Ketamine Drug for Pain Management

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Introduction

Ketamine is a dissociative anesthetic developed in the 1960s and introduced into clinical practice as an intravenous or intramuscular agent for anesthesia. The original essay correctly identified its continuing use in emergency, disaster, surgical, and veterinary settings and its growing role in difficult pain management. However, ketamine's regulatory status and evidence must be stated carefully. In the United States, approved ketamine products are indicated primarily for general anesthesia. Intravenous ketamine for acute or chronic pain is commonly used off label by qualified clinicians, meaning that the use is not the specific indication approved on the product label. Evidence supports benefit in selected conditions and settings, but results vary, long-term data are limited, and treatment requires monitoring. Ketamine is not a routine first-line drug for every painful condition and should not be obtained or administered without licensed medical supervision (Schwenk et al., 2018; Cohen et al., 2018; U.S. Food and Drug Administration, 2026).

How Ketamine Produces Analgesia

Ketamine is best known as a noncompetitive antagonist at the N-methyl-D-aspartate (NMDA) receptor, where it binds within the receptor-associated ion channel and reduces excitatory glutamate signaling. NMDA activity contributes to central sensitization, "wind-up," and amplification of pain after repeated or intense stimulation. By reducing this process, subanesthetic ketamine may lessen pain and opioid tolerance or hyperalgesia. Its effects are more complex than one receptor: ketamine also influences opioid, monoaminergic, cholinergic, inflammatory, and other signaling systems. The drug's analgesic, anesthetic, dissociative, and psychotropic effects overlap but are not identical. Dose, rate, route, patient condition, and concurrent medicines influence which effects predominate (Schwenk et al., 2018; Cohen et al., 2018).

Difference Between Anesthetic and Analgesic Doses

At anesthetic doses, ketamine produces profound dissociation and loss of awareness while often preserving spontaneous breathing and cardiovascular tone better than some alternatives. At lower, subanesthetic doses, it may provide analgesia without full general anesthesia. "Low dose" is not a guarantee of no risk, and dosing protocols vary across acute-pain, chronic-pain, procedural, and psychiatric settings. A clinician must consider body size, comorbidities, opioid exposure, previous

response, and the treatment environment. Patients should not compare doses from unrelated clinics or indications because route and infusion duration alter exposure (Schwenk et al., 2018; Cohen et al., 2018).

Ketamine Infusion

A ketamine infusion delivers a controlled amount of medicine intravenously using an infusion pump. The original description of cannula placement and monitoring remains accurate in broad terms. Before treatment, clinicians review diagnosis, medications, cardiovascular history, psychiatric history, substance-use risk, liver function where relevant, pregnancy status, and previous adverse reactions. During infusion, the level of monitoring depends on dose and risk but may include blood pressure, heart rate, oxygen saturation, respiratory status, sedation, pain, and mental state. Personnel must be able to respond to airway, cardiovascular, and behavioral complications. The setting should provide resuscitation equipment and clear discharge criteria (Schwenk et al., 2018; Cohen et al., 2018).

Ketamine in Acute Pain

Consensus guidelines support considering intravenous ketamine as part of multimodal analgesia for selected acute-pain patients, especially people who are opioid tolerant, undergoing painful surgery, or experiencing refractory pain. It can reduce opioid requirements and improve analgesia in some perioperative settings. Ketamine may be given as a small bolus, infusion, or combination depending on protocol. It does not eliminate the need for assessment of the underlying cause of pain, regional anesthesia, non-opioid medicine, physical care, or appropriate opioid use. The treatment plan should target function and recovery rather than one pain score alone (Schwenk et al., 2018).

Ketamine and Opioids

The original essay stated that ketamine may be administered with opioids but then incorrectly suggested that opioid infusion alone minimizes opioid tolerance. Ketamine, rather than prolonged opioid exposure, may help reduce opioid requirements and counter some mechanisms of tolerance or opioid-induced hyperalgesia. Combining drugs can improve analgesia through different mechanisms, but it can also increase sedation and monitoring needs. Ketamine should not be used simply to permit uncontrolled opioid dosing. Clinicians should review respiratory risk, other sedatives, and the patient's functional response (Schwenk et al., 2018; Cohen et al., 2018).

Chronic Neuropathic Pain

Ketamine is sometimes used for severe neuropathic pain that has not responded adequately to established treatments. Neuropathic pain results from disease or injury affecting the somatosensory

nervous system and may involve burning, electric-shock sensations, allodynia, numbness, or exaggerated pain. Evidence for ketamine varies by condition, dose, and follow-up duration. Temporary reduction can occur, but durable benefit is less certain. A specialist should confirm the diagnosis and review options such as antidepressants used for pain, anticonvulsant medicines, topical treatment, rehabilitation, psychological support, interventional procedures, and management of the underlying disorder. Calling ketamine a universal “third-line agent” is too simple because guidelines differ (Cohen et al., 2018).

Complex Regional Pain Syndrome

Complex regional pain syndrome (CRPS) is among the chronic conditions for which ketamine infusions have been studied. CRPS can involve disproportionate regional pain, sensory change, swelling, temperature or color difference, motor dysfunction, and trophic change. Some trials and clinical series report pain reduction after multi-hour or multi-day infusions, but response is inconsistent and adverse effects increase with dose. Ketamine should be integrated with physical and occupational rehabilitation because avoiding movement can worsen disability. An infusion that reduces pain temporarily may create a window for functional therapy, but it does not address every aspect of CRPS (Cohen et al., 2018).

Other Chronic-Pain Conditions

Ketamine has been investigated in spinal-cord injury pain, phantom-limb pain, fibromyalgia, cancer-related pain, ischemic pain, and other difficult syndromes. The quality of evidence is uneven, and a positive result in one condition cannot be transferred automatically to another. The risk–benefit calculation may be more favorable when pain is severe, alternatives have failed, and treatment occurs in an experienced program. Clinics should define what counts as a meaningful response—such as improved sleep, mobility, participation, or reduced rescue medicine—rather than continue treatment based only on transient dissociation or vague subjective change (Cohen et al., 2018).

Patient Selection

Appropriate selection is essential because ketamine can worsen certain conditions or create unnecessary risk. Relative or absolute contraindications depend on dose and indication but may include poorly controlled cardiovascular disease, severe liver dysfunction, active psychosis, pregnancy, increased intracranial or intraocular pressure in particular situations, and uncontrolled substance-use disorder. A psychiatric history does not automatically exclude treatment, but clinicians should assess whether dissociation or perceptual effects could destabilize the patient. Selection should also consider whether reliable follow-up and transportation are available (Schwenk et al., 2018; Cohen et al., 2018).

Short-Term Cardiovascular Effects

Ketamine commonly increases sympathetic activity, which can raise blood pressure and heart rate. This may be useful in some anesthesia situations but dangerous in people with unstable cardiovascular disease. Palpitations and chest discomfort require prompt evaluation rather than being listed as expected psychological effects. Continuous electrocardiographic monitoring is not required for every low-risk protocol, but vital signs must be monitored according to dose and clinical status. Severe hypertension, arrhythmia, or ischemia are uncommon but important potential complications (World Health Organization, 2015; Cohen et al., 2018).

Respiratory and Airway Effects

Ketamine tends to preserve respiratory drive and airway reflexes better than many anesthetics, but it can still produce hypoventilation, apnea, airway obstruction, laryngospasm, or excessive secretions, particularly with rapid administration, high dose, or other sedatives. Increased salivation can be uncomfortable and may complicate airway management. The belief that ketamine never affects breathing is unsafe. Administration belongs in a setting with trained staff and appropriate rescue capability (World Health Organization, 2015; Schwenk et al., 2018).

Nausea, Vomiting, and Neurologic Effects

Nausea, vomiting, dizziness, blurred vision, nystagmus, impaired coordination, slurred speech, and sedation may occur. Rapid involuntary eye movements are a recognized sign, but seizures are not a routine expected effect and require medical evaluation. Patients should not drive, operate machinery, sign important documents, or make safety-sensitive decisions until the treating team confirms recovery. Discharge instructions should account for concurrent medicines and the duration of residual impairment (World Health Organization, 2015; U.S. Food and Drug Administration, 2026).

Dissociation and Perceptual Effects

Ketamine can alter perception of body, time, sound, and environment and may produce vivid imagery, derealization, depersonalization, or hallucination-like experiences. These effects are often called dissociation or psychotomimetic effects. Some patients find them neutral or pleasant; others experience fear, confusion, or loss of control. A calm environment, explanation, dose adjustment, and trained observation can reduce distress. Comparing medically supervised ketamine directly with LSD is imprecise because mechanisms, duration, dose, and clinical context differ. The relevant point is that perceptual alteration can be intense and requires preparation (World Health Organization, 2015; Cohen et al., 2018).

Cognitive Effects

During and shortly after an infusion, attention, memory, judgment, and reaction time may be impaired. Repeated heavy nonmedical use has been associated with cognitive problems, although the degree and reversibility vary. Clinical protocols should avoid assuming that intermittent supervised treatment carries no cumulative risk. Patients receiving repeated courses need review of function, memory concerns, frequency, and whether benefit persists. Treatment should stop when risk or burden exceeds meaningful improvement (World Health Organization, 2015).

Urinary and Bladder Toxicity

Chronic frequent ketamine misuse can cause painful urinary symptoms, inflammation, reduced bladder capacity, and upper urinary-tract damage. This condition is sometimes called ketamine-induced cystitis. Risk appears related to cumulative exposure, but precise thresholds are uncertain. Patients receiving repeated treatment should be asked about urinary frequency, urgency, pain, blood in urine, or pelvic discomfort. Symptoms require investigation and reconsideration of exposure. This important long-term harm was missing from the original article (World Health Organization, 2015).

Liver Effects

Repeated or prolonged infusions can be associated with elevated liver enzymes and, rarely, biliary or hepatic injury. Monitoring practices vary with treatment intensity, history, and cumulative dose. A patient with existing liver disease may require additional caution. Abnormal laboratory findings should not be ignored simply because pain has improved. The purpose of repeated assessment is to detect harm before it becomes severe (Cohen et al., 2018).

Abuse, Dependence, and Diversion

Ketamine is a Schedule III controlled substance in the United States and has nonmedical-use and diversion potential. Tolerance, craving, compulsive use, and escalating exposure can occur. A therapeutic program should screen risk without stigmatizing patients, maintain controlled storage and administration, document response, and avoid unsupervised products from unverified internet sources. The FDA has warned against websites offering unapproved ketamine products. Medical treatment and nonmedical use have different contexts, but controlled status remains relevant to safety (World Health Organization, 2015; U.S. Food and Drug Administration, 2026).

Ketamine and Depression Are Different Clinical Uses

Ketamine has received attention for rapid antidepressant effects, but racemic ketamine is not FDA-approved for a psychiatric indication. Esketamine, a related S-enantiomer nasal product, is approved for specific adult depressive indications under a restricted monitoring program. Pain treatment and psychiatric treatment use different protocols and goals. Evidence about depression should not be cited as proof that ketamine will control chronic pain, nor should an analgesic infusion be assumed to treat a mood disorder. Patients with both conditions need coordinated care (U.S. Food and Drug Administration, 2026).

Informed Consent

Informed consent should explain that pain use may be off label, what evidence exists for the specific condition, expected duration of benefit, alternatives, cost, adverse effects, driving restrictions, monitoring, and what would cause treatment to stop. Marketing terms such as “reset,” “cure,” or guaranteed long-term relief should be avoided. Patients should know whether the clinic provides comprehensive pain care or only an infusion. Financial vulnerability can be significant when repeated private treatment is expensive and insurance coverage is limited (Cohen et al., 2018; U.S. Food and Drug Administration, 2026).

Outcome Monitoring

A baseline should document pain characteristics, function, sleep, medicines, mental health, and goals. Follow-up should evaluate the same outcomes at planned intervals. A statistically or subjectively lower pain rating may not justify continued exposure if mobility, participation, or quality of life remain unchanged. Conversely, a modest pain-score change may be valuable if the person returns to rehabilitation or reduces harmful medication. Standardized monitoring improves decisions and allows comparison across treatments (Cohen et al., 2018).

Conclusion

Ketamine is an important anesthetic and a useful analgesic option in selected acute and chronic pain settings. It acts principally through NMDA-receptor antagonism and can reduce central sensitization and opioid requirements. Infusions require controlled dosing, patient selection, monitoring, and personnel prepared for cardiovascular, respiratory, dissociative, and other adverse effects. Evidence is strongest for particular short-term applications and more limited for sustained relief across many chronic conditions. Repeated exposure raises concerns about urinary, hepatic, cognitive, and abuse-

related harm. Ketamine should therefore be one component of a comprehensive, goal-directed pain plan rather than a stand-alone cure. Safe use depends on specialist judgment, informed consent, verified medication, and continued assessment of whether meaningful benefit outweighs risk (Schwenk et al., 2018; Cohen et al., 2018; U.S. Food and Drug Administration, 2026).

References

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