

On-Label and Off-Label Uses of Ketamine

Question

What are the common uses of ketamine, and what are the associated benefits and risks of on-label and off-label use of this drug?

Answer

Ketamine is a Schedule III nonnarcotic drug that the U.S. Food and Drug Administration (FDA) has approved for anesthesia and procedural sedation. It has been used in surgical settings for about 50 years, and providers can administer it alone or in combination with other anesthetic agents.¹

Ketamine is beneficial in many ways. It does not have a significant impact on breathing or heart function during surgery, and it may reduce postoperative pain and the need for pain medication.² Using ketamine as an anesthetic also might be advantageous for children, patients with asthma and life-threatening acute bronchial constriction, patients with unstable hemodynamics, patients with burns, and patients undergoing caesarean sections.³

Like all anesthetic drugs, however, ketamine is not without risks. To ensure safety during ketamine administration, an anesthesiologist should be present to monitor the patient's health and vital signs.⁴ Monitoring is essential because ketamine may produce side effects, including increases in blood pressure and pulmonary arterial pressure as well as neurological effects.⁵ Surgical teams should prepare for these possibilities and how to respond.

From a safety and liability perspective, providers also should consider the risks associated with off-label ketamine use. The drug sometimes is prescribed and administered to treat pain and psychiatric conditions (e.g., depression and posttraumatic stress disorder), but it is not FDA approved for these uses or for recreational use.⁶ One exception is a derivative of ketamine called esketamine, which comes in the form of a nasal spray. The FDA approved esketamine in 2019, but only for treatment-

resistant, severe unipolar major depression without psychotic features. A trained prescriber should oversee patients who are receiving the medication for this purpose.⁷

Unfortunately, ketamine providers and clinics may not administer the drug in accordance with recognized or well-researched safety protocols. For example, they may not use isolated ketamine or the FDA-approved nasal spray. Some patients are treated at these clinics without any supervision from a psychiatrist or a physician, and the drug isn't always given for true treatment-resistant depression.⁸

The American Association of Nurse Anesthesiology's [Ketamine Infusion Therapy Considerations Checklist](#) offers helpful risk management guidance and practice considerations related to scope of practice, treatment and management, clinic infrastructure, operations, and policies. Additionally, providers should consider the following strategies and precautions in relation to on-label and off-label use of ketamine:

- Healthcare providers who prescribe and/or administer ketamine (e.g., anesthesiologists, certified registered nurse anesthetists, registered and advanced practice nurses, emergency department physicians, pain specialists, psychiatrists, dentists, and paramedics) should collaborate as part of interdisciplinary teams to optimize use of the medication and prevent adverse outcomes.
- Healthcare providers should be well informed of ketamine's indications and contraindications, potential side effects, and patient eligibility criteria for ketamine treatment.
- Healthcare providers should receive appropriate education and training related to ketamine as part of onboarding and ongoing education. Healthcare organizations should routinely assess provider competency and provide feedback.
- Nurses and pharmacists should receive training to help to guard against improper ketamine dosing and to recognize and react to adverse drug events and drug interactions.
- Healthcare providers who are using ketamine for off-label purposes should have thorough informed consent discussions with patients. These discussions should include a review of the risks, benefits, and alternatives to the proposed ketamine treatment.
- When ketamine is used, a qualified provider should monitor the patient's neuropsychiatric function, cardiac function, blood pressure, pulse, breathing, and oxygen saturation.

- Healthcare providers should be trained and prepared to intubate patients in case it becomes necessary during ketamine administration. Providers and staff should verify prior to administration that appropriate resuscitative equipment is available.
- Healthcare organizations should establish documentation standards and protocols, including expectations for documenting informed consent, patient assessments, and patient monitoring; using procedure-specific forms; and completing documentation in specified timeframes.
- Healthcare providers should ensure that patients' neuropsychiatric function and vital signs have returned to baseline prior to discharge, and patients should not be discharged unless they are under the supervision of a responsible adult.⁹

Resources

- [American Association of Nurse Anesthesiology: Ketamine Infusion Therapy Overview](#)
- [American Psychiatric Nurses Association: APNA Position: Ketamine Infusion Therapy](#)
- [American Psychiatric Nurses Association: Ketamine Infusion Therapy Treatment Considerations](#)
- [JAMA Network: A Consensus Statement on the Use of Ketamine in the Treatment of Mood Disorders](#)

Endnotes

¹ Rosenbaum, S. B., Gupta, V., Patel, P., & Palacios, J. L. (2023, May 26). Ketamine. *StatPearls* [Internet]. Retrieved from www.ncbi.nlm.nih.gov/books/NBK470357/; Medical News Today. (2023, July 25 [last updated]). *What are the uses of ketamine?* Retrieved from www.medicalnewstoday.com/articles/302663; Gao, M., Rejaei, D., & Liu, H. (2016, March 28). Ketamine use in current clinical practice. *Acta Pharmacologica Sinica*, 37:865–872.

² Moawad, H. (2022, July 20 updated). What is ketamine? An anesthetic drug that can also be abused. *Verywell Health*. Retrieved from www.verywellhealth.com/ketamine-5077592

³ Gao, et al., Ketamine use in current clinical practice.

⁴ Moawad, What is ketamine?

⁵ Bravenec, B. (2022, October 26 [last updated]). General anesthesia: Intravenous induction agents. *UpToDate*. Retrieved from www.uptodate.com/contents/general-anesthesia-intravenous-induction-agents

⁶ Rosenbaum, et al., Ketamine; American Association of Nurse Anesthesiology. (2019). *Ketamine infusion therapy: Considerations checklist*. Retrieved from www.aana.com/wp-content/uploads/2023/01/ketamine-infusion-therapy-checklist.pdf

⁷ Das, Smita. (2023, February 5). Ketamine clinics are jumping ahead of the evidence. *MedPage Today*. Retrieved from www.medpagetoday.com/opinion/second-opinions/102956; U.S. Department of Justice, Drug Enforcement Administration. (2020). *Drug fact sheet: Ketamine*. Retrieved from www.dea.gov/sites/default/files/2020-06/Ketamine-2020.pdf

⁸ Das, Ketamine clinics are jumping ahead of the evidence.

⁹ Rosenbaum, et al., Ketamine; American Association of Nurse Anesthesiology. (2019). *Ketamine infusion therapy: Considerations checklist*.

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