

Intravenous Anesthetics for the Treatment of Chronic Pain and Psychiatric Disorders

Policy # 00463

Original Effective Date: 02/18/2015

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

Note: esketamine (Spravato™) is addressed separately in medical policy 00681.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers intravenous (IV) infusion of anesthetics (e.g., ketamine or lidocaine) for the treatment of chronic pain, including, but not limited to chronic neuropathic pain, chronic daily headache, and fibromyalgia to be **investigational**.*

Based on review of available data, the Company considers intravenous infusion (IV) of anesthetics (eg, ketamine or lidocaine) for the treatment of psychiatric disorders, including but not limited to treatment-resistant depression and obsessive-compulsive disorder, and post-traumatic stress disorder, to be **investigational**.*

Background/Overview

Intravenous Anesthetic Agents

Courses of intravenous (IV) anesthetic agents may be given in the inpatient or outpatient setting as part of a pain management program, with the infusion of a subanesthetic dose preceded by a bolus infusion to achieve desired blood levels sooner. Treatment protocols for the initial cycle may include infusion of subanesthetic doses for 1 to 6 hours for up to 10 days.

Lidocaine

Lidocaine, which prevents neural depolarization through effects on voltage-dependent sodium channels, is also used systemically for the treatment of arrhythmias. Adverse events for lidocaine are common, can be mild to moderate, and include general fatigue, somnolence, dizziness, headache, periorbital and extremity numbness and tingling, nausea, vomiting, tremors, and changes in blood pressure and pulse. Severe adverse events may include arrhythmias, seizures, loss of consciousness, confusion, or even death. Lidocaine should only be given IV to patients with normal conduction on

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electrocardiography and normal serum electrolyte concentrations to minimize the risk of cardiac arrhythmias.

Ketamine

Ketamine is an antagonist of the *N*-methyl-D-aspartate receptor and is a dissociative anesthetic. Respiratory depression may occur with overdosage or a rapid rate of ketamine administration. Ketamine is a schedule III controlled substance. Psychological manifestations vary in severity from pleasant, dream-like states to hallucinations and delirium; further, these manifestations can be accompanied by confusion, excitement, aggression, or irrational behavior. The occurrence of adverse events with IV anesthetics may be reduced by the careful titration of subanesthetic doses. However, the potential benefits must be carefully weighed against the potential for serious, harmful adverse events.

Indications

The IV administration of anesthetics has been reported for various conditions, including chronic headache, chronic pain of neuropathic origin, fibromyalgia, depression, and obsessive-compulsive disorders.

Chronic daily headache is defined as a headache disorder that occurs 15 or more days a month for more than 3 months. Chronic daily headache includes chronic migraine, new daily persistent headache, hemicranias continua, and chronic tension-type headache.

Neuropathic pain is often disproportionate to the extent of the primary triggering injury and may consist of thermal or mechanical allodynia, dysesthesia, and/or hyperalgesia. Allodynia is pain that occurs from a stimulus that normally does not elicit a painful response (eg, light touch, warmth). Dysesthesia is a constant or ongoing unpleasant or electrical sensation of pain. Hyperalgesia is an exaggerated response to normally painful stimuli. In the latter, symptoms may continue longer (eg, ≥ 6 months) than clinically expected after an illness or injury. It is proposed that chronic neuropathic pain results from peripheral afferent sensitization, neurogenic inflammation, and sympathetic afferent coupling, along with sensitization and functional reorganization of the somatosensory, motor, and autonomic circuits in the central nervous system. Therefore, treatments focus on reducing activity and desensitizing pain pathways, thought to be mediated through *N*-methyl-d-aspartate receptors in the peripheral and central nervous system. Sympathetic ganglion blocks with lidocaine have been used to treat sympathetically maintained chronic pain conditions, such as complex regional pain syndrome (previously known as reflex sympathetic dystrophy). Test infusion of an anesthetic has also been used in treatment planning to assess patient responsiveness to determine whether medications, such as oral mexiletine or oral ketamine, may be effective. A course of IV lidocaine or ketamine, usually at subanesthetic doses, has also been examined. This approach for treating chronic neuropathic pain differs from continuous subcutaneous or IV infusion of anesthetics for managing chronic pain conditions, such as terminal cancer pain, which is not discussed herein.

Fibromyalgia is a chronic state of widespread pain and tenderness. Although fibromyalgia is generally considered a disorder of central pain processing or central sensitization, others have proposed that the nerve stimuli causing pain originates mainly in the muscle, causing both

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widespread pain and pain on movement. There are focal areas of hyperalgesia, or tender points, which tend to occur at muscle-tendon junctions. Biochemical changes associated with fibromyalgia include alterations in *N*-methyl-d-aspartate receptors, low levels of serotonin, suppression of dopamine-releasing neurons in the limbic system, dysfunction of the hypothalamic-pituitary-adrenal axis, and elevated substance P levels. Fibromyalgia is typically treated with neuropathic pain medications such as pregabalin, non-narcotic pain relievers, or low doses of antidepressants.

The use of IV ketamine has also been reported for treatment-resistant depression, defined as depression that does not respond adequately to appropriate courses of antidepressant medications. Particularly challenging are patients with treatment-resistant depression with suicidal ideation. Several studies are ongoing to test the efficacy of IV ketamine in patients with suicidal ideation who present to the emergency department.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Intravenous lidocaine is approved by the U.S. Food and Drug Administration for systemic use in the acute treatment of arrhythmias and locally as an anesthetic; IV lidocaine for the treatment of chronic pain or psychiatric disorders is considered off-label use.

Ketamine hydrochloride injection is approved for diagnostic and surgical procedures that do not require skeletal muscle relaxation, for the induction of anesthesia before the administration of other general anesthetic agents, and to supplement low-potency agents, such as nitrous oxide. IV ketamine for the treatment of chronic pain or psychiatric disorders is an off-label use.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Description

Intravenous (IV) infusion of lidocaine or ketamine has been investigated for the treatment of migraine and chronic daily headache, fibromyalgia, and chronic neuropathic pain. Chronic neuropathic pain disorders include phantom limb pain, post-herpetic neuralgia, complex regional pain syndrome, diabetic neuropathy, and pain related to stroke or spinal cord injuries. An IV infusion of ketamine has also been investigated for treatment-resistant depression and obsessive-compulsive disorder (OCD).

Summary of Evidence

For individuals who have chronic pain syndromes (eg, neuropathic pain or fibromyalgia) who receive a course of IV anesthetics (eg, lidocaine, ketamine), the evidence includes systematic reviews, several randomized controlled trials (RCTs), and observational studies. Relevant outcomes

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are symptoms, change in disease status, morbid events, functional outcomes, quality of life (QOL), medication use, and treatment-related morbidity. Several RCTs have been performed using IV lidocaine for post-herpetic neuralgia (PHN), complex regional pain syndrome (CRPS), and diabetic neuropathy. These trials have failed to show a durable effect of lidocaine infusion on chronic pain. Two trials with a total of 100 patients provide limited evidence that courses of IV ketamine may provide temporary relief (2 to 4 weeks) to some chronic pain patients in some settings. Neither of the RCTs used an active control, raising concerns about placebo effects. A third trial found no benefit from a single infusion of ketamine or ketamine/magnesium. Overall, the intense treatment protocols, the severity of adverse events, and the limited treatment durability raise questions about the net health benefit of this therapy. Additional clinical trials are needed to evaluate the long-term efficacy and safety of repeat courses of IV anesthetics for chronic pain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have treatment-resistant depression who receive a course of IV ketamine, the evidence consists of systematic reviews, RCTs, and case series. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. Two publications of double-blind trials were identified that compared repeated ketamine infusion with an infusion of saline for treatment-resistant depression. Additionally, 2 open-label, randomized trials comparing ketamine infusion to electroconvulsive therapy (ECT) were identified. There is a possibility of publication bias due to the lack of publication of many other small trials. Systematic reviews in patients with unipolar depression or depression related to bipolar disorder have identified numerous studies evaluating the efficacy of ketamine infusion. While the analyses indicate depression improvement in the short-term, there is limited evidence beyond a single infusion. One study with 26 patients found no significant difference in a depression scale at the end of infusion. A larger RCT (N=68) found a significantly greater improvement in a depression scale during the 4-week infusion period, but the effect diminished over 3 weeks post-infusion. The trial did not use an active control, raising the possibility of placebo effects and unblinding of patients and investigators. The open-label, randomized trials comparing ketamine with ECT produced mixed results, with the first trial indicating ketamine was not noninferior to ECT in inducing remission and the second trial indicating ketamine was noninferior to ECT in inducing response. These divergent findings may be attributable to differences in the populations studied, as the first trial was conducted in severely ill inpatients and the second trial was conducted in a less severely ill, predominantly outpatient sample. Large observational studies in patients with depression indicate improvement on depression rating scales following ketamine infusions; however, these studies lack a control group, and no firm conclusions on the effectiveness or safety of serial ketamine infusions can be drawn from this evidence. Common side effects of ketamine infusion include headache, anxiety, dissociation, nausea, and dizziness. The intense treatment protocols, the severity of adverse events, and the short treatment durability limit the clinical utility of the treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have other psychiatric disorders (eg, obsessive-compulsive disorder [OCD], post-traumatic stress disorder [PTSD]) who receive a course of IV ketamine, the evidence consists of RCTs and case series. Relevant outcomes are symptoms, change in disease status, morbid events,

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functional outcomes, quality of life, medication use, and treatment-related morbidity. One double-blind, placebo-controlled trial and case series for OCD treatment, and 1 double-blind trial comparing multiple ketamine infusions with midazolam in chronic PTSD were identified. There is a possibility of publication bias due to the lack of publication of many other small trials. One double-blind, crossover RCT in patients with serotonin reuptake inhibitor-resistant OCD (N=15) found that ketamine infusion provided a higher frequency of Yale-Brown Obsessive Compulsive Scale (YBOCS) response at day 7 compared with placebo; however, unblinding was suspected and only data from the first phase were analyzed because of a carryover effect of ketamine. A case series (N=14) identified only 1 patient who demonstrated prespecified significant YBOCS response after 2 to 3 weeks. A single RCT in patients with chronic PTSD (N=30) found that ketamine infusion produced significantly greater improvements in a PTSD symptom scale at 2 weeks compared to midazolam. Common side effects of ketamine infusion include headache, anxiety, dissociation, nausea, and dizziness. The intense treatment protocols, the severity of adverse events, and the short treatment durability limit the clinical utility of the treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Society of Regional Anesthesia and Pain Medicine et al

In 2018, the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine and the American Society of Anesthesiologists issued a joint consensus guideline on the use of intravenous (IV) ketamine for treatment of chronic pain. The guideline found:

- Weak evidence supporting use of IV ketamine for short-term improvement in patients with spinal cord injury pain
- Moderate evidence supporting use of IV ketamine for improvement in patients with chronic regional pain syndrome up to 12 weeks
- Weak or no evidence for immediate improvement with IV ketamine use for other pain conditions, including mixed neuropathic pain, fibromyalgia, cancer pain, ischemic pain, headache and spinal pain

American Psychiatric Association

In 2017, the American Psychiatric Association (APA) published an evidence review and consensus opinion of the use of ketamine in treatment-resistant depression. The APA noted that "while ketamine may be beneficial to some patients with mood disorders, it is important to consider the limitations of the available data and the potential risk associated with the drug when considering the treatment option."

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U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Over 100 trials evaluating IV infusion of ketamine for depression are listed on clinicaltrials.gov. The majority are completed but not published. Some currently ongoing and unpublished trials that include over 50 participants are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT05339074	Maintenance Ketamine Infusions for Treatment-Resistant Bipolar Depression: An Open-Label Extension Trial	60	Feb 2026
NCT05045378	Low-dose Ketamine Infusion Among Adolescents With Treatment-resistant Depression: a Randomized, Double-blind Placebo-control Study	54	Dec 2026
NCT05973851	A Randomised, Controlled Trial to Investigate the Effect of a Six week Intensified Pharmacological Treatment for Major Depressive Disorder Compared to Treatment as Usual in Subjects Who Had a First-time Treatment Failure on Their First-line Treatment.	418	Jun 2026
NCT06034821	Rapid Reversal of Suicidal Depression: Comparative Effectiveness of ECT vs. KETAMINE Over the Lifespan (REaKT-SD)	1500	Mar 2030
NCT04032301	Characterization of Comorbid Post-traumatic Stress Disorder and Major Depressive Disorder Utilizing Ketamine as an Experimental Medicine Probe	108	Apr 2025
<i>Unpublished</i>			
NCT02461927	Ketamine for The Rapid Treatment of Major Depression and Alcohol Use Disorder	65	Oct 2023

NCT: national clinical trial.

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References

1. Yousefshahi F, Predescu O, Francisco Asenjo J. The Efficacy of Systemic Lidocaine in the Management of Chronic Pain: A Literature Review. *Anesth Pain Med.* Jun 2017; 7(3): e44732. PMID 28856112
2. Israel JE, St Pierre S, Ellis E, et al. Ketamine for the Treatment of Chronic Pain: A Comprehensive Review. *Health Psychol Res.* 2021; 9(1): 25535. PMID 34746491
3. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia.* Jan 2018; 38(1): 1-211. PMID 29368949
4. Gwathmey KG, Pearson KT. Diagnosis and management of sensory polyneuropathy. *BMJ.* May 08 2019; 365: 11108. PMID 31068323
5. Winslow BT, Vandal C, Dang L. Fibromyalgia: Diagnosis and Management. *Am Fam Physician.* Feb 2023; 107(2): 137-144. PMID 36791450
6. McIntyre RS, Alsuwaidan M, Baune BT, et al. Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. *World Psychiatry.* Oct 2023; 22(3): 394-412. PMID 37713549
7. Wertli MM, Kessels AG, Perez RS, et al. Rational pain management in complex regional pain syndrome 1 (CRPS 1)--a network meta-analysis. *Pain Med.* Sep 2014; 15(9): 1575-89. PMID 25234478
8. Schwartzman RJ, Alexander GM, Grothusen JR, et al. Outpatient intravenous ketamine for the treatment of complex regional pain syndrome: a double-blind placebo controlled study. *Pain.* Dec 15 2009; 147(1-3): 107-15. PMID 19783371
9. Sigtermans MJ, van Hilten JJ, Bauer MCR, et al. Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1. *Pain.* Oct 2009; 145(3): 304-311. PMID 19604642
10. O'Connell NE, Wand BM, McAuley J, et al. Interventions for treating pain and disability in adults with complex regional pain syndrome. *Cochrane Database Syst Rev.* Apr 30 2013; 2013(4): CD009416. PMID 23633371
11. Ferraro MC, Cashin AG, Wand BM, et al. Interventions for treating pain and disability in adults with complex regional pain syndrome- an overview of systematic reviews. *Cochrane Database Syst Rev.* Jun 12 2023; 6(6): CD009416. PMID 37306570
12. Lee JH, Koutalios EP, Leimer EM, et al. Intravenous Lidocaine in Chronic Neuropathic Pain: A Systematic Review. *Clin J Pain.* Dec 01 2022; 38(12): 739-748. PMID 36288104
13. Kim YC, Castañeda AM, Lee CS, et al. Efficacy and Safety of Lidocaine Infusion Treatment for Neuropathic Pain: A Randomized, Double-Blind, and Placebo-Controlled Study. *Reg Anesth Pain Med.* May 2018; 43(4): 415-424. PMID 29381569
14. Liu H, Lu F, Zhou D, et al. The Analgesic and Emotional Response to Intravenous Lidocaine Infusion in the Treatment of Postherpetic Neuralgia: A Randomized, Double-Blinded, Placebo-controlled Study. *Clin J Pain.* Nov 2018; 34(11): 1025-1031. PMID 29698250
15. Moulin DE, Morley-Forster PK, Pirani Z, et al. Intravenous lidocaine in the management of chronic peripheral neuropathic pain: a randomized-controlled trial. *Can J Anaesth.* Jul 2019; 66(7): 820-827. PMID 31098961

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16. Amr YM. Multi-day low dose ketamine infusion as adjuvant to oral gabapentin in spinal cord injury related chronic pain: a prospective, randomized, double blind trial. *Pain Physician*. 2010; 13(3): 245-9. PMID 20495588
17. Pickering G, Pereira B, Morel V, et al. Ketamine and Magnesium for Refractory Neuropathic Pain: A Randomized, Double-blind, Crossover Trial. *Anesthesiology*. Jul 2020; 133(1): 154-164. PMID 32384291
18. Przeklasa-Muszyńska A, Kocot-Kępska M, Dobrogowski J, et al. Intravenous lidocaine infusions in a multidirectional model of treatment of neuropathic pain patients. *Pharmacol Rep*. Oct 2016; 68(5): 1069-75. PMID 27552062
19. Vacher E, Kosela M, Song-Smith C, et al. Lidocaine infusions in chronic pain management: A prospective case series analysis. *Br J Pain*. Jun 2022; 16(3): 270-280. PMID 35646339
20. Patil S, Anitescu M. Efficacy of outpatient ketamine infusions in refractory chronic pain syndromes: a 5-year retrospective analysis. *Pain Med*. Feb 2012; 13(2): 263-9. PMID 21939497
21. Mangnus TJP, Dirckx M, Bharwani KD, et al. Effect of intravenous low-dose S-ketamine on pain in patients with Complex Regional Pain Syndrome: A retrospective cohort study. *Pain Pract*. Nov 2021; 21(8): 890-897. PMID 34233070
22. de Carvalho JF, Skare TL. Lidocaine in fibromyalgia: A systematic review. *World J Psychiatry*. Apr 19 2022; 12(4): 615-622. PMID 35582338
23. Noppers I, Niesters M, Swartjes M, et al. Absence of long-term analgesic effect from a short-term S-ketamine infusion on fibromyalgia pain: a randomized, prospective, double blind, active placebo-controlled trial. *Eur J Pain*. Oct 2011; 15(9): 942-9. PMID 21482474
24. Dean RL, Hurducas C, Hawton K, et al. Ketamine and other glutamate receptor modulators for depression in adults with unipolar major depressive disorder. *Cochrane Database Syst Rev*. Sep 12 2021; 9(9): CD011612. PMID 34510411
25. Dean RL, Marquardt T, Hurducas C, et al. Ketamine and other glutamate receptor modulators for depression in adults with bipolar disorder. *Cochrane Database Syst Rev*. Oct 08 2021; 10(10): CD011611. PMID 34623633
26. Grasso V, Gutierrez G, Alzbeidi N, et al. Cognitive changes in patients with unipolar TRD treated with IV ketamine: A systematic review. *Prog Neuropsychopharmacol Biol Psychiatry*. Dec 20 2024; 135: 111095. PMID 39032855
27. Singh JB, Fedgchin M, Daly EJ, et al. A Double-Blind, Randomized, Placebo-Controlled, Dose-Frequency Study of Intravenous Ketamine in Patients With Treatment-Resistant Depression. *Am J Psychiatry*. Aug 01 2016; 173(8): 816-26. PMID 27056608
28. Ekstrand J, Fattah C, Persson M, et al. Racemic Ketamine as an Alternative to Electroconvulsive Therapy for Unipolar Depression: A Randomized, Open-Label, Non-Inferiority Trial (KetECT). *Int J Neuropsychopharmacol*. May 27 2022; 25(5): 339-349. PMID 35020871
29. Anand A, Mathew SJ, Sanacora G, et al. Ketamine versus ECT for Nonpsychotic Treatment-Resistant Major Depression. *N Engl J Med*. Jun 22 2023; 388(25): 2315-2325. PMID 37224232
30. Ionescu DF, Bentley KH, Eikermann M, et al. Repeat-dose ketamine augmentation for treatment-resistant depression with chronic suicidal ideation: A randomized, double blind, placebo controlled trial. *J Affect Disord*. Jan 15 2019; 243: 516-524. PMID 30286416
31. McInnes LA, Qian JJ, Gargeya RS, et al. A retrospective analysis of ketamine intravenous therapy for depression in real-world care settings. *J Affect Disord*. Mar 15 2022; 301: 486-495. PMID 35027209

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32. Oliver PA, Snyder AD, Feinn R, et al. Clinical Effectiveness of Intravenous Racemic Ketamine Infusions in a Large Community Sample of Patients With Treatment-Resistant Depression, Suicidal Ideation, and Generalized Anxiety Symptoms: A Retrospective Chart Review. *J Clin Psychiatry*. Sep 12 2022; 83(6). PMID 36112599
33. Zhou Y, Wang C, Lan X, et al. The effectiveness of repeated intravenous ketamine on subjective and objective psychosocial function in patients with treatment-resistant depression and suicidal ideation. *J Affect Disord*. May 01 2022; 304: 78-84. PMID 35176337
34. Pfeiffer PN, Geller J, Ganoczy D, et al. Clinical Outcomes of Intravenous Ketamine Treatment for Depression in the VA Health System. *J Clin Psychiatry*. Jan 08 2024; 85(1). PMID 38206011
35. Gutierrez G, Kang MJY, Vazquez G. IV low dose ketamine infusions for treatment resistant depression: Results from a five-year study at a free public clinic in an academic hospital. *Psychiatry Res*. May 2024; 335: 115865. PMID 38518518
36. Rodriguez CI, Kegeles LS, Levinson A, et al. Randomized controlled crossover trial of ketamine in obsessive-compulsive disorder: proof-of-concept. *Neuropsychopharmacology*. Nov 2013; 38(12): 2475-83. PMID 23783065
37. Feder A, Costi S, Rutter SB, et al. A Randomized Controlled Trial of Repeated Ketamine Administration for Chronic Posttraumatic Stress Disorder. *Am J Psychiatry*. Feb 01 2021; 178(2): 193-202. PMID 33397139
38. Sharma LP, Thamby A, Balachander S, et al. Clinical utility of repeated intravenous ketamine treatment for resistant obsessive-compulsive disorder. *Asian J Psychiatr*. Aug 2020; 52: 102183. PMID 32554207
39. Cohen SP, Bhatia A, Buvanendran A, et al. Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. *Reg Anesth Pain Med*. Jul 2018; 43(5): 521-546. PMID 29870458
40. Sanacora G, Frye MA, McDonald W, et al. A Consensus Statement on the Use of Ketamine in the Treatment of Mood Disorders. *JAMA Psychiatry*. Apr 01 2017; 74(4): 399-405. PMID 28249076
41. Peyrovian B, McIntyre RS, Phan L, et al. Registered clinical trials investigating ketamine for psychiatric disorders. *J Psychiatr Res*. Aug 2020; 127: 1-12. PMID 32315806

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02/05/2015 Medical Policy Committee review

02/18/2015 Medical Policy Implementation Committee approval. New policy.

08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.

02/04/2016 Medical Policy Committee review

02/17/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes

02/01/2018 Medical Policy Committee review

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02/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/07/2019	Medical Policy Committee review
02/20/2019	Medical Policy Implementation Committee approval. Added psychiatric disorders to the investigational statement.
02/06/2020	Medical Policy Committee review
02/12/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Title changed from “Intravenous Anesthetics for the Treatment of Chronic Pain” to “Intravenous Anesthetics for the Treatment of Chronic Pain and Psychiatric Disorders”. INV statement separated into two statements one for pain and the other for psychiatric disorders, including but not limited to depression and obsessive-compulsive disorder.
02/04/2021	Medical Policy Committee review
02/10/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/22/2021	Coding update
02/03/2022	Medical Policy Committee review
02/09/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/01/2024	Medical Policy Committee review
02/14/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2025	Medical Policy Committee review
02/12/2025	Medical Policy Implementation Committee approval. Added treatment-resistant to describe depression and post-traumatic stress disorder as investigational indications for intravenous infusion (IV) of anesthetics (eg, ketamine or lidocaine) for the treatment of psychiatric disorders.
09/02/2025	Coding update
02/05/2026	Medical Policy Committee review
02/11/2026	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 02/2027

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2025 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	01999, 96365, 96366, 96367, 96368
HCPCS	No codes
ICD-10 Diagnosis	F0150-F99, Z8651-Z8659

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.