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<b>Subject:</b>	Opioid Antagonists Under Heavy Sedation or General Anesthesia as a Technique of Opioid Detoxification		
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## Description/Scope

This document addresses the use of relatively high doses of opioid antagonists, such as naltrexone or naloxone, under deep sedation with benzodiazepines or general anesthesia. This strategy has been referred to as "ultra-rapid," "anesthesia-assisted," or "one-day" detoxification.

## Position Statement

### Investigational and Not Medically Necessary:

Administration of opioid antagonists under heavy sedation or general anesthesia, as a technique of opioid detoxification, is considered **investigational and not medically necessary**.

## Rationale

Evaluation of the safety and effectiveness of ultra-rapid treatment of opioid withdrawal using sedation or general anesthesia involves consideration of a variety of outcomes. For example, one might consider the number of dependent individuals enrolling in detoxification programs. Many opioid addicts may be fearful of prolonged detoxification programs and thus may only seek treatment in an accelerated detoxification program. Advocates of ultra-rapid detoxification point out that an increasing enrollment in detoxification programs is an important outcome (Bovill, 2000; Gooberman, 1998). In addition, proponents suggest that the procedure is a rapid and painless method of detoxification. Therefore, an important outcome is the comparison of the duration and severity of withdrawal symptoms associated with ultra-rapid detoxification and other detoxification strategies.

The completion rate of a detoxification program is another possible outcome. As noted by Scherbaum and colleagues (1998), up to 30% of individuals may drop out of traditional inpatient detoxification programs. Using sedation or anesthesia, one is assured of 100% completion of detoxification. However, as is commonly pointed out, detoxification is only the first step in treating opiate addiction, and ultra-rapid detoxification programs may offer different types of long-term follow-up care, based on ongoing psychosocial support with or without additional medication, such as naltrexone. Therefore, the rate of abstinence during both the short-term 6-month period of protracted withdrawal symptoms and longer-term abstinence are also important outcomes. For example, traditional methods of withdrawal (for instance, tapering doses of methadone or buprenorphine) require the individual to be in a therapeutic environment for a prolonged period of time, potentially reducing the risk of long-term relapse.

In addition, the success of any detoxification program must be evaluated according to the populations requiring treatment. For example, individuals addicted to heroin may respond differently than those addicted to oxycodone, and response may vary according to duration of addiction or prior attempts at traditional detoxification. Also, ultra-fast detoxification may be offered to individuals on methadone maintenance in an effort to render these individuals drug free. Methadone withdrawal after abrupt drug discontinuation tends to be prolonged compared to ultra-rapid detoxification and withdrawal from other opioids. However, methadone maintenance can be an important element in diminishing the risk of illicit opioid use as well as support other

desirable outcomes. Switching to buprenorphine and naloxone or a slow methadone taper are widely employed alternatives to ultra-rapid detoxification from methadone.

The major safety considerations regarding ultra-rapid detoxification are the risks associated with general anesthesia in combination with opioid antagonists. While participants are generally intubated and ventilated, eliminating the risk of choking, intravenous naloxone has been associated with cardiovascular complications such as cardiac arrest and pulmonary edema. These potential safety issues are particularly important since opioid withdrawal itself is not associated with life-threatening complications. Advocates of ultra-rapid detoxification point out, however, that detoxification is a painful procedure, and that the risk of anesthesia has generally been considered acceptable when used to relieve pain (Brewer, 1998).

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

A search of the peer-reviewed literature did not identify any studies that directly compared the outcomes of ultra-rapid detoxification with other methods of detoxification. As also noted by two published reviews, the majority of the published literature consists of single institution case series including heterogeneous populations and a variety of protocols, varying in the opioid antagonist used, the dose and mode of administration, the anesthetic agent, duration of anesthesia, and adjunct medications used (Gowing, 2010; O'Connor, 1998). Two randomized studies were identified; however, these studies focused on treatment regimens that varied only in the level of sedation used and did not include a conventionally treated control group (Kienbaum, 2000; Seoane, 1997).

Regarding severity and duration of withdrawal symptoms, Gowing and colleagues' review (2010) suggests that most individuals experienced moderate withdrawal symptoms lasting a few days post-anesthesia or sedation, including nausea, vomiting, diarrhea, and sleep disturbances. In addition, withdrawal severity may also be related to the anesthetic used. However, without a controlled trial, no conclusion can be made regarding the duration or severity of withdrawal symptoms compared to other techniques of detoxification.

Most of the studies did not report short-term or long-term follow-up of abstinence, and those studies that did include follow-up have reported conflicting results. For example, Seoane and colleagues (1997) reported that 279 of the 300 participants treated were abstinent after 1 month, while in Cucchia and colleagues' study (1998) of 20 participants, 16 reported some resumption of heroin in the 6 months following detoxification, with 60% considered to have relapsed. Albanese and colleagues (2000) assessed relapse at 6 months in 120 participants. Relapse data was available for 111 participants; 55% were relapse free. Again, without controlled studies in similar populations of subjects, no conclusions can be drawn about the relative long-term efficacy of ultra-rapid detoxification compared with other treatment strategies.

A variety of adverse events have been reported in a small number of participants including vomiting while under anesthesia or sedation, various cardiac rhythmic disturbances, pulmonary dysfunction, and renal insufficiency (Gowing, 2010). 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 afterward have been reported (Bearn, 1999; Dyer, 1998; Gold, 1999; Solomont, 1997). In addition, deaths subsequent to ultra-rapid detoxifications have been reported (Brewer, 1998). Of particular concern is the fact that the use of opioid antagonists results in loss of tolerance to opioids, rendering the individuals susceptible to overdose if the individual returns to his/her pre-detoxification dosage of illicit drugs (O'Connor, 1998).

In a trial by Collins and colleagues (2005), 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 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 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. A randomized trial from a European center reported that the initial improvement in the rate of opiate detoxification and abstinence (3 months) with anesthesia was not maintained with long-term follow-up; both groups (36 participants treated with anesthesia and 34 with classical clonidine detoxification) showed less than 5% abstinence after 12 months (Favrat, 2006). In addition, a Cochrane review on heavy sedation or anesthesia for opioid withdrawal concluded that:

Heavy sedation compared to light sedation does not confer additional benefits in terms of less severe withdrawal or increased rates of commencement on naltrexone maintenance treatment. Given that the adverse events are potentially life-threatening; the value of antagonist-induced withdrawal under heavy sedation or anesthesia is not supported (Gowing, 2010).

In 2000, The American Society of Addiction Medicine (ASAM) released a policy statement titled “Rapid and Ultra Rapid Opioid Detoxification” that states:

1. 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.
2. 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.
3. 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.

This document was last reviewed in April of 2005, probably reflecting the lack of scientific progress regarding the safety and efficacy of various rapid opioid detoxification techniques. This document still stands as an active position of the ASAM.

In a practice guideline addressing ultra-rapid opioid detoxification (Kleber, 2006), the American Psychiatric Association (APA) states:

Although some small uncontrolled studies have reported good long-term outcomes with this method, it appears to be no more effective than methadone detoxification in achieving beneficial outcomes such as maintenance of abstinence. In addition, complications associated with such rapid withdrawal procedures (e.g., general anesthesia) coupled with the lack of better long-term results suggest that the procedure should not be commonly used.

A treatment improvement protocol from The Substance Abuse and Mental Health Services Administration (SAMSHA) (2006; revised 2015) states that rapid and ultra-rapid detoxification “remains unproven regarding effectiveness and long-term abstinence rates and is very controversial.”

Forozeshfard and colleagues (2014), evaluated 1-month relapse outcomes of 64 subjects who underwent ultra-rapid opiate detoxification. The relapse rate observed was very high: 75% (n=48) of subjects reported relapse, with 4 subjects in the non-relapsed group reporting at least one episode of opiate use.

In summary, additional controlled trials and a standardized approach to ultra-rapid detoxification are required to permit scientific conclusions regarding the safety or efficacy of ultra-rapid detoxification compared to other approaches that do not involve deep sedation or general anesthesia.

## **Background/Overview**

The traditional treatment of opioid addiction involves substituting for the opiate (for example, heroin) an equivalent dose of a longer acting opioid antagonist (for example, 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 individuals in treatment, and a decrease in the risk of transmitting HIV or hepatitis. However, critics of methadone maintenance point out that this strategy is a substitution of 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 an individual on methadone maintenance. Detoxification is associated with acute symptoms followed by a longer period of protracted symptoms. 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 individual support and oral medications are offered, detoxification is associated with an individual's discomfort, and many dependent individuals 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.

Ultra-rapid and rapid detoxification are approaches for detoxifying opioid-dependent individuals using opioid antagonists, such as naltrexone used typically under general anesthesia or heavy sedation. The aim is to flood the brain with an opioid antagonist to remove all agonists very rapidly while the anesthesia or sedation minimizes the discomfort. The individual is then maintained on naltrexone, which has been referred to as rapid antagonist induction. Since the individual is under anesthesia during the procedure, he/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 octreotide acetate (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 with programs typically consisting 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, demerol, dilaudid, fentanyl, oxycodone, hydrocodone, or butorphanol. Once acute detoxification is complete, the opioid antagonist naltrexone is often continued to decrease drug craving, thus reducing the incidence of relapse.

## **Definitions**

Buprenorphine: A partial opioid agonist and analgesic that can be administered once a day to block withdrawal symptoms.

Detoxification: A short-term approach designed to help selected individuals achieve a drug-free state.

Naltrexone: An opioid antagonist used for maintenance treatment of opioid dependence.

Opioids: A class of drugs that are the most powerful known pain relievers and can produce euphoria. Opioids can be classified as the following:

- Naturally occurring opium derivatives - morphine, codeine
- Partially synthetic derivatives of morphine - heroin, oxycodone, oxymorphone
- Synthetic compounds - fentanyl, alfentanil, levorphanol, meperidine, methadone, propoxyphene

Opioid antagonists: Agents which block opioid effects, thereby eliminating opioid-induced euphoria, diminishing the reinforcing effects of heroin, and potentially extinguishing the association between conditioned stimuli and opioid use; opioid antagonists offer the advantage of treatment with medications that have no addictive potential or tolerance.

Opioid maintenance agonists: Long-acting noneuphorogenic opioids with relative steady-state pharmacokinetics that are used to replace heroin, a short-acting, euphorogenic opioid that is characterized by rapidly changing serum levels.

## Coding

*The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.*

### **When Services are Investigational and Not Medically Necessary:**

When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

#### **CPT**

No specific code for rapid or ultra-rapid opioid detoxification procedure under anesthesia

#### **HCPCS**

H0047

Alcohol and/or other drug abuse services, not otherwise specified [when describing rapid or ultra-rapid opioid detoxification under anesthesia]

#### **ICD-10 Procedure**

HZ2ZZZZ

Detoxification services for substance abuse treatment [when specified as rapid or ultra-rapid opioid detoxification under anesthesia]

#### **ICD-10 Diagnosis**

F11.10-F11.99

Opioid related disorders, dependence, use unspecified

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2. Bearn J, Gossop M, Strang J. Rapid opiate detoxification treatments. *Drug Alcohol Rev.* 1999; 18(1):75-81.
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16. 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; 171:340-345.
17. Solomont JH. Opiate detoxification under anesthesia. *JAMA.* 1997; 278(16):1318-1319.
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### Government Agency; Medical Society; and Other Authoritative Publications:

1. American Society of Addiction Medicine. National practice guideline for the use of medications in the treatment of addiction involving opioid use. May 2015. Anesthesia-assisted withdrawal management. Available at: <http://www.asam.org/magazine/read/article/2015/06/02/asam-releases-national-practice-guideline-for-the-use-of-medications-in-the-treatment-of-addiction-involving-opioid-use>. Accessed on November 11, 2017.
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### Websites for Additional Information

- American Society of Addiction Medicine. Available at: <http://www.asam.org/>. Accessed on November 11, 2017.
- Substance Abuse and Mental Health Services Administration (SAMHSA). Available at: <http://www.samhsa.gov/>. Accessed on November 11, 2017.

### Index

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Ultra-Rapid Detoxification

**The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.**

### Document History

Status	Date	Action
Reviewed	02/23/2018	Behavioral Health Subcommittee review. The document header wording updated from "Current Effective Date" to "Publish Date." Updated the Rationale, Definitions, Index, Websites, and References sections.
Reviewed	01/25/2018	Medical Policy & Technology Assessment Committee (MPTAC) review.
Reviewed	02/02/2017	MPTAC review.
Reviewed	01/20/2017	Behavioral Health Subcommittee review. Updated the Rationale and Reference sections.
Reviewed	02/04/2016	MPTAC review.
Reviewed	01/29/2016	Behavioral Health Subcommittee review. Updated Description, Background and References. Removed ICD-9 codes from Coding section.
Reviewed	02/05/2015	MPTAC review.
Reviewed	01/30/2015	Behavioral Health Subcommittee review. Updated Description, Background and References.
Reviewed	02/13/2014	MPTAC review.

Reviewed	02/07/2014	Behavioral Health Subcommittee review. Updated Rationale, References and Websites.
Reviewed	02/14/2013	MPTAC review.
Reviewed	02/08/2013	Behavioral Health Subcommittee review. Updated References and Websites.
Reviewed	02/16/2012	MPTAC review.
Reviewed	02/10/2012	Behavioral Health Subcommittee review. Updated References and Websites.
Reviewed	02/17/2011	MPTAC review.
Reviewed	02/11/2011	Behavioral Health Subcommittee review. Updated Description, Rationale, References and Websites.
Reviewed	05/13/2010	MPTAC review. References updated.
Reviewed	05/21/2009	MPTAC review. References updated.
Reviewed	05/15/2008	MPTAC review. Updated background and references.
	02/21/2008	The phrase "investigational/not medically necessary" was clarified to read "investigational and not medically necessary." This change was approved at the November 29, 2007 MPTAC meeting.
Reviewed	05/17/2007	MPTAC review. Rationale and references updated.
Reviewed	06/08/2006	MPTAC review. Updated references.
	11/22/2005	Added reference for Centers for Medicare and Medicaid Services (CMS) – National Coverage Determination (NCD).
Revised	07/14/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

<b>Pre-Merger Organizations</b>	<b>Last Review Date</b>	<b>Document Number</b>	<b>Title</b>
Anthem, Inc.	03/20/2003	BEH.00001	Opioid Antagonists Under Heavy Sedation or General Anesthesia as a Technique of Opioid Detoxification
WellPoint Health Networks, Inc.	06/24/2004	2.01.19	Opioid Antagonists Under Sedation or General Anesthesia as a Technique of Opioid Detoxification

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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. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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