BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

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

Policy #: 091
Category: Mental Health Pharmacology

Latest Review Date: August 2019
Policy Grade: **Effective January 28, 2016: Active Policy but no longer scheduled for regular literature reviews and updates.**

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).*

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 ultrarapid detoxification. It is a potential alternative to standard detoxification that allows patients to avoid the acute symptoms associated with initial detoxification. Ultrarapid 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 patients in treatment, and a decrease in the risk of transmitting HIV or hepatitis. However, critics of methadone maintenance point out that this strategy substitutes 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 patients 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 patient support and oral medications are offered, detoxification is associated with patient discomfort, and many patients 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 "ultrarapid," "anesthesia-assisted," or "one-day" detoxification.

A rapid opioid detoxification (RD) 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 patients 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. Patients 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.

URD 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 patients 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.

Policy:

Effective for dates of service on or after July 1, 2005:

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.

Key Points:

The following information is a summary of the key literature to date.

Favrat et al published a randomized controlled trial in 2006 from a European center. The trial reported that the initial improvement in rate of opiate detoxification and abstinence (three months) with anesthesia was not maintained with longer-term follow-up; both groups (36 patients treated with anesthesia and 34 with classical clonidine detoxification) showed less than 5% abstinence after 12 months.

In 2010, an updated Cochrane review by Gowing et al on opioid antagonists under heavy sedation or anesthesia for opioid withdrawal was published. A total of nine studies including

1109 participants were eligible for inclusion; there were eight randomized controlled trials (RCTs) and one non-randomized controlled trial. Four studies compared the intervention to conventional approaches of withdrawal and five compared different regimes of antagonist-induced withdrawal. In five of the studies, all participants were withdrawing from heroin or other short-acting opioids, in three studies, they were using heroin and/or methadone and, in one study, all participants were withdrawing from methadone.

Due to differences in study designs (e.g., antagonist and anesthesia or sedation regimens, comparison interventions, outcome variables, etc.), few pooled analyses could be conducted. Findings from three trials (total n=240) comparing antagonist-induced and conventional withdrawal were pooled for several outcome variables. The number of participants completing maintenance treatment was significantly higher in the antagonist-induced group than conventional treatment (relative risk [RR] = 4.28, 95% confidence interval [CI] =2.91 to 6.30). The number of participants who continued maintenance treatment or were abstinent at 12 months also favored the antagonist-induced group (RR=2.77, 95% CI=1.37 to 5.61). Safety data from these three studies were not pooled. One of the studies reported no adverse effects and one only reported adverse effects in patients who received octreotide during the anesthetic procedure; seven out of these 11 patients (64%) experienced vomiting and/or diarrhea. The third study reported three serious adverse events, all of which occurred in the anesthesia group. There were no pooled analyses of the results of studies evaluating the efficacy differing opioid antagonist withdrawal regiments. One meta-analysis of safety data from two studies (total n=572) found a statistically significantly higher rate of adverse events with heavy sedation compared to light sedation (RR=3.21, 95% CI=1.13 to 9.12). Other adverse events included high rates of vomiting in several studies and, in one study, episodes of irregularities in respiratory patterns during withdrawal.

The authors of the Cochrane review commented that, due to variability among the trials, "it is not possible to identify 'standard' treatment regimens for antagonist-induced withdrawal in conjunction with heavy sedation or anesthesia." They concluded that "the increased risk of clinically significant adverse events associated with withdrawal under heavy sedation or anesthesia make the value of anesthesia-assisted antagonist-induced withdrawal questionable."

A representative RCT included in the Cochrane review was a 2005 trial by Collins et al. In this study, 106 heroin addicts were randomized to undergo detoxification with an anesthesia-assisted rapid opioid detoxification, buprenorphine-assisted rapid opioid detoxification, or clonidine-assisted opioid detoxification. All patients received an additional 12 weeks of outpatient naltrexone maintenance. Mean withdrawal severities were similar among the three groups, and treatment retention in the 12-week follow-up period was also similar. However, the anesthesia procedure was associated with three potentially significant life-threatening adverse events. The authors concluded that the data did not support the use of general anesthesia for heroin detoxification.

Among the AEs reported in the Cochrane review, vomiting under sedation is particularly worrisome due to the threat of aspiration. Techniques reported to minimize this risk include intubation, use of prophylactic antibiotics, and the use of medication to diminish the volume of gastric secretions. Several deaths occurring either during anesthesia or immediately thereafter

have been reported. Also, deaths subsequent to ultrarapid detoxification have been reported. Of particular concern is the fact that the use of opioid antagonists results in loss of tolerance to opioids, rendering patients susceptible to overdose if they return to predetoxification dosage of illicit drugs.

Relapse after ultrarapid detoxification was examined in a 2014 study by Salimi et al. A total of 424 patients with self-reported opioid use entered a treatment program at a single institution in Iran. Treatment consisted of rapid detoxification under general anesthesia and naltrexone maintenance therapy. Four hundred of the 424 patients (94%) completed two years of follow-up. Among completers, 97 patients (24%) experienced at least one incident of relapse. Patients who relapsed had significantly lower rates of long-term compliance with naltrexone therapy, and all of the patients who relapsed had discontinued naltrexone use prior to relapse. Mild AEs were common and did not differentiate between patients with successful abstinence versus relapse. For example, 52% of those with treatment success and 56% who relapsed ($p>0.05$) experienced mild muscle pain in the first three months after withdrawal. This study was uncontrolled and does not provide data on the relative efficacy of detoxification methods.

A follow up study was done by Forozesshfard et al to evaluate relapse after Ultrarapid detoxification. This was a prospective study done in Iran and included 64 patients undergoing the procedure with general anesthesia, followed by outpatient treatment using naltrexone oral therapy, and free-of-charge monthly psychiatric visits. Of the 64 patients undergoing treatment, 48 patients (75%) suffered relapse within the first month, with 12 patients returning to opioid abuse at three months, and the remaining four patients by six months. Four patients (6%) had life-threatening complications during the procedure, including pulmonary edema, pneumothorax, bradycardia, and refractory delirium with hypertension and cardiac arrhythmia. None of these patients had a fatal event.

Summary
The evidence for ultrarapid 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 ultrarapid 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
In 2007, the National Institute for Health and Clinical Excellence issued clinical practice guideline on “drug misuse, opioid detoxification.” The guidelines include the following statement regarding ultra-rapid detoxification. “Ultra-rapid detoxification under general anesthesia or heavy sedation (where the airway needs to be supported) must not be offered. This is because of the risk of serious adverse events, including death.”

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."

In 2005, the American Society of Addiction Medicine published a public policy statement regarding opiate detoxification under sedation or anesthesia (OADUSA) (update of their 2000 statement). It included the following position statements:

- Opioid detoxification alone is not a treatment of opioid addiction. ASAM does not support the initiation of acute opioid detoxification interventions unless they are part of an integrated continuum of services that promote ongoing recovery from addiction.

- 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 (RD), ultra-rapid opioid detoxification (URD), general anesthesia, opioid antagonist agent detoxification under sedation or anesthesia (OADUSA), one day detox

Approved by Governing Bodies:
Not applicable

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

Coding:

CPT codes:

01999 Unlisted anesthesia procedure

References:

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Policy History:

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Medical Policy Group, March 2006
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Medical Policy Group, March 2008
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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, August 2019

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.