PTSD 2024

ICER SNAPSHOT

The ICER Snapshot is a summary designed to help patients and the broader community learn about the key results and recommendations from ICER's 2024 Final Evidence Report on MDMA-Assisted Psychotherapy for PTSD.

The information included is up to date as of June 2024. New information about this therapy may become available, but is not captured here.

Let's Take a Look

What is PTSD?

Impact on Individuals and Families

Treatment: Benefits and Risks

Treatment: What We Still Don't Know

Policy Recommendations & Impact of Engagement

What is PTSD?

Post-traumatic stress disorder (PTSD) is a mental health disorder that can happen from experiencing a traumatic event. It can cause nightmares and flashbacks, and people may avoid things that remind them of a traumatic event. People with PTSD are at higher risk of developing other mental health conditions like depression, anxiety, and substance abuse.



In the United States, around 13 million adults experience PTSD symptoms each year. PTSD is more common in some groups, including women, veterans, and people of color. PTSD is often treated with antidepressant drugs and certain types of talk therapy (also called psychotherapy). However, the current treatments do not work well enough for many PTSD patients.

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Impact on Individuals and Families

What ICER Learned from the Community

Patients shared that successful PTSD therapy would help reduce symptom severity, suicidal ideation, and reliance on medications.

Symptoms of PTSD can impact every part of a person's life, making daily activities, travel, employment, and relationships with family and friends extremely difficult.

After trying many treatment options and coping strategies over the years, many patients continue to report persistent PTSD symptoms.



Patients with PTSD have expressed concerns over the lack of new FDA-approved treatments in the past two decades.

PTSD can also place a significant burden on caregivers, which in itself can be a traumatic experience. and require sharing or giving up responsibilities.

The potential for having other mental health conditions such as anxiety, depression, and suicidal thoughts make living with PTSD even more challenging.

Due to issues with accessing treatment options, some individuals feel compelled to self-medicate through substance use or to experiment with compounds that are either illegal or lack research evidence.

Treatment of Focus

MDMA-ASSISTED PSYCHOTHERAPY (MDMA-AP)

Proposed by Lykos Therapeutics

MDMA-AP is under FDA review as of June 2024.

What is MDMA-AP?

MDMA stands for midomafetamine (also known as "ecstasy" or "molly") and is being studied as a **potential treatment to be taken in combination with psychotherapy** (talk therapy) **led by a professional therapist.** This combination treatment is known as **MDMA-assisted psychotherapy (MDMA-AP)**.

How does it work?

It is believed that MDMA **may reduce an individual's fear response** and allow people with PTSD to engage in therapy sessions that deal with trauma.

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What Did Clinical Trials Show?

TRIAL NAMES	**MAPP 1 and MAPP 2**
PARTICIPANTS	**Studied in 194 adults with moderate-to-severe PTSD lasting at least 6 months**
TREATMENT GROUPS	**MDMA + talk therapy** vs. **Placebo + talk therapy**
RESULTS	Outcomes for patients receiving **MDMA-AP**:

10-point average reduction* in CAPS-5 score
(fewer PTSD symptoms)

40% of patients no longer had PTSD diagnosis
(achieved remission)

*compared to placebo

Helpful Clinical Terms

Placebo:
An inactive treatment intended to hide whether a patient received the studied drug

CAPS-5:
A scale used to measure how often and how severe a patient experiences PTSD symptoms

Higher score = more PTSD symptoms

Lower score = less PTSD symptoms

These represent some, but not all outcomes that were measured in the clinical trials.

Safety of MDMA-AP

Patients receiving MDMA-AP had symptoms like **muscle tightness, decreased appetite, teeth grinding, excessive sweating, fatigue, restlessness, and insomnia**. It also **increased blood pressure, body temperature, and heart rate**. The potential long-term effects of MDMA use remain unclear, including whether it may increase the risk of suicide, heart problems, liver damage, or addiction.

ICER's report findings are NOT recommendations that support the use of MDMA-AP. Individuals and families should always talk with their doctors to make shared decisions about treatment for PTSD.

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What We Still Don't Know

The way that Lykos Therapeutics designed and conducted the clinical trials for MDMA-AP raise several important questions about the accuracy of the results. See below for some of ICER's main concerns when reviewing the available data on MDMA-AP. You can find the full list of concerns in the Final Evidence Report, pages 3-7 and 21-22.

CONCERN #1: The strong beliefs in favor of MDMA held by researchers, therapists, and participants may have influenced how benefits and harms of MDMA-AP were reported in the MAPP trials. We heard repeatedly that some participants felt pressured to report good outcomes and not report bad outcomes when they took MDMA in the MAPP trials. Many of the people who participated or helped conduct the trials came from a community with strong beliefs about the positive value of psychedelic treatment. In fact, 40% of patients in the MAPP trials had prior MDMA experience which also made it difficult to know how the results of the trial apply to patients who are new to psychedelics.

CONCERN #2: Trial participants could guess whether they received MDMA or a placebo based on the strong psychedelic effects of MDMA. This makes it difficult to compare the results between those who received MDMA and placebo, since a patient knowing that they received MDMA might behave or respond differently during the trial.

CONCERN #3: The psychotherapy (talk therapy) used with MDMA in the MAPP trials has not been tested or proven to work. The talk therapy used for both the treatment and placebo groups in the trials was developed by Lykos Therapeutics and does not have evidence to support its use among people with PTSD.

Based on the limited number of participants, ICER is very uncertain about how often patients experienced harms or benefits in the trials, how accurate the trial results are, and how MDMA-AP may impact patients outside of the pro-psychedelic community. Because ICER calculates a fair price range for a treatment based on how well it works, ICER could not proceed with a price calculation for MDMA-AP since we could not assume the clinical trials results were accurate or reliable.

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Key Policy Recommendations

The Policy Roundtable at the ICER public meeting informed several policy recommendations for pricing, access, and future research in PTSD. A few key recommendations are summarized below.

1 **All stakeholders have an important role to play in identifying people living with PTSD across diverse communities and engaging them to make sure that any new and effective treatment option is introduced in a way that will help reduce health inequities.**



Safe and effective treatment for PTSD, especially for those with moderate to severe disease, remains a significant unmet health care need for all Americans. **Underserved communities including veterans, women, and people of color suffer more than others.** These groups are often diagnosed with PTSD at a higher rate and also have more barriers to accessing evidence-based PTSD treatments.



- **All stakeholders:** Should creatively engage with people with PTSD by making **new connections with community volunteers and people in rural and urban networks**.
- **Insurance providers**: Should develop coverage policies that **also provide childcare and travel assistance** when needed to **ensure equitable access** for all people with PTSD.

Clinical societies: Should develop **culturally-competent educational materials and evidence-based training** for health care providers to help them identify the different forms of PTSD across ethnically and culturally diverse groups.

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2 Looking forward, clinical researchers and life science companies in this space should pursue future research to help all stakeholders understand how psychedelic therapies can help treat people living with PTSD.

There are many important evidence gaps in our understanding of the safety and effectiveness of MDMA-AP. Future research should:

- Test MDMA in combination with different evidence-based psychotherapies. These studies would ideally include a placebo group that uses medications producing similar effects to psychedelics that **make it more difficult for patients not receiving MDMA to recognize the treatment versus the placebo**.



- Conduct trials to directly compare MDMA-AP and evidence-based psychotherapy in patients new to psychedelics and patients with known history of previous psychedelic use.
- **When recruiting patients to future studies, be inclusive of culturally diverse populations**, such as women, veterans, people with personality disorder, people with chronic pain, and people with hypertension.

Impact of Patient Engagement

Discussions with a few patients who participated in the MAPP trials brought to light how trial design and misconduct may have impacted the **reliability of the results.**

Patient community input raised uncertainty about frequency of benefits and harms and ultimately **led ICER to rate the evidence for MDMA-AP as "Insufficient."**

Patient and advocacy group testimony at the public meeting helped inform ICER's policy recommendation for **increased cultural diversity in future research.**

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit organization that does research on how well new treatments work and what a fair price should be. Patients and families should always talk with their doctor to make shared decisions about the best treatment option for them.

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