FDA Takes New Steps to Encourage Development of Novel Medicines for Opioid Use Disorder

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FDA takes new steps to encourage the development of novel medicines for the treatment of opioid use disorder

The U.S. Food and Drug Administration today issued new scientific recommendations aimed at encouraging more widespread innovation and development of novel medication-assisted treatment (MAT) drugs for the treatment of opioid use disorder (OUD). New draft guidance issued today outlines new ways for drug developers to consider measuring and demonstrating the effectiveness and benefits of new or existing MAT products. This new draft guidance is part of the FDA's ongoing commitment to promote more widespread development, access to and adoption of MAT.

"The Trump Administration is pursuing every opportunity to address our country's opioid epidemic and support patients struggling with opioid use disorder. This work at HHS includes placing a special priority on ensuring access to a full range of safe and effective options for medication-assisted treatment," said HHS Secretary Alex Azar. "The evidence is clear: medication-assisted treatment works, and it is a key piece of defeating the drug crisis facing our country. The FDA's new guidances have the potential to bring new medications to market that are more closely tailored to patient needs and help give Americans facing addiction a better chance at recovery."

MAT for opioid dependence relies on prescription drugs, including buprenorphine, methadone and naltrexone, to stabilize brain chemistry; reduce or block the euphoric effects of opioids; relieve physiological cravings; and normalize body functions. Regular adherence to MAT helps patients gain control over their use of opioids, without causing the cycle of highs and lows associated with opioid misuse or abuse. MAT, coupled with relevant social, medical and psychological services, is a highly effective treatment for OUD. Additionally, patients receiving MAT cut their risk of death from all causes in half, according to the Substance Abuse and Mental Health Services Administration.

"As we seek to help those with an opioid use disorder transition to lives of sobriety, we recognize

there's great interest in new treatment options that result in meaningful outcomes for patients. For example, we must consider new ways to gauge success beyond simply whether a patient in recovery has stopped using opioids, such as reducing relapse overdoses and infectious disease transmission. Treatments that can impact these aspects of addiction can be important parts of a comprehensive approach to the treatment of opioid use disorder. This new guidance is an important step in fostering the development of new treatment options that help patients achieve these and other real-world outcomes, by providing a pathway for how innovators can use these clinically relevant measures as part of new drug development programs," said FDA Commissioner Scott Gottlieb, M.D. "We're committed to doing our part to expand access to high-quality, effective medication-assisted treatments and encouraging health care professionals to ensure patients with opioid use disorder are offered an adequate chance to benefit from these therapies. This work also includes improving understanding about the treatment options available for patients and countering the unfortunate stigma that's sometimes associated with their use."

Clinical trials to evaluate effectiveness of MAT for the purposes of FDA approval have generally used reduction in drug-taking behavior (drug use patterns) as an endpoint. The new draft guidance, "Opioid Use Disorder: Endpoints for Demonstrating Effectiveness of Drugs for Medication-Assisted Treatment," identifies several additional potential clinical endpoints and other outcome measures that drug developers may consider.

In the guidance, for example, the FDA encourages drug sponsors to consider a variety of ways to evaluate the effect and clinical benefit of MAT. These include the impact of a new drug on adverse outcomes like mortality (overall mortality or overdose mortality), emergency medical interventions and hepatitis C seroconversion (the period during which antibodies develop and become detectable). Efficacy may also be measured by studying the proportion of patients that transition from meeting criteria for being diagnosed with moderate to severe OUD – based on both drug use and its impact on patient wellbeing – at baseline to being considered in remission at the end of the study. Improvements in the ability to resume work, school, or other productive activity may also demonstrate clinical benefit.

While understanding that many of these outcomes could be highly valuable, the agency recognizes that evaluating them could require larger trials than those usually conducted for marketing approval. To that end, the FDA is encouraging sponsors to discuss their plans with the agency early in the drug development process. The agency is also committed to providing assistance to sponsors interested in developing a validated measurement of patient-reported experiences, such as "craving" or "urge to use" opioids, which make it difficult for patients with OUD to sustain recovery. Patient-reported experiences could be used to complement other endpoints and help determine how a new treatment's effects on such experiences support the goal of sustained clinical response.

Today's action builds on another draft guidance issued by the FDA in April that outlines the agency's current thinking about drug development and trial design issues relevant to the study of depot buprenorphine products (i.e., modified-release products for injection or implantation). The FDA also recently published a paper with the National Institute on Drug Abuse that describes

efforts to overcome some of the barriers to new drug development and the issues with determining effectiveness. In an effort to adequately incorporate patient experience into the drug development and review paradigm, the agency also held a meeting in April to hear from directly from those with OUD on a wide range of topics, including the effects on their health and well-being that have the greatest impact on daily life, their experience using prescription medical treatments and other treatments or therapies for OUD, and challenges or barriers to accessing or using medical treatments for OUD.

As part of HHS' Five-Point Strategy to Combat the Opioid Crisis, the FDA remains committed to addressing the epidemic on all fronts, with a significant focus on decreasing exposure to opioids and preventing new addiction by taking new steps to encourage more appropriate prescribing; supporting the treatment of those with OUD and promoting the development of improved as well as lower cost forms of MAT; fostering the development of novel pain treatment therapies that may not be as addictive as opioids, and opioids more resistant to abuse and misuse; and taking action against those who contribute to the illegal importation and sale of opioid products. The FDA will also continue to evaluate how drugs currently on the market are used, in both medical and illicit settings, and take regulatory action where needed.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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