MDMA Close to Being Legal Medicine as FDA Grants Priority Review

BY ALEXANDER LEKHTMAN FEBRUARY 15, 2024

MDMA is getting ever closer to becoming a legal medicine. The federal Food and Drug Administration (FDA) is now expediting review of an application which, if approved, would allow doctors to prescribe the psychedelic for people experiencing post-traumatic stress disorder (PTSD). Federal approval for an often-demonized drug would be historic, and the Drug Enforcement Administration (DEA) would then have to reschedule it. But the next challenge would be finding a way to make the treatment affordable for people in need.

On February 9, pharmaceutical company Lykos Therapeutics announced that the FDA has accepted and is reviewing its

application, submitted in December, for "[MDMA] capsules used in combination with psychological intervention, which includes psychotherapy (talk therapy) and other supportive services provided by a qualified healthcare provider for individuals with [PTSD]." The FDA has now granted the application "priority review" status as requested, meaning it should make a decision by August 11.

"Securing priority review for our investigational MDMA-assisted therapy is a significant accomplishment and underscores the urgent unmet need for new innovation in the treatment of PTSD," stated Lykos CEO Amy Emerson. "We remain focused on working with the FDA through the review process and preparing for a controlled launch with an emphasis on quality should this potential treatment be approved."

The company, formerly known as MAPS Public Benefit Corporation, was created by the nonprofit Multidisciplinary Association for Psychedelic Studies (MAPS). The company's application includes results from its recent clinical research, which builds on nearly 30 years of work. Its "Phase 3" research, the final experimental stage before you gather and submit data to the FDA, was published in the *Nature Medicine* journal in September 2023.

The future of this MDMA treatment could be impacted by a change in the company seeking to bring it to market. MAPS PBC, as it was then, was a wholly owned subsidiary of MAPS, and raised funds from philanthropic donors. But in January, it announced it had completed an "oversubscribed" stock sale, raising over $100 million from private investors.

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The transformed entity re-branded as Lykos Therapeutics, with CEO Emerson retaining that role. Six members of Lykos' board of directors are to be appointed by MAPS, with two (including Emerson) representing shareholders. MAPS is the largest shareholder in Lykos, but holds less than half of the total stock.

"The decisions to be made at Lykos, even though it is a public benefit corporation, will, of necessity, include responsibilities to private stockholders," said Rick Doblin, the founder and former executive director of MAPS, and a Lykos board member. "These decisions will not always be the decisions that the nonprofit MAPS would have made if we had remained the sole owner … responsible only to our donors and to advancing public benefit."

The company's Phase 3 research included two studies, one for patients with severe PTSD, the other for people with "moderate to severe" cases. The latter looked at a group of 104 adult patients, who were

randomly split into two groups—one given the drug MDMA, the other a placebo—and all received the same psychotherapy. Compared to placebo, MDMA resulted in improved scores for PTSD symptoms and disability over 18 weeks. At the end of the study, over 71 percent of these patients no longer met the diagnostic criteria for PTSD.

"MDMA simultaneously induces prosocial feelings and softens responses to emotionally challenging and fearful stimuli," the researchers wrote, "potentially enhancing the ability of individuals with PTSD to benefit from psychotherapy by reducing sensations of fear, threat and negative emotionality."

No major safety issues came up during the study, the researchers stated. That said, the drug was not risk-free—most participants experienced at least one negative side effect from the treatment, though none life-threatening. Side effects included heart symptoms like palpitations, elevated blood pressure, muscle tightness, nausea, sweating or decreased appetite. Psychiatric side effects included anxiety and insomnia. Some participants also experienced suicidal ideation, but MDMA was not found to increase the risk of it (the study excluded people deemed to be at high suicide risk).

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The FDA will take the next several months to review these findings, and decide if the drug "[provides] benefits that outweigh its known and potential risks for the intended population." If the FDA approves the application, the DEA will have to take the important next step of rescheduling MDMA.

Currently, the drug is in Schedule I, the most restrictive of five federal categories for controlled substances—illegal for any use, including medical. The DEA would need to categorize it as Schedule II or lower, making it legal for a doctor to prescribe it.

In that event, the DEA would have to hold public hearings before making its decision within 90 days. This is an important step, because it would determine the level of restrictions and scrutiny to be placed on doctors and pharmacists.

Schedule II, which includes cocaine, methamphetamine and fentanyl, sets the strictest rules on writing prescriptions, which cannnot be refilled—it's one and done. Schedule III drugs, including ketamine and anabolic steroids, can be prescribed orally, and can be refilled for up to six months, though no more than five times.

MDMA becoming a legal medicine could be very positive for people with PTSD. They'd be able to receive a regulated dose of known composition—nothing like buying on the unregulated market. They

would use it with therapeutic support, and evidence indicates most would benefit.

But making MDMA legal is not the same as making it accessible. When MDMA treatment is projected to cost thousands or even tens of thousands of dollars, large numbers of people will be excluded. A 2022 review estimated that MDMA therapy, as conducted in the trials, costs over $11,000 per patient—although it would generates significant lifetime *savings* in health care costs.

The price tag is due to a number of factors—all related to the broken US for-profit health care system. Most projected costs relate to the services that would be required to accompany the drug, rather than the drug itself. You'd likely have to visit a clinic, potentially involving an overnight stay, and use MDMA under supervision of one or more trained and licensed psychotherapists, paid to sit with you for hours while you're under the influence.

Treatment guidelines in the Phase 3 research involved three 90-minute "preparation" sessions before taking the drug, then three eight-hour "dosing" sessions. Finally there was a 90-minute "integration" session, to talk about your feelings on how it went.

If you've ever gone to see a counselor, you know it's not cheap, even with health insurance. And it's not entirely clear if health insurance companies would pay for MDMA treatment, in full or partially—though that could change.

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Much would depend on factors like if the medical establishment embraces MDMA treatment, costs versus demonstrated savings of treatment, and how clinical outcomes compare to existing PTSD treatments. But ultimately, health insurance companies will have a great deal of discretion. And of course none of this would do anything for the estimated 27 million Americans without health insurance. Many people from lower-income and marginalized backgrounds—the very populations that might benefit most from PTSD treatment—will simply not have access, unless large numbers of providers are prepared to eat at least some of the cost of treatment.

"There are so many different ways people are seeking to answer this question, beyond MAPS, [that] I'm really inspired by," Betty Aldworth, communications director for MAPS, told *Filter*. **"**You've got nonprofit therapy clinics popping up, perhaps currently providing ketamine therapy but with the intent to provide other psychedelic-assisted therapies as they become available, on a sliding scale or with scholarship programs. There are a variety of different foundations and

philanthropic efforts to address the cost of the therapy itself. You see individual organizations and clinics working together across the field to see how we're going to answer that question."

Despite that major issue, the rapid progress toward legalization of medical MDMA is a victory for the psychedelic movement. It validates literally decades of work—from activists, underground providers, community organizers, academics and clinicians—to show that a vilified drug has real therapeutic value.

"I do think this is a beacon of hope for people researching the potential benefits of psychedelics to address very serious mental health conditions that have insufficient treatments available," Aldworth said. "The fact the FDA accepted this application certainly sends a signal that other studies that have similarly careful research methods might lead to more new drug applications for other substances and other conditions."