KETAMINE

Ketamine is a dissociative anesthetic used medically in both humans and animals as a short-acting painkiller since the 1970s. More recently, in 2019, the U.S. Food and Drug Administration approved esketamine, an isomer of ketamine, as a medication for treatment-resistant depression (brand name Spravato®). Ketamine is classified as a dissociative anesthetic because it causes patients to feel detached from their pain and environment. Ketamine's chemical structure and mechanism of action resembles phencyclidine (PCP), although ketamine has less than 10 percent of the potency of pure PCP. Because ketamine can produce dissociative sensations, feelings of euphoria, and hallucinations, it is popular as a "club drug" among teens and young adults at dance clubs and raves. Most of the ketamine illicitly distributed in the U.S. is either diverted or stolen from legitimate sources, particularly veterinary clinics, or smuggled into the U.S. from Mexico. Ketamine is sold illicitly under various street names, including Special K, Vitamin K, Cat Tranquilizer, Cat Valium, and Kit Kat. In 1999, the Drug Enforcement Administration (DEA) listed ketamine as a Schedule III non-narcotic substance under the federal Controlled Substances Act.[1]

Illicit ketamine is found either as a clear liquid or as a white or off-white powder. Liquid ketamine can be injected or mixed into drinks, while powdered ketamine can be snorted, smoked, or pressed into pills. The onset of ketamine's effects happens quickly – within one minute if injected, within five to 15 minutes if snorted, and within 30 minutes if swallowed. The effects of ketamine are shorter in duration than PCP, lasting approximately 30 to 60 minutes after onset as opposed to several hours. People who use ketamine report experiencing dream-like states and hallucinations, with sensations ranging from floating to being separated from their bodies. Ingesting a large dose of ketamine can result in an individual becoming completely detached from reality; ketamine users call this terrifying experience the "k-hole" and compare it to a near death experience. In rare cases, an individual may develop Hallucinogen Persisting Perception Disorder in which the person experiences visual disturbances days, weeks, or even years after using ketamine.

Long term or chronic use of ketamine can lead to lasting psychiatric effects such as depression and impaired memory and concentration. Additionally, chronic ketamine use can cause ulcerative cystitis, a shrinking of the bladder resulting in pelvic pain, increased urinary frequency, blood in the urine, and incontinence. Researchers estimate that more than 20 percent of ketamine users experience urinary tract symptoms.[2] The risk of overdose death from ketamine alone is uncommon due to the drug's ability to cause unconsciousness with minimal impact on breathing or blood circulation. The risk of death from accidents, such as falling, drowning, or vehicular accidents, while intoxicated with ketamine, however, is increased. Ketamine is often misused in combination with other substances, including alcohol, amphetamines, MDMA (commonly known as ecstasy), and cocaine, which increase the likelihood of serious complications or death. There is also an increased risk of adverse effects when ketamine is combined with caffeine or alcohol. This presents a particular concern to consumers and policymakers because individuals often mix liquid ketamine into alcoholic beverages or caffeinated energy drinks.

[1] Schedules of Controlled Substances: Placement of Ketamine into Schedule III, 64 Fed. Reg. 37,673 (July 13, 1999).
[2] Shalom Srirangam and Joe Mercer, "Ketamine Bladder Syndrome: An Important Differential Diagnosis when Assessing a Patient with Persistent Lower Urinary Tract Symptoms," *BMJ Case Reports* 2012 (Sept. 2012), https://doi.org/10.1136/bcr-2012-006447.

In 2020, the United Nations Office on Drugs and Crime received reports of ketamine misuse from 56 countries.[3] While illicit ketamine use has been increasing in the United Kingdom, ketamine misuse in the U.S. remains low.[4] The Substance Abuse and Mental Health Services Administration's 2021 National Survey on Drug Use and Health notes that only 1.8 percent of Americans aged 18 and over reported using ketamine in their lifetime.[5] Further, the University of Michigan's 2022 "Monitoring the Future" study, which looks at drug use in secondary school students, reported that the prevalence of past-12 month use of ketamine among 12th grade students is below two percent, the same level at which it has been since 2004.[6] While misuse of ketamine is low in the U.S., drug experts have concerns that novel ketamine analogs will gain popularity in the U.S. drug market.

One such novel ketamine analog is methoxetamine, which is abbreviated MXE and referred to on the street as M-ket, Kmax, and Mexxy. Unlike ketamine, methoxetamine has no approved medical use in the U.S. Anecdotal reports suggest that methoxetamine is more potent than ketamine. There are also reports of individuals using methoxetamine in lieu of ketamine in order to avoid developing ketamine-associated ulcerative cystitis. However, because methoxetamine and ketamine are chemically related, they are likely to produce similar long-term effects. In March 2016, during the 59th session of the United Nations Commission on Narcotic Drugs, members voted to place methoxetamine in Schedule II of the 1971 Convention on Psychotropic Substances due to its dependence and abuse potential.[7] In June 2022, the DEA permanently listed methoxetamine as a Schedule I substance due to its high potential for abuse and lack of accepted medical use.[8] As of May 2023, 23 states and the District of Columbia similarly schedule methoxetamine.

While ketamine misuse is rare in the U.S., public health and safety officials should continue to advise their communities about the dangers associated with the use of illicit ketamine and novel ketamine analogs. LAPPA will continue to monitor the spread of novel ketamine analogs and any new regulatory responses at the state and federal levels.

RESOURCES

"Drug Fact Sheet: Ketamine," Drug Enforcement Administration, last modified April 2020, https://www.dea.gov/sites/default/files/2020-06/Ketamine-2020_1.pdf.

"Ketamine Abuse," Drugs.com, accessed April 27, 2023, https://www.drugs.com/illicit/ketamine.html.

[3] United Nations Office on Drugs and Crime, "Drug Market Trends: Cocaine, Amphetamine-type Stimulants, and New Psychoactive Substances," *2022 World Drug Report* (June 2022) 96, https://www.unodc.org/res/wdr2022/MS/WDR22_Booklet_4.pdf.
[4] *Id.* at 97
[5] "2021 National Survey on Drug Use and Health-Table 1.106A," Substance Abuse and Mental Health Services Administration, Jan. 4, 2023, https://www.samhsa.gov/data/report/2021-nsduh-detailed-tables.
[6] Richard A. Miech, et al., "Monitoring the Future: National Survey Results on Drug Use, 1975-2022, Secondary School Students," June 2023, 44, https://monitoringthefuture.org/wp-content/uploads/2022/12/mtf2022.pdf. Researchers added ketamine to the survey in 2000. Because of the very low level of use of this drug, by 2011, researchers dropped questions about its use from the questionnaires administered to 8th and 10th graders.
[7] Schedules of Controlled Substances: Placement of Methoxetamine (MXE) in Schedule I, 87 Fed. Reg. 34,166 (June 6, 2022). The United States is a party to the 1971 United Nations Convention on Psychotropic Substances (1971 Convention; 32 U.S.T. 543). When the United States receives notification of a scheduling decision pursuant to Article 2 of the 1971 Convention indicating that a drug or other substance has been added to a specific schedule, the Secretary of the Department Health and Human Services, after consultation with the Attorney General, shall determine whether existing legal controls under subchapter I of the Controlled Substances Act and the Federal Food, Drug, and Cosmetic Act meet the requirements of the schedule specified in the notification with respect to the specific drug or substance.
[8] *Id.*

"Ketamine," Drug Enforcement Administration, last modified September 2019, https://www.deadiversion.usdoj.gov/drug_chem_info/ketamine.pdf.

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