MEDICAL POLICY

POLICY TITLE	OPIOID ANTAGONISTS UNDER HEAVY SEDATION OR GENERAL ANESTHESIA AS A TECHNIQUE OF OPIOID DETOXIFICATION
POLICY NUMBER	MP-2.303

Original Issue Date (Created):	**December 8, 2003**
Most Recent Review Date (Revised):	**March 25, 2014**
Effective Date:	**June 1, 2014**

I. POLICY

Opioid antagonists under heavy sedation or anesthesia is considered **investigational** as a technique for opioid detoxification (i.e., ultra-rapid detoxification), as there is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Cross-reference:

MP-2.301 Treatment of Opiate and Alcohol Addiction

II. PRODUCT VARIATIONS

TOP

[N] = No product variation, policy applies as stated
[Y] = Standard product coverage varies from application of this policy, see below

- [N] Capital Cares 4 Kids
- [N] PPO
- [N] HMO
- [Y] SeniorBlue HMO*
- [Y] SeniorBlue PPO*
- [N] Indemnity
- [N] SpecialCare
- [N] POS
- [N] FEP PPO

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*For coverage information, refer to:

Centers for Medicare and Medicaid (CMS) National Coverage Determination (NCD) 130.6, Treatment of Drug Abuse (Chemical Dependency).

Centers for Medicare and Medicaid (CMS) National Coverage Determination (NCD) 130.7, Withdrawal Treatments for Narcotic Addictions.

III. DESCRIPTION/BACKGROUND

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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.

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 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.

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Dissatisfaction with current approaches to detoxification has led to interest in using relatively high doses of opioid antagonists, such as naltrexone, naloxene, 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. The use of opioid antagonists accelerates the acute phase of detoxification, which can be completed within 24–48 hours. Since the patient is under anesthesia, the patient 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. Neuraad™ Treatment Centers, Nutmeg Intensive Rehabilitation, and Center for Research and Treatment of Addiction (CITA) are examples. These programs typically consist of 3 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, demerol, dilaudid, 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 a buprenorphine monotherapy product, Subutex®, and a buprenorphine/naloxone combination product, Suboxone®, for use in opioid addiction treatment.

IV. RATIONALE

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This policy is updated regularly with searches of the MEDLINE database. The most recent literature search was performed for the period October 2012 through November 4, 2013. Following is a summary of the key literature to date:

This assessment of ultra-rapid opioid detoxification, 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 and colleagues 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-

randomized controlled trial. 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]: 2.91-6.30). 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: 1.37-5.61). Safety data from these 3 studies were not pooled. One of the studies reported no adverse effects, and 1 only reported adverse effects in patients who received octreotide during the anesthetic procedure; 7 out 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 adverse events with heavy sedation compared to light sedation (RR: 3.21; 95% CI: 1.13- 9.12). Other adverse events 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."

Several of the trials are described in more detail below:

Collins and colleagues reported on the results of a trial of 106 persons addicted to heroin who were randomly assigned to undergo detoxification with an anesthesia-assisted rapid opioid detoxification, buprenorphine-assisted rapid opioid detoxification, or clonidine-assisted opioid detoxification. (2) All patients 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 adverse events. The authors concluded that the data did not support the use of general anesthesia for heroin detoxification. Favrat and colleagues published an RCT from a European center in 2006. The trial reported that the initial improvement in rate of opiate detoxification and abstinence (3 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. (3)

Among the published RCTs are several that focused on treatment regimens that varied only in the level or type of sedation used and did not include a control group of patients who did receive rapid detoxification. (4-6) In 2011, Nasr and colleagues in Egypt compared ultra-rapid detoxification under general anesthesia with and without dexmedetomidine. (6) Another study, by Seoane and colleagues, compared rapid intravenous detoxification treatment under either monitored light intravenous sedation or unmonitored deep intravenous sedation. (5) No conclusions can be drawn from these studies about the relative efficacy of rapid detoxification and standard methods.

Among the adverse events 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. (7-10) Also, deaths subsequent to ultra-rapid detoxification have been reported. (11) 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. (12)

Summary

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 to 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

In 2007, the National Institute for Health and Clinical Excellence issued clinical practice guidelines on "drug misuse, opioid detoxification." (13) 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." The guideline was reviewed in 2011 and it was determined to be up-to-date.

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. (14) The practice guideline included 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. (15) 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."

V. DEFINITIONS

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OPIOID refers to any synthetic narcotic not derived from opium

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital for benefit information.

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VII. DISCLAIMER

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Capital's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

No specific CPT codes

ICD-9-CM Diagnosis Code*	Description
304.0	Opioid type dependence

The following ICD-10 diagnosis codes will be effective October 1, 2015:

ICD-10-CM Diagnosis Code*	Description
F11.10	Opioid abuse, uncomplicated
F11.20	Opioid dependence, uncomplicated
F11.220	Opioid dependence with intoxication, uncomplicated
F11.221	Opioid dependence with intoxication delirium
F11.222	Opioid dependence with intoxication with perceptual disturbance
F11.229	Opioid dependence with intoxication, unspecified
F11.23	Opioid dependence with withdrawal

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F11.24	Opioid dependence with opioid-induced mood disorder
F11.250	Opioid dependence with opioid-induced psychotic disorder with delusions
F11.251	Opioid dependence with opioid-induced psychotic disorder with hallucinations
F11.259	Opioid dependence with opioid-induced psychotic disorder, unspecified
F11.281	Opioid dependence with opioid-induced sexual dysfunction
F11.282	Opioid dependence with opioid-induced sleep disorder
F11.288	Opioid dependence with other opioid-induced disorder
F11.29	Opioid dependence with unspecified opioid-induced disorder

IX. REFERENCES

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1. *Gowing L, Ali R, White J. Opioid antagonists under heavy sedation or anesthesia for opioid withdrawal. Cochrane Database Syst Rev 2010; (1):CD002022.*
2. *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.*
3. *Favrat B, Zimmermann G, Zullino D et al. Opioid antagonist detoxification under anesthesia versus traditional clonidine detoxification combined with an additional week of psychosocial support: a randomised clinical trial. Drug Alcohol Depend 2006; 81(2):109-16.*
4. *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.*
5. *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.*
6. *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.*
7. *Bearn J, Gossop M, Strang J. Rapid opiate detoxification treatments. Drug Alcohol Rev 1999; 18(1):75-81.*
8. *Dyer C. Addict died after rapid opiate detoxification. BMJ 1998; 316(7126):170.*
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. *Solomont JH. Opiate detoxification under anesthesia. JAMA 1997; 278(16):1318-9.*
11. *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.*

12. *American Society of Addiction Medicine. Public Policy Statement on Opioid Antagonist Agent Detoxification Under Sedation Or Anesthesia (OADUSA). J Addict Dis 2000; 19(4):109-12.*
13. *National Institute for Health and Clinical Evidence. Drug misuse, opioid detoxification. NICE Clinical Guideline 52. Available online at: http://www.nice.org.uk/Guidance/CG52. Accessed January 9, 2014.*
14. *Kleber HD, Weiss RD, Anton RF et al. Work Group on Substance Use Disorders. Treatment of patients with substance use disorders. American Psychiatric Association. Am J Psychiatry 2006; 163(8 suppl):5-82.*
15. *American Society of Addiction Medicine. Public Policy Statement on Rapid and Ultra Rapid Opioid Detoxification. Available online at: http://www.asam.org/advocacy/find-a-policy-statement/view-policy-statement/public-policy-statements/2011/12/15/rapid-and-ultra-rapid-opioid-detoxification. Accessed January 9, 2014.*
16. *Centers for Medicare and Medicaid Services (CMS) National Coverage Decision (NCD) 130.6, Treatment of Drug Abuse (Chemical Dependency). CMS [Website: http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=28&ncdver=1&DocID=130.6+&bc=gAAAAAgAAAAA& Accessed January 9, 2014.*
17. *Centers for Medicare and Medicaid Services (CMS) National Coverage Decision (NCD) 130.7, Withdrawal Treatments for Narcotic Addictions. CMS [Website]: http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=59&ncdver=1&DocID=130.7&bc=gAAAAAgAAAAA& Accessed January 9, 2014.*

X. POLICY HISTORY

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MP 2.203	**CAC 5/27/03**
	CAC 4/26/05
	CAC 4/25/06
	CAC 4/24/07 Consensus
	CAC 5/27/08 Consensus
	CAC 5/26/09 Consensus
	CAC 5/25/10 Consensus
	CAC 9/10 Adopted BCBSA Guidelines
	CAC 7/26/11 Consensus
	CAC 8/28/12 Consensus, no change to policy statements, references updated Codes reviewed 8/20 /12 klr
	CAC 07/30/13- Consensus review. Admin code review complete.
	CAC 3-25-14 Consensus. No change to policy statements. References updated. Rationale section added. Coding complete.

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