Midomafetamine-Assisted Psychotherapy for Post-Traumatic Stress Disorder: Final Policy Recommendations

June 27, 2024

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the May 30th, 2024 New England CEPAC public meeting on the use of MDMA-AP for the treatment of patients with moderate to severe PTSD. At the meeting, ICER presented the findings of its revised report on these treatments and the New England CEPAC voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations, and long-term value for money at a placeholder prices. Following the votes, ICER convened a Policy Roundtable of two patients, two clinical experts, and two payers to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed here, and a recording of the voting portion of the meeting can be accessed here. More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the Report.

The roundtable discussion was facilitated by Dr. Steven Pearson, MD, MSc, special advisor to ICER.

Improving Health Equity

Recommendation 1

All stakeholders have a responsibility and an important role to play in improving the identification of people living with PTSD across diverse communities and in engaging with them in new ways to ensure that any effective new 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. Marginalized communities including veterans, women, and people of color suffer disproportionately, since they are diagnosed with PTSD at a higher rate while facing underlying social and health access challenges that likely lead to underreporting of true PTSD prevalence among these groups and barriers to accessing evidence-based PTSD treatments when diagnosis is confirmed. People living with PTSD in rural communities also face inequities in diagnosis and access to clinicians with expertise in treating this condition. When new, effective interventions for PTSD are being launched in practice, all stakeholders should seize the opportunity to address existing disparities in diagnosis and care, and should take specific

steps to ensure that new interventions are made available in ways that minimize the risk that these disparities are accentuated.

To achieve these goals:

All stakeholders have a responsibility to improve the identification of people with PTSD across diverse communities and should take the following actions:

- Develop a variety of approaches to engage with people with PTSD through collaborative outreach efforts and forging new connections with community volunteers and people on the ground among rural and urban networks. Outreach and education should include efforts to overcome the shame and intergenerational shame that is often a barrier to effective identification of PTSD.

Payers should take the following actions:

- Develop comprehensive insurance coverage policies that provide treatment coverage in addition to childcare and travel assistance when needed to ensure equitable access to evidence-based treatment options for all people with PTSD.

Clinical specialty societies should take the following actions:

- Develop and disseminate culturally competent educational materials for diverse providers and create measurable goals to help identify people with PTSD, especially among marginalized communities.
- Develop evidence-based training for diverse providers to help them identify the different manifestations of PTSD across ethnically and culturally diverse groups.

Steps to ensure safety and effectiveness of psychedelic treatment for PTSD

Based on the currently available evidence, ICER's evidence ratings and the votes of the New England CEPAC suggest that there are too many questions about the safety and effectiveness of MDMA-AP to support regulatory approval and/or insurance coverage. Detailed public comments from participants in the clinical trial, along with other testimony, highlighted deep concerns about inappropriate clinician behavior and lapses in the integrity of the clinical trial itself. However, given that regulatory approval of MDMA-AP is still a possibility at this time, and that other treatments that incorporate psychedelic agents are on the horizon, it is important to consider potential steps that can be taken to help ensure the safety and effectiveness of treatment for patients who are

already vulnerable, and who may be rendered even more vulnerable through the short-term effects of a psychedelic agent.

Recommendation 1

For any approved therapy using a psychedelic agent, the FDA should establish an expansive Risk Evaluation and Mitigation Strategies (REMS) program with components including tracking of adverse outcomes and which requires rigorous certification of all healthcare providers involved in treatment.

Rigorous certification and oversight of providers is of the highest importance and should include entities other than the manufacturer, such as the American Psychiatric Association and American Psychological Association, to reduce potential conflicts of interest in maintaining the highest standards.

Regulators, clinical specialty societies, and payers should collaborate to ensure a consistent approach to certification of providers in treatments using psychedelic agents. It is possible that the manufacturer may also play a role, but it is important that they not be the sole agent of certification. Different models for certification could include a two-step process, with manufacturer certification as a first step, followed by specialty society certification. Training, certification and oversight is needed for both the medical providers who will prescribe psychedelic agents and for therapists who will provide psychedelic-assisted psychotherapy. This is of utmost importance because psychedelic agents can increase patient vulnerability. It is critical to ensure strong training and oversight to minimize the risk of therapist misbehavior. Payers should also consider augmenting any certification process by identifying a limited network of centers of excellence for the provision of psychedelic treatments. There will always be tension between the goals of providing broad access to new treatments and efforts to ensure appropriate care by limiting available providers through certification and insurance networks, but especially when new treatments are first launched it may be most important to control access to prioritize patient safety.

Recommendation 2

As soon as possible following regulatory approval, clinical specialty societies, and large integrated provider groups such as the VA, should rapidly develop clinical practice guidelines to guide optimal practice with novel treatments.

Guidelines put out by clinical specialty societies and influential large integrated provider groups, such as the VA, are the most authoritative sources of guidance on appropriate care following the introduction of new therapies. Payers look to see if guidelines exist when developing early coverage policies, and therefore it will be important for all stakeholders to have rigorous guidelines to help align evidence, practice, and insurance coverage across the diverse payers in the US health system.

Recommendation 3

Payers should translate the findings from pivotal trials of psychedelic treatments and the recommendations from available clinical guidelines into transparent, evidence-based coverage policies that provide a rationale for specific clinical eligibility criteria and any step therapy approaches.

In the context of the uncertainty at this time regarding MDMA-AP, if the treatment gains FDA approval, it will be reasonable for payers to draw relatively tight boundaries around coverage, based on the inclusion and exclusion criteria of the clinical trials. In general, for any new treatments based on psychedelic agents, it is likely that payers will leverage pivotal trial criteria as part of the effort to assure an appropriate risk/benefit balance of treatment.

It will also be reasonable for payers to consider step therapy for new treatments involving psychedelic agents. New treatments will lack the longer-term track record of safety and effectiveness that has been demonstrated by several short-term trauma-focused psychotherapies (TFP). And, if new treatments require greater clinical resources, such as the dual-provider protocol for MDMA-AP, it is also reasonable for payers to favor approaches requiring less clinician time to maximize access to an accepted form of therapy.

If payers do apply step therapy to new psychedelic treatment options, it will highlight the responsibility they bear to take all efforts to increase the availability of clinicians providing first-step therapeutic options for PTSD. In addition, payers will need to institute mechanisms to ensure that patients who do not receive adequate benefit from first-step options or who have specific contraindications can rapidly gain coverage for approved psychedelic treatment options. Lastly, if MDMA-AP is approved by the FDA, payers should be aware of ongoing research studying the use of MDMA within protocols using not AP but other evidence-approved psychotherapy approaches. If and when this research demonstrates equal or better outcomes, payers should consider rapidly expanding coverage to include these options, which will likely help expand access and require fewer clinical resources.

Future Research Recommendations

Recommendations

There are many important evidence gaps in our understanding of the safety and effectiveness of MDMA-AP. Looking forward, clinical researchers and life science companies in this space should attend to the following key recommendations regarding the research needed to help all stakeholders understand the appropriate place of psychedelic therapies in the care of people living with PTSD.

Future research should:

- Test MDMA in combination with different evidence-based TFP in prospective comparative studies. These studies would ideally include placebo arms that use medications producing systemic effects that make it more difficult for MDMA-naïve patients to recognize that they are not receiving active MDMA.
- Conduct direct head-to-head trials comparing MDMA-AP and first-line recommended evidence-based TFP in psychedelic-naive patients and those with known history of previous psychedelic use.
- Utilize randomized trial designs that ensure balance between the treatment groups and allow assessment of the impact of known prognostic factors that could influence treatment responsiveness. These factors include intensity of trauma events, dissociative PTSD subtype, PTSD among racially/ethnically and socio economically diverse groups and different genders.
- Evaluate innovative models of delivery in prospective studies including the effect of utilizing single therapists, and fewer or more frequent therapy sessions.
- Ensure inclusivity when recruiting patients to future studies, including culturally diverse populations, women, veterans, people with personality disorder, people with chronic pain, and people with hypertension.

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the May 30, 2024 Public meeting of New England CEPAC.

Appendix Table 1. ICER Staff and Consultants and COI Disclosures

ICER Staff and Consultants*	
Sarah Emond, MPP, President and CEO, ICER	**Michael Distefano, PhD, M.Bioethics**, Assistant Professor, University of Colorado Anschutz Medical Campus
Grace Ham, MSc, Program and Events Coordinator, ICER	**Brett McQueen, PhD**, Associate Professor, University of Colorado Anschutz Medical Campus
Reem Mustafa, MD, MPH, PhD, Professor of Medicine, University of Kansas Medical Center	**Emily Nhan, BA**, Senior Research Assistant, ICER
Dmitriy Nikitin, MSPH, Senior Research Lead, Evidence Synthesis, ICER	**Steve Pearson, MD, MSc**, Special Advisor, ICER
David Rind, MD, MSc, Chief Medical Officer, ICER	**Liis Shea, MA**, Senior Program Director, ICER
Antal Zemplenyi, PhD, MSc, Visiting Research Associate, University of Colorado Anschutz Medical Campus	

*No conflicts of interest to disclose, defined as individual health care stock ownership (including anyone in the member's household) in any company with a product under study, including comparators, at the meeting in excess of $10,000 during the previous year, or any health care consultancy income from the manufacturer of the product or comparators being evaluated.

Appendix Table 2. New England CEPAC Panel Member Participants and COI Disclosures

Participating Members of New England CEPAC*	
Rob Aseltine, PhD, Professor and Chair, UConn Health	**Austin Frakt, PhD**, Professor, Boston University School of Public Health
Rebecca Kirch, JD, EVP Policy and Programs, National Patient Advocate Foundation	**Stephen Kogut, PhD, MBA, RPh**, Professor of Pharmacy Practice, University of Rhode Island College of Pharmacy
Donald Kreis, MS, JD, Patient Advocate, New Hampshire Office of the Consumer Advocate	**Julie Kueppers, PhD, NP**, Clinical Vice President, Alera Group
Tara Lavelle, PhD, Assistant Professor, Tufts Medical Center	**Aaron Mitchell, MD, MPH**, Medical Oncologist, Memorial Sloan Kettering Cancer Center
Stephanie Nichols, PharmD, MPH, BCPP, FCCP, Associate Professor, University of New England	**Jo Porter, MPH**, Chief Strategy Officer, New Hampshire Center for Justice and Equity
Joseph Ross, MD, MHS, Professor of Medicine and Public Health, Yale University	**Jeanne Ryer, MSc, EdD**, Director, NH Citizens Health Initiative
Jason L. Schwartz, PhD, Associate Professor of Health Policy, Yale School of Public Health	**Jason Wasfy, MD**, Associate Professor, Harvard Medical School and Mass General Hospital
Rishi Wadhera, MD, MPP, MPhil, Associate Professor of Medicine, Harvard Medical School	

*No conflicts of interest to disclose, defined as individual health care stock ownership (including anyone in the member's household) in any company with a product under study, including comparators, at the meeting in excess of $10,000 during the previous year, or any health care consultancy income from the manufacturer of the product or comparators being evaluated.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Participant	Conflict of Interest
Diana Chao, Executive Director, Letters to Strangers	Diana serves as an advisor on the Mental Health America Youth Council, who has received funding from healthcare companies. Letters to Strangers has received a $5000 donation from an executive member at Pfizer as a private individual donation.
Peter Glassman, MBBS, MSc, Chair, Medical Advisory Panel, VA Pharmacy Benefits Management Services	Peter Glassman is a full-time employee at the U.S. Department of Veterans Affairs.
Jessica Maples-Keller, PhD, Assistant Professor, Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine	Dr. Maples-Keller has received funding from healthcare companies, such as COMPASS Pathways and Multidisciplinary Association of Psychedelic Studies (MAPS) for research trials on MDMA-assisted exposure therapy for PTSD.
Naomi M. Mathis, Assistant National Legislative Director, Disabled American Veterans	No conflicts to disclose.
Joar Øveraas Halvorsen, PhD, Associate Professor and Consultant Clinical Psychologist, Norwegian University of Science and Technology, and St. Olav's University Hospital	No conflicts to disclose.
Marina Sehman, PharmD, CSP, Clinical Director, IPD Analytics	Marina Sehman is a full-time employee at IPD Analytics.