Pinney Associates

31 May 2024

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
Via https://www.regulations.gov

Re: Docket No. FDA-2024-N-1938 for Psychopharmacologic Drugs Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments – Midomafetamine Capsules

Dear Food and Drug Administration and Psychopharmacologic Drugs Advisory Committee,

These comments are submitted in response to the Request for Comments – Midomafetamine Capsules (Docket No. FDA-2024-N-1938).

I am Marion Coe, Director, Clinical Development and Postmarketing Surveillance at Pinney Associates in Bethesda Maryland.

My work has included pharmaceutical development, including scientific and regulatory support of the research and development of psychedelic substances and products, including 3,4-Methylenedioxymethamphetamine (MDMA), for sponsors including the Multidisciplinary Association for Psychedelic Studies (MAPS) and Lykos Therapeutics (see more at www.PinneyAssociates.com). My opinions are my own and no pharmaceutical sponsor has had input or has provided financial support for my comment. Additionally, these comments were not vetted with anyone outside of our company, nor did any outside organization compensate us for our time to prepare these comments.

I support approval of midomafetamine (MDMA) capsules for the treatment of post-traumatic stress disorder (PTSD). This medication assisted therapy holds significant potential for public health benefit by providing an effective treatment for PTSD, a condition affecting millions of people. It is likely to contribute to a decrease in PTSD-related suicides and homelessness, offering substantial societal benefits. Its approval could also reduce the burden on healthcare systems by lowering associated costs and improving patients' quality of life.

The risks of MDMA administration have been effectively managed in the Lykos clinical trials, and adhering to these same therapeutic conditions after approval should mitigate potential risks in the real world. Nonetheless, MDMA does pose potential serious safety concerns that can and should be addressed by a risk evaluation and mitigation strategy (REMS) program which goes beyond labeling to address serious safety concerns. Specifically, as recently discussed by FDA (2023): “A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration can require for a certain medication with serious safety concerns to help ensure the benefits of the medication outweigh its risks. REMS use risk minimization tools to

reinforce behaviors and actions that support the safe use of that medication…. It is important for health care professionals, patients, and all others whom REMS affect to be aware that these strategies can provide safe access for patients to certain drugs with serious risks that may otherwise not be approved and available on the market." (at https://www.fda.gov/drugs/our-perspective/our-perspective-two-part-series-risk-evaluation-and-mitigation-strategies-rems-program)

The MDMA REMS is essential to ensure that this medicine is only given to patients who meet the labeled criteria for treatment, by health care providers that are certified to follow the identified elements to assure safe use (ETASU), and in healthcare settings that are certified to adhere to the ETASU and can ensure patient safety. These and other concerns have been recently discussed by FDA (2023): "Risk evaluation and mitigation strategy (REMS) programs focus on preventing, monitoring, and/or managing a specific serious risk(s) associated with certain drugs by informing, educating, and/or reinforcing actions to reduce the frequency and/or severity of a particular adverse event(s)." at https://www.fda.gov/drugs/our-perspective/risk-evaluation-and-mitigation-strategies-rems#:~:text=Risk%20evaluation%20and%20mitigation%20strategy,particular%20adverse%20event(s)

We note that if MDMA is approved by FDA, that action will include a recommendation for rescheduling that will have input from the National Institute on Drug Abuse (NIDA) that will be submitted to the Drug Enforcement Administration (DEA) for consideration for its scheduling action. As discussed by my Pinney Associates colleague, Dr. Jack E. Henningfield, in his comment to this docket, MDMA should and likely will remain a controlled substance in the Controlled Substances Act (CSA). Although it appears to carry lower overall abuse potential and public safety risks than its chemically related Schedule II amphetamine products, it is not clear whether the differences are sufficient to merit less restrictive scheduling such as placement in Schedule III. Regardless, CSA control itself will substantially restrict access and will support the need for vigilant real-world monitoring of MDMA prescribing, as well as potential diversion and nonmedical use of the drug product. The REMS can help ensure that such measures are implemented.

Pinney Associates has extensive experience in REMS and understands that REMS development and execution must balance the statutory prohibition of regulating the practice of medicine, and the statutory requirement of the legislation that established REMS for drugs in which it is determined by FDA (often with input from an Advisory Committee) that a REMS is necessary to ensure that the benefits of the medication outweigh the risks but that the REMS is not unnecessarily burdensome and does not compromise patient care. This is a complex balancing act and must be guided by medical and scientific evidence with appropriate monitoring and surveillance to ensure evolution of the REMS to improve effectiveness and address unintended consequences such as hindering patient care or contributing to healthcare disparities.

For those who are concerned about illicit use of MDMA for treatment of PTSD and other medical conditions, I would note that not approving MDMA and keeping all forms of the medication in CSA Schedule I will not prevent such use, it will simply mean that for patients who are desperate for such therapy will have no potentially reimbursable option in the United States (US); and furthermore that only those with sufficient financial resources will be able to travel outside of the US to clinics that might possibly provide high quality care. This will only serve to hinder patient care and contribute to healthcare

disparities, which as noted above are exactly the types of unintended consequences that must be avoided where possible.

In closing, we hope that FDA will not impose such severe restrictions on MDMA use that would ultimately exacerbate health disparities related to socioeconomic status, race, ethnicity, and/or geographical location. This medication has the potential to be transformative in the lives of so many Americans, and it is our hope that it will not just be accessible and available to a wealthy minority but rather to all who need it.

Thank you very much for the opportunity to provide these comments. Please contact me at mcoe@pinneyassociates.com if you have any questions or need further information.

Sincerely,

Marion A Coe, PhD
Director, Clinical Development and Postmarketing Surveillance
Pinney Associates, Inc.