A, Catillon M, Fan Q, Williams GR, Marden JR, Anderson A, Kirson N, Dembek C. The Economic Burden of Schizophrenia in the United States. J Clin Psychiatry. 2022 Oct 10;83(6):22m14458. doi: 10.4088/JCP.22m14458. PMID: 36244006.

[2] https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/antipsychotic-medications

[3] https://pmc.ncbi.nlm.nih.gov/articles/PMC11886451/

[4] Neporent, L "Emergent Trial Data For KarXT Shows Promise in Schizophrenia" Psychiatrist.com, May 30, 2023, https://www.psychiatrist.com/news/emergent-trial-data-for-karxt-shows-promise-in-schizophrenia/.

encouraging adherence profile for a patient population that has historically struggled to maintain continuity on oral treatments.[5]

When considering the unique mechanism by which xanomeline and trospium chloride operates, the lack of negative symptoms is critical. Because xanomeline and trospium chloride does not directly impact dopamine or serotonin receptors, these negative symptoms are far less common than with the current standard of care. As these symptoms and related conditions, including unexpected weight gain, tardive dyskinesia, sexual dysfunction and hyperarousal, among others, can lead to discontinuation of treatment, xanomeline and trospium chloride provides a clear alternative to patients who otherwise would stop pursuing treatment or were unsuccessful on previous treatments. Even when patients did show signs of metabolic side effects, these were often mild to moderate in severity and resolved themselves over a 52-week course of treatment.[6] This demonstrates a significant improvement in the current standard of care, particularly for patients with a history of extensive antipsychotic use, ultimately allowing for long-term symptom reduction and improved tolerability from current options.

Conclusion

Considering the above information, AfPA encourages CMS to prioritize policies that allow and encourage new treatment options for the treatment of serious mental illness. New treatment options with novel mechanisms of action offer hope to millions living with schizophrenia. However, with restrictions in place, people will not be able to benefit from these treatment advances. We urge you to take this into account when considering the New Technology Add-On Payment application for xanomeline and trospium chloride.

If AfPA can provide further details, please contact us at 202-951-7097 or cmcpherson@allianceforpatientaccess.org.

Sincerely,

[5] Cutler, A.J., Zhong, Y., Gillard, K., Appio, J., Gao, C., Laliberte ´, F., Rubio, J.M. Real-World Use of Xanomeline-Trospium in Schizophrenia: Patient Characteristics and Antipsychotic Treatment Patterns. Presentation at Psych Congress, September 17–21, 2025, San Diego, CA

[6] https://www.psychiatrictimes.com/view/new-data-demonstrates-karxt-positive-long-term-metabolic-profile