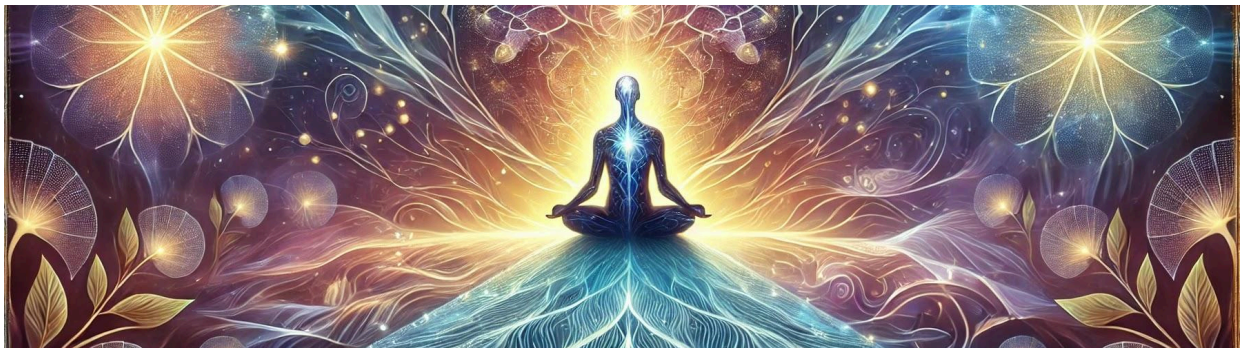

A Guide for Integrative Clinicians: Safe & Conscious Psychedelic Use

Comparative Chart of Ketamine, Psilocybin, MDMA, and Ayahuasca*

Substance	Mechanism of Action & Acute Effect Duration	Evidence-Informed Indications	Contraindications & Interactions	Drug Schedule & Legal Status - Notes (USA)
Ketamine	NMDA receptor antagonist, increases glutamate release, induces neuroplasticity via BDNF receptor activation. 1-3h	Treatment-resistant depression, suicidality, PTSD, chronic pain, OCD, SUD (Research ongoing).	Schizophrenia, uncontrolled hypertension, interstitial cystitis, history of psychosis; history of recreational abuse, caution with benzodiazepines and lamotrigine (blunts effects).	Schedule III (FDA-approved for depression as esketamine, other legal uses are considered off-label).
Psilocybin	Serotonin 5-HT2A agonist, enhances neuroplasticity, alters default mode network (DMN) connectivity. 4-6h	Major depressive disorder, end-of-life anxiety, cluster headaches, PTSD (Research ongoing)	Contraindicated in schizophrenia, bipolar disorder; interacts with SSRIs use, MAOIs use (risk of serotonin syndrome).	Schedule I (Oregon & Colorado legalized for therapeutic use).

MDMA	Increases serotonin, dopamine, norepinephrine release, promotes oxytocin-driven emotional bonding & fear extinction. 3-5h	PTSD, social anxiety (e.g., in autism), couples therapy (Research ongoing).	Contraindicated in cardiovascular disease, QTc prolongation, active substance abuse disorder, eating disorder, active suicidality, personality disorder, interacts with SSRIs, MAOIs (serotonin syndrome risk).	Schedule I
Ayahuasca	DMT (5-HT2A agonist) + β-carbolines (MAOIs) prevent DMT breakdown, leading to visionary and neuroplastic effects. 4-8h	Studied for depression, addiction, grief, anxiety (Research ongoing, more limited than above 3)	Contraindicated in psychotic disorders, bipolar disorder (mania risk), cardiovascular disease; interaction with SSRIs, MAOIs (hypertensive crisis risk). Emesis and diarrhea increase risk of hypotension and dehydration.	Schedule I (DMT is illegal; religious exemptions for certain groups like Santo Daime & Uniao do Vegetal). Most often served in groups ceremonially - often in evenings/overnight

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***(2025 current summary, not comprehensive)**

Shared Considerations for All Substances

1. **Set & Setting:** Mind-heartset (set) and environment/who is present (setting) significantly influence outcomes.
2. **Preparation:** Screening for contraindications, intention-setting, and pre-session guidance improve safety and efficacy.
3. **Facilitator Role:** Skilled guides/clinicians help ensure safety, emotional support, and meaning-making during the experience.
4. **Integration:** Post-experience processing through therapy, journaling, and community support enhances long-term benefits.

Guiding Patients Through Safe & Conscious Psychedelic Use

A Clinical Framework for Integrative Medicine Practitioners when seeing patients bringing up psychedelics as a complementary therapy for their care.

Phase	Key Questions to consider	Guidance
Pre-Experience and seeking counsel (Assessment & Risk-Benefit Harm Reduction)	. Inquiry into their intentions and psychological readiness . Has the patient tried evidence-based standard treatments first or plan to concomitantly? . Medication interaction review [see table] . PMH review for contra-indications or side effects consideration. [see table] . Discuss non-drug alternative psychedelic states suitability: breathwork, meditation retreats, fasting, drumming. -Cost vs perceived benefits compared to other care options.	-Refer to a psychedelic medicine trained MD. Often psychiatry, internal/family medicine who has trained with for e.g. MAPS, CIIS, Polaris, Fluence or worked at clinics offering ketamine/legal psychedelics - savvy in harm reduction. -Be sure to encourage a medical evaluation before any psychedelic journey for harm reduction.
Patient set on trying something - Preparation (Set, Setting, Logistics, Safety)	**Explore the risks profile of the different settings** ● **Research study** (e.g. university or drug development sponsored study with IRB and guidelines) [low risk] ● **Clinic-Based** (e.g., ketamine therapy, clinical trials, Oregon psilocybin services) [low risk, look for nursing/MD supervision and having psychotherapy required clinics] ● **Retreat-Based or Underground**: Greater	**Outside of research or clinic based psychedelic medicine care:** ● Look for facilitators with **medical or licensed mental health training** (if clinical) - e.g. CIIS, Fluence, Polaris ● Ethics, safety, and harm reduction training (avoid financial/sexual exploitation risks) Explore if they seem appropriately prepared for the proposed experience.

	variability in standards and safety [low to high risk] ● **International Retreats**: Ayahuasca (Peru, Brazil), psilocybin (Jamaica, Netherlands) for e.g. [low to high risk]	-Driver to and from the experience. - Have they prepared like they would for surgery with a medical pre-op visit? -What's the facility standards? -Is emergency planning in place? -Who is running the operation, how have they been vetted? -If out of the country, have travel insurance and have travel visit.
During the Experience (Session Structure & Safety)	Other Questions to explore regarding the session: - Facilitation Approach: Sitting presence vs. active therapy. Touch or not. -Who will lead the experience, and who else will be there. Group or 1:1/1:2. - Somatic Experience: Movement allowed? Eyes open/closed? - Music vs. Silence: Intentional auditory input planned? - Emergency Protocol: Who's in charge if distress occurs?	
Post-Experience (Recovery & Integration)	- Immediate Aftercare: Hydration, food, rest. - Neuroplasticity Window: Attention to inputs, avoiding overstimulation. - Emotional Processing: Art, journaling, therapy, nature. - Avoiding Impulsivity: No major life decisions immediately post-experience. - Integration Support: Therapists, spiritual guides, ongoing work.	- What is their post-op plan? Who is checking in? - How are they planning to process & make sense of the experience [ie integration]? - Monitoring for over-identifying with the experience itself, and psychological attachment?

Long-Term Healing & Growth (Sustained Transformation)	- Avoid "Chasing the Experience": Integration is key, not repeated use. Yet different medicines work better for sequential experiences over time. - Continued Work: Trauma healing, therapy, mindfulness practices. - Support System: Finding mentors, elders, community. - Reconnecting with Intentions: What was the deeper lesson?	- What's next? How do they continue integrating? - Are they leaning on community & guides to sustain growth? - How do they avoid or work with attachment to the peak experience itself?

Key Takeaways for Clinicians

- Think of psychedelic journeys like elective surgery → Not usually first-line, requires screening, preparation, skilled facilitation, and structured recovery.
- Safety matters → Provider qualifications, medical risks, ethical considerations, and harm reduction principles are critical.
- Set, setting, and integration determine outcomes more than the psychedelic medicine itself → Guide patients through preparation and post-experience meaning-making.
- Healing is a process, not a peak moment → Encourage sustainable transformation, not dependence on psychedelic states.
- Refer to a clinician trained in psychedelic medicine

References:

1. **Set and Setting in Psychedelic Therapy**: The importance of mindset and environment in influencing psychedelic experiences has been well-documented. Optimizing these factors can significantly impact therapeutic outcomes.
    a. Carhart-Harris RL, Roseman L, Haijen E, et al. **Psychedelics and the essential importance of context.** Journal of Psychopharmacology. 2018;32(7):725-731. doi:10.1177/0269881118754710 https://journals.sagepub.com/doi/abs/10.1177/0269881118754710
2. **Integration Practices**: Post-experience integration is crucial for translating psychedelic experiences into lasting therapeutic benefits. Engaging in activities like therapy, journaling, and community support facilitates this process.
    a. Nielson, E. M., Guss, J., Files, J. M., Friedman, H., & Williams, M. T. (2022). **Psychedelic harm reduction and integration: A transtheoretical model for clinical practice**. *Frontiers in Psychology, 13*, 824077. https://doi.org/10.3389/fpsyg.2022.824077 https://www.frontiersin.org/journals/psychology/articles/10.3389/fpsyg.2022.824077/full
3. **Ethical and Legal Considerations:** Clinicians must navigate complex ethical and legal landscapes when supporting patients in psychedelic use, emphasizing the need for clear guidelines and harm reduction approaches.

   a. Pilecki, B., Luoma, J.B., Bathje, G.J. et al. **Ethical and legal issues in psychedelic harm reduction and integration therapy.** Harm Reduct J 18, 40 (2021). https://doi.org/10.1186/s12954-021-00489-1
   b. McGuire AL, Cohen IG, Sisti D, et al. **Developing an Ethics and Policy Framework for Psychedelic Clinical Care: A Consensus Statement.** *JAMA Netw Open.* 2024;7(6):e2414650. doi:10.1001/jamanetworkopen.2024.14650
4. **Facilitator Competencies:** Therapeutic alliance and facilitator ethics and skill play important role on experience and outcomes
   a. Levin, A. W., *et al*. (2024) **The therapeutic alliance between study participants and intervention facilitators is associated with acute effects and clinical outcomes in a psilocybin-assisted therapy trial for major depressive disorder.** *PLOS ONE*. doi.org/10.1371/journal.pone.0300501
   b. Carlin, S., & Scheld, S. (2019). **Developing ethical guidelines in psychedelic psychotherapy**. *MAPS Bulletin, 30*(3), 27–34. https://maps.org/wp-content/uploads/2020/12/v30n3-p27-34.pdf
5. Psychedelic substances in clinical use:
   a. De Gregorio, D., Aguilar-Valles, A., Preller, K. H., Heifets, B. D., Hibicke, M., Mitchell, J., & Gobbi, G. (2021). ***Hallucinogens in mental health: Preclinical and clinical studies on LSD, psilocybin, MDMA, and ketamine.*** Journal of Neuroscience, 41(5), 891-900. https://doi.org/10.1523/JNEUROSCI.1659-20.2020
   b. Wilkinson, S. T., et al. (2017). **The effects of ketamine in treatment-resistant depression: A double-blind, placebo-controlled study.** *American Journal of Psychiatry*, **174**(10), 1002-1010. https://doi.org/10.1176/appi.ajp.2017.17060691
   c. Feder, A., et al. (2021). **Efficacy of repeated ketamine infusions in PTSD: A randomized controlled trial.** *JAMA Psychiatry*, **78**(9), 893-902. https://doi.org/10.1001/jamapsychiatry.2021.1218
   d. Michelet, D., et al. (2018). **Ketamine for chronic pain: A meta-analysis. *Anesthesia & Analgesia*, 127**(1), 180-188. https://doi.org/10.1213/ANE.0000000000003235
   e. Griffiths, R. R., et al. (2016). **Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer.** *Journal of Psychopharmacology*, **30**(12), 1181-1197. https://doi.org/10.1177/0269881116675513
   f. Johnson, M. W., et al. (2014). **Psilocybin-assisted smoking cessation: A pilot study.** *Journal of Psychopharmacology*, **28**(11), 983-992. https://doi.org/10.1177/0269881114548296
   g. Mithoefer, M. C., et al. (2018). **MDMA-assisted psychotherapy for PTSD: A phase 3 trial.** *Nature Medicine*, **27**(6), 1025-1033. https://doi.org/10.1038/s41591-021-01336-3
   h. Danforth, A. L., et al. (2018). **Reduction in social anxiety after MDMA-assisted psychotherapy in autistic adults: A randomized, double-blind, placebo-controlled pilot study.** *Psychopharmacology*, **235**(11), 3137-3148. https://doi.org/10.1007/s00213-018-5010-9
   i. Palhano-Fontes, F., et al. (2019). **Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: A randomized placebo-controlled trial.** *Psychological Medicine*, **49**(4), 655-663. https://doi.org/10.1017/S0033291718001356
   j. Sharma, R., Batchelor, R., & Sin, J. (2023)**. Psychedelic Treatments for Substance Use Disorder and Substance Misuse: A Mixed Methods Systematic Review.** Journal of Psychoactive Drugs, 55(5), 612–630. https://doi.org/10.1080/02791072.2023.2190319