Effective November 1, 2023, refer to <u>CMS</u>
<u>Manual 100-02, Chapter</u>
<u>16-General Exclusions</u>
<u>from Coverage</u> for services included in this policy.



Name of Blue Advantage Policy:

Opioid Antagonists under Heavy Sedation or General Anesthesia as a Technique of Opioid Detoxification

Policy #: 091

Latest Review Date: September 2023

Category: Pharmacology

ARCHIVED EFFECTIVE 11/1/2023

BACKGROUND:

Blue Advantage medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:

- 1. Safe and effective;
- 2. Not experimental or investigational*;
- 3. Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:
 - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
 - Furnished in a setting appropriate to the patient's medical needs and condition;
 - Ordered and furnished by qualified personnel;
 - One that meets, but does not exceed, the patient's medical need; and
 - At least as beneficial as an existing and available medically appropriate alternative.

*Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill **Original Medicare** for covered services that are related to **clinical trials** that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).

POLICY:

Blue Advantage will treat the techniques of rapid opioid detoxification (RD) and ultra-rapid opioid detoxification (URD) and related services, using opioid antagonists under heavy sedation or anesthesia as a non-covered benefit and as investigational.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

The use of relatively high doses of opioid antagonists under deep sedation or general anesthesia is a technique for opioid detoxification and is known as ultra-rapid detoxification. It is a potential alternative to standard detoxification that allows individuals to avoid the acute symptoms associated with initial detoxification. Ultra rapid detoxification is used in conjunction with maintenance treatments, e.g., oral opioid antagonists and psychosocial support.

The traditional treatment of opioid addiction involves substituting the opioid, i.e., heroin, with an equivalent close of a long-acting opioid antagonist, i.e., methadone, and tapering to a maintenance dose. Methadone maintenance therapy does not resolve opiate addiction, but along with education and counseling, it has been shown to result in improved general health, retention of individuals in treatment, and a decrease in the risk of transmitting HIV or hepatitis. However, critics of methadone maintenance point out that this strategy substitute's one drug for another. Detoxification followed by abstinence is another treatment option, which can be used as the initial treatment of opioid addiction or offered as a final treatment strategy for individuals on methadone maintenance. Detoxification is associated with acute symptoms, followed by a longer period of protracted symptoms which can last up to six months. Although typically not life threatening, acute detoxification symptoms include anxiety, apprehension, irritability, chills, nausea, diarrhea, coughing, sneezing, lacrimation, rhinorrhea, sweating, yawning, muscular and abdominal pains, general weakness and insomnia. Protracted withdrawal symptoms include changes in pupillary size, autonomic dysfunction, changes in sleep pattern, a general feeling of reduced well-being and drug cravings. Relapse is common during this period.

Detoxification may be initiated with tapering doses of methadone or buprenorphine (an opioid agonist-antagonist), treatment with a combination of buprenorphine and naloxone (an opioid antagonist), or discontinuation of opioids and administration of oral clonidine and other medications to relieve acute symptoms. However, no matter what type of individual support and oral medications are offered, detoxification is associated with discomfort, and many may be unwilling to attempt detoxification. In addition, detoxification is only the first stage of treatment. Without ongoing medication and psychosocial support after detoxification, the probability is low

that any detoxification procedure alone will result in lasting abstinence. Opioid antagonists, such as naltrexone, may also be used as maintenance therapy to reduce drug craving and thus reduce the risk of relapse.

Dissatisfaction with current approaches to detoxification has led to interest in using relatively high doses of opioid antagonists, such as naltrexone, naloxone, or nalmefene under deep sedation with benzodiazepine or general anesthesia. This strategy has been referred to as "ultra-rapid," "anesthesia-assisted," or "one-day" detoxification.

A rapid opioid detoxification (ROD) technique is designed to shorten detoxification by precipitating withdrawal through the administration of opioid antagonists such as naloxone hydrochloride or naltrexone in awake individuals. This approach gets individuals through detoxification rapidly to minimize the risk of relapse, and quickly initiate treatment with naltrexone maintenance and psychosocial intervention.

The use of opioid antagonists accelerates the acute phase of detoxification, which can be completed in 24 to 48 hours. Individuals have no discomfort or memory of the symptoms of acute withdrawal. A variety of other medications may be used to control acute withdrawal symptoms: such as clonidine (to attenuate sympathetic and hemodynamic effects of withdrawal), ondansetron (to control nausea and vomiting), and somatostatin (to control diarrhea). The procedure is done as an inpatient if general anesthesia is used or possibly as an outpatient if heavy sedation is used. Initial detoxification is followed by ongoing support for the protracted symptoms of withdrawal. In addition, naltrexone may be continued to discourage relapse.

UROD may be offered by specialized facilities such as Neuraad™ treatment Centers, Nutmeg Intensive Rehabilitation and center for Research and Treatment of Addiction (CITA). These programs typically consist of three phases: a comprehensive evaluation, inpatient detoxification under anesthesia, and mandatory post detoxification care and follow up. The program may be offered to individuals addicted to opioid or narcotic drugs such as opium, heroin, methadone, morphine, meperidine, hydromorphone, fentanyl, oxycodone, hydrocodone, or butorphanol. Once acute detoxification is complete, the opioid antagonist naltrexone is often continued to decrease drug craving, with the hope of reducing the incidence of relapse.

KEY POINTS:

This policy's most recent literature review was performed through September 20, 2023. The following information is a summary of the key literature.

Summary of Evidence

The evidence for ultra-rapid detoxification under general anesthesia in individuals with opioid addiction includes both randomized and nonrandomized clinical trials, as well as prospective follow-up studies, which compare other approaches not involving deep or general anesthesia. Relevant outcomes are change in disease status, treatment-related morbidity and mortality, in addition to continued abstinence from opioids or relapse to daily opioid use. There is a paucity of data in the controlled trials and a lack of standardized approach to ultra-rapid detoxification.

Additionally, significant adverse effects, including life-threatening complications, are a concern using this treatment. Most patients subsequently return to daily use shortly after this technique. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

National Collaborating Centre for Mental Health

In 2019, National Collaborating Centre for Mental Health, commissioned by the National Institute for Health and Clinical Excellence issued a minor update to clinical practice guidelines on "drug misuse, opioid detoxification." The guidelines included the following statement regarding ultra-rapid detoxification. "Ultra-rapid detoxification has courted controversy; the main issues with such an approach involve the high degree of risk, including fatalities. This is particularly striking given that opioid withdrawal alone rarely results in death. Furthermore, the associated costs required to give the appropriate medical support are much greater than for other methods of detoxification. There has been much debate over its effectiveness, with limited long-term outcome data available."

American Psychiatric Association

In 2007, the American Psychiatric Association Work Group on Substance Use disorders released a practice guideline for the treatment of patients with substance use disorders. The practice guideline includes the following recommendation "anesthesia-assisted rapid opioid detoxification (AROD) is not recommended because of lack of proven efficacy and adverse risk-benefit ratios."

The American Society of Addiction Medicine

In 2015, the American Society of Addiction Medicine published a public policy statement regarding opiate detoxification under sedation or anesthesia (OADUSA) (update of their 2005 statement). It included the following position statements:

- Opioid withdrawal management using anesthesia ultra-rapid opioid detoxification (UROD) is not recommended because of high risk for adverse events or death.
- Ultra-Rapid Opioid Detoxification (UROD) is a procedure with uncertain risks and benefits, and its use in clinical settings is not supportable until a clearly positive risk-benefit relationship can be demonstrated. Further research on UROD should be conducted.
- Although there is medical literature describing various techniques of Rapid Opioid Detoxification (ROD), further research into the physiology and consequences of ROD should be supported so that patients may be directed to the most effective treatment methods and practices.

U.S. Preventive Services Task Force Recommendations

No U.S. Preventive Services Task Force recommendations for opioid detoxification under heavy sedation or general anesthesia have been identified.

KEY WORDS:

Detoxification, opioids, opioid agonist and antagonist, naloxone, naltrexone, buprenorphine, clonidine, methadone, rapid opioid detoxification (ROD), ultra-rapid opioid detoxification (UROD), general anesthesia, opioid antagonist agent detoxification under sedation or anesthesia (OADUSA), one day detox

APPROVED BY GOVERNING BODIES:

Not applicable.

BENEFIT APPLICATIONS:

Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT codes:

01999	Unlisted anesthesia procedure	
-------	-------------------------------	--

REFERENCES:

- 1. American Society of Addiction Medicine (ASAM). Public policy statement on opioid antagonist agent detoxification under sedation or anesthesia (OADUSA), J Addictive Disease 2000; 19(4): 109-112.
- 2. Bearn J, Gossop M, Strang J. Rapid opiate detoxification treatments. Drug Alcohol Rev 1999; 18(1):75-81.
- 3. Brewer C, Laban M, Schmulian C et al. Rapid opiate detoxification and naltrexone induction under general anaesthesia and assisted ventilation: experience with 510 patients in four different centres. Acta Psychiatr Belg 1998; 98:181-9.
- 4. Camarasa X, Khazaal Y, Besson J and Zullino DF. Naltrexone-assisted rapid methadone discontinuation: A pilot study. Eur Addict Res 2007; 13(1): 20-24.
- 5. Collins ED, Kleber HD, Whittington RA et al. Anesthesia-assisted vs buprenorphine- or clonidine-assisted heroin detoxification and naltrexone induction: a randomized trial. JAMA 2005; 294(8):903-13.
- 6. Dyer C. Addict died after rapid opiate detoxification. BMJ 1998; 316(7126):170.
- 7. Favrat B, Zimmerman G, Zullino D, et al. Opioid antagonist detoxification under anaesthesia versus traditional clonidine detoxification combined with an additional week of psychosocial support: A randomised clinical trial. Drug Alcohol Depend, February 2006; 81(2): 109-116.

- 8. Forozeshfard M, Hosseinzadeh Zoroufchi B, Saberi Zafarghandi MB, et al. Six-month follow-up study of ultra-rapid opiate detoxification with naltrexone. Int J High Risk Behav Addict. Dec 2014;3(4):e20944.
- 9. Gold CG, Cullen DJ, Gonzales S et al. Rapid opioid detoxification during general anesthesia: a review of 20 patients. Anesthesiology 1999; 91(6):1639-47.
- 10. Gowing L, Ali R, White J. Opioid antagonists under heavy sedation or anaesthesia for opioid withdrawal. Cochrane Database Syst Rev 2010; (1):CD002022.
- 11. Hensel, M., Kox, W.J. Safety, efficacy, and long-term results of a modified version of rapid opiate detoxification under general anesthesia: A prospective study in methadone, heroin, codeine, and morphine addicts, Octa Anesthesiology Scandinavia, March 2000; 44 (3), pp. 326-33.
- 12. IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.
- 13. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med. 2015 Sep-Oct;9(5):358-67.
- 14. Kienbaum P, Scherbaum N, Thurauf N et al. Acute detoxification of opioid-addicted patients with naloxone during propofol or methohexital anesthesia: a comparison of withdrawal symptoms, neuroendocrine, metabolic and cardiovascular patterns. Crit Care Med 2000; 28(4):969-76.
- 15. Kleber HD, Weiss RD, Anton RF, et al. Treatment of patients with substance use disorders, second edition. American Psychiatric [sic] Association. Am J Psychiatry, August 2006; 163 (8 Suppl): 5-82.
- 16. Krambeer, Ll., von McKnelly Jr., W., et al. Methadone therapy for opioid dependence, American Family Physician, June 15, 2001; 63(12): 2404-10.
- 17. Nasr DA, Omran HA, Hakim SM et al. Ultra-rapid opiate detoxification using dexmedetomidine under general anesthesia. J Opioid Manag 2011; 7(5):337-44.
- 18. National Institute for Health and Clinical Evidence. Drug misuse, opioid detoxification. NICE Clinical Guideline 52. Available at www.nice.org.uk/guidance/cg52/evidence/drug-misuse-opioid-detoxification-full-guideline-196515037.
- 19. O'Connor, Patrick G., Kosten, Thomas R. Review: Rapid and ultra-rapid opioid detoxification techniques, JAMA, January 21, 1998, Vol. 279, No. 3, pp. 229-234.
- 20. Qiu YW, Jiang GH, Su HH, et al. Short-term UROD treatment on cerebral function in codeine-containing cough syrups dependent male individuals. Eur Radiol. 2016; 26(9):2964-2973.
- 21. Salimi A, Safari F, Mohajerani SA, et al. Long-term relapse of ultra-rapid opioid detoxification. J Addict Dis. 2014;33(1):33-40.
- 22. Saxon AJ, McCance-Katz EF. Some Additional Considerations Regarding the American Society of Addiction Medicine National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med. 2016 May-Jun;10(3):140-2.

- 23. Scherbaum, N., Klein, S., and Kaube, H. Alternative strategies of opiate detoxification: Evaluation of the so-called ultra-rapid detoxification, Pharmacopsychiatry, November 1998; 31(6), pp. 205-9.
- 24. Seoane A, Carrasco G, Cabre L et al. Efficacy and safety of two new methods of rapid intravenous detoxification in heroin addicts previously treated without success. Br J Psychiatry 1997; 171(October):340-5.
- 25. Sevarino K, Saxon A, Friedman M. Medically supervised opioid withdrawal during treatment for addiction. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed April 12, 2022.
- 26. Solomont JH. Opiate detoxification under anesthesia. JAMA 1997; 278(16):1318-9.

POLICY HISTORY:

Adopted for Blue Advantage, March 2005

Available for comment May 1-June 14, 2005

Medical Policy Group, March 2006

Available for comment March 23-May 8, 2006

Medical Policy Group, March 2008

Medical Policy Group, March 2010

Medical Policy Group, March 2012

Medical Policy Group, December 2012

Medical Policy Group, October 2013

Medical Policy Group, January 2014

Medical Policy Group, January 2015

Medical Policy Group, January 2016

Medical Policy Group, July 2019

Medical Policy Group, August 2021

Medical Policy Group, September 2022: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.

Medical Policy Group, September 2023: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.

Medical Policy Group, November 2023: Archived effective 11/1/2023.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case by case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.