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

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Replaces 3.01.02

*Medicare has a policy.

Policy

Opioid antagonists under heavy sedation or anesthesia are considered investigational as a technique for opioid detoxification (i.e., ultra-rapid detoxification).

Related Policies/Guidelines

2.04.513 Urine Drug Testing in Pain Management and Substance Abuse Treatment Settings
3.01.515 Behavioral Health: Residential/Sub-Acute Detoxification

Policy Guidelines

Specialized facilities that offer ultra-rapid detoxification include but are not limited to:
- Center for Research and Treatment of Addiction (CITA)
- Neuraad™ Treatment Centers
- Nutmeg Intensive Rehabilitation Centers

Description

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 patients 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.
Background
The traditional treatment of opioid addiction involves substituting the opiate (i.e., heroin) with an equivalent dose of a longer-acting opioid antagonist, (i.e., methadone) followed by tapering to a maintenance dose. Methadone maintenance therapy does not resolve opioid addiction but has been shown to result in improved general health, retention of patients in treatment, and a decrease in the risk of transmitting human immunodeficiency virus (HIV) or hepatitis. However, critics of methadone maintenance point out that this strategy substitutes one drug of dependence for the indefinite use of 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 (i.e., 6 months) of withdrawal. Although typically not life-threatening, acute detoxification symptoms include irritability, anxiety, apprehension, muscular and abdominal pains, chills, nausea, diarrhea, yawning, lacrimation, sweating, sneezing, rhinorrhea, general weakness, and insomnia. Protracted withdrawal symptoms include a general feeling of reduced well-being and drug craving. 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 nalmefine under deep sedation with benzodiazepine or general anesthesia. This strategy has been referred to as “ultra-rapid,” “anesthesia-assisted,” “one-day assisted” or “one-day” detoxification. The use of opioid antagonists accelerates the acute phase of detoxification, which can be completed within 24 to 48 hours. Because the patient is under anesthesia, he or she has no discomfort or memory of the symptoms of acute withdrawal. Various other drugs are also administered 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). Hospital admission is required if general anesthesia is used. If heavy sedation is used, the program can potentially be offered on an outpatient basis. Initial detoxification is then followed by ongoing support for the protracted symptoms of withdrawal. In addition, naltrexone may be continued to discourage relapse.

Ultra-rapid detoxification may be offered by specialized facilities. These programs typically consist of three phases: a comprehensive evaluation, inpatient detoxification under anesthesia, and finally, 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.

Regulatory Status
In October 2002, Reckitt Benckiser received U.S. Food and Drug Administration (FDA) approval to market the following for use in opioid addiction treatment:
- Subutex® , a buprenorphine monotherapy product
- Suboxone®, a buprenorphine/naloxone combination product

Scope
Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject
to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

### Benefit Application

Opioid dependence is considered a mental disorder, thus claims for ultra-rapid detoxification may be adjudicated under the mental health benefits.

### Rationale

This assessment of ultra-rapid opioid detoxification (UROD) focuses on data reporting the severity and duration of withdrawal symptoms and the short- and long-term outcomes of maintenance of abstinence in distinct populations of patients, based on type and duration of addiction. Efficacy outcomes will be balanced against the safety considerations of deep sedation or general anesthesia in conjunction with naloxone.

In 2010, Gowing et al. published a Cochrane review on opioid antagonists under heavy sedation or anesthesia for opioid withdrawal.\(^1\) A total of 9 studies including 1,109 participants were eligible for inclusion; there were 8 randomized controlled trials (RCTs) and 1 non-RCT. Four studies compared the intervention to conventional approaches of withdrawal, and 5 compared different regimens of antagonist-induced withdrawal. In 5 of the studies, all participants were withdrawing from heroin or other short-acting opioids; in 3 studies, they were using heroin and/or methadone and, in 1 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 3 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 in the conventional treatment group (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 3 studies were not pooled. One of the studies reported no adverse effects (AEs), and 1 only reported AEs in patients who received octreotide (a somatostatin analog) during the anesthetic procedure; 7 of these 11 patients (64%) experienced vomiting and/or diarrhea. The third study reported 3 serious adverse events, all of which occurred in the anesthesia group. There were no pooled analyses of the results of studies that evaluated the efficacy of differing opioid antagonist withdrawal regimens. One meta-analysis of safety data from 2 studies (total n=572) found a statistically significantly higher rate of AEs with heavy sedation compared with light sedation (RR=3.21; 95% CI: 1.13 to 9.12). Other AEs included high rates of vomiting in several studies and, in 1 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.\(^2\) In this study, 106 persons addicted to heroin were randomly assigned to undergo detoxification with an anesthesia-assisted rapid opioid detoxification, buprenorphine-assisted rapid opioid detoxification, or clonidine-assisted opioid detoxification. All study participants received an additional 12 weeks of outpatient naltrexone maintenance. Mean withdrawal severities were similar among the 3 groups, and treatment retention in the 12-week follow-up period was also similar. However, the anesthesia procedure was associated with 3 potentially significant life-threatening AEs. 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. (3-6) Also, deaths subsequent to ultra-rapid detoxification have been reported. (7) 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 pre-detoxification dosage of illicit drugs. (8)

Relapse after ultrarapid detoxification was examined in a 2014 study by Salimi et al. (9) 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 2 years of follow-up. Among completers, 97 patients (24%) experienced at least 1 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 3 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 Forozesshfrad et al to evaluate relapse after Ultrarapid detoxification. (10) 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 3 months, and the remaining 4 patients by 6 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.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in February 2017 did not identify any ongoing or unpublished trials that would likely influence this review.

Summary of Evidence
Ultra-rapid detoxification is an opioid detoxification technique that uses relatively high doses of opioid antagonists under deep sedation or general anesthesia. The paucity of controlled trials and lack of a standardized approach to ultra-rapid detoxification does not permit scientific conclusions regarding the safety or efficacy of ultra-rapid detoxification compared with other approaches that do not involve deep sedation or general anesthesia. Moreover, there are concerns about adverse effects, including life-threatening or potentially life-threatening events. Thus, this technology is considered investigational.

Practice Guidelines and Position Statements

National Institute for Health and Clinical Excellence (NICE)
In 2007, the NICE issued clinical practice guidelines on “drug misuse, opioid detoxification.” (11) 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.”

American Psychiatric Association (APA)
In 2007, the APA Work Group on Substance Use Disorders released a practice guideline for the treatment of patients with substance use disorders. (12) The practice guideline included the following recommendation: “Anesthesia-assisted rapid opioid detoxification is not recommended because of lack of proven efficacy and adverse risk-benefit ratios.”

American Society of Addiction Medicine (ASAM)
In 2005, the ASAM published a public policy statement regarding opiate detoxification under sedation or
anesthesia. 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.

**Medicare National Coverage**

Medicare Policy on this issue is as follows:

Section 130.7, of the Medicare Coverage Issues Manual (Medical Procedures), Withdrawal Treatment for Narcotic Addictions, states:

“Withdrawal is an accepted treatment for narcotic addiction, and Part B payment can be made for these services if they are provided by the physician directly or under his personal supervision and if they are reasonable and necessary. In reviewing claims, reasonableness and necessity are determined with the aid of the B/Medicare Administrative Contractor’s medical staff.

Drugs that the physician provides in connection with this treatment are also covered if they cannot be self-administered and meet all other statutory requirements. “

Cross-reference:


Section 130.6, Treatment of Drug Abuse (Chemical Dependency), states:

“The Centers for Medicare & Medicaid Services recognizes that there are similarities between the approach to treatment of drug abuse and alcohol detoxification and rehabilitation. However, the intensity and duration of treatment for drug abuse may vary (depending on the particular substance(s) of abuse, duration of use, and the patient’s medical and emotional condition) from the duration of treatment or intensity needed to treat alcoholism. Accordingly, when it is medically necessary for a patient to receive detoxification and/or rehabilitation for drug substance abuse as a hospital inpatient, coverage for care in that setting is available. Coverage is also available for treatment services that are provided in the outpatient department of a hospital to patients who, for example, have been discharged from an inpatient stay for the treatment of drug substance abuse or who require treatment but do not require the availability and intensity of services found only in the inpatient hospital setting. The coverage available for these services is subject to the same rules generally applicable to the coverage of outpatient hospital services. (See the Medicare Benefit Policy Manual (BPM), Chapter 6, “Hospital Services Covered Under Part B,” §§20.) The services must also be reasonable and necessary for treatment of the individual’s condition. (See the Medicare BPM, Chapter 16, “General Exclusions from Coverage,” §90.) Decisions regarding reasonableness and necessity of treatment, the need for an inpatient hospital level of care and length of treatment, should be made by A/B Medicare Administrative Contractors (MACs) based on accepted medical practice with the advice of their medical consultant. (In hospitals under Quality Improvement Organization (QIO) review, QIO determinations of medical necessity of services and appropriateness of the level of care at which services are provided are binding on A/B MACs for purposes of adjudicating claims for payment.)”
References


Appendix

N/A

History

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<th>Date</th>
<th>Reason</th>
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<tbody>
<tr>
<td>04/12/16</td>
<td>New Policy. Replaces 3.01.02 which is archived. Coverage statements remain unchanged.</td>
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<tr>
<td>03/14/17</td>
<td>Annual review. No changes made to policy.</td>
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200 Independence Avenue SW, Room S09F, HHH Building
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