Clinical Policy Title: Medication-assisted treatment for opioid use disorder

Clinical Policy Number: 18.02.08

Effective Date: March 1, 2018
Initial Review Date: January 11, 2018
Most Recent Review Date: February 6, 2018
Next Review Date: February 2019

Related policies:

CP# 00.01.03 Drug testing for substance abuse and misuse
CP# 03.02.11 Multidisciplinary treatments to address neonatal abstinence syndrome

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas considers the use of medication-assisted treatment to be clinically proven and, therefore, medically necessary for medically supervised withdrawal and maintenance of opioid dependency when the following criteria are met:

- Member has a confirmed diagnosis of an opioid use disorder by the provider with prescribing authority and who recommends medication use (Kampman, 2015).
- Pharmacotherapy is approved by the U.S. Food and Drug Administration (FDA) for use in medication-assisted treatment: methadone monotherapy; buprenorphine monotherapy; buprenorphine-naloxone combination therapy; and naltrexone monotherapy.
- Choice of medication and form of delivery should be individualized in accordance with FDA approval criteria, current best practices, local formulary requirements, and member’s preferences (American Congress of Obstetricians and Gynecologists [ACOG], 2017; Srivastava, 2017; American Academy of Pediatrics [AAP], 2016; American Society of Addiction Medicine [ASAM], 2016; Substance Abuse and Mental Health Services...
Where available, generic products are preferred over brand name products.

Medication-assisted treatment is most effective when combined with counseling and behavioral therapies. The decision to require counseling should be individualized according to the member’s needs, regulatory requirements, and current best practices (ACOG, 2017; AAP, 2016; SAMHSA, 2015a, 2015b, and 2015c).

Limitations:

The following treatments for opioid use disorder are not medically necessary due to insufficient evidence of safety and effectiveness:

- Rapid or ultra-rapid opioid medically supervised withdrawal under anesthesia (Kampman, 2015; SAMHSA, 2006).
- Naltrexone subcutaneous implants (Larney, 2014).
- Extended-release injectable naltrexone in the adolescent population (SAMHSA, 2015b).
- Buprenorphine sublingual tablets in members younger than age 16 (SAMHSA, 2015b).
- Buprenorphine subcutaneous implants in pregnant women (ACOG, 2017).

Few psychiatric or medical diagnoses should rule out admission to an opioid treatment program or access to pharmacotherapy for opioid use disorder. However, absolute contraindications to medication-assisted treatment for opioid dependency include (SAMHSA, 2015b):

- Hypersensitivity or allergy to methadone, buprenorphine, naltrexone, or naloxone, or to any ingredient in their preparations.
- Methadone only — Respiratory depression (in the absence of resuscitative equipment or in unmonitored settings), acute bronchial asthma or hypercarbia, or a paralytic ileus (present or suspected).
- Extended-release naltrexone only — Current opioid use based on self-report or a positive urine drug screen, current long-term opioid therapy, currently undergoing opioid withdrawal, on buprenorphine or methadone maintenance therapy, a body mass that precludes intramuscular injection with the 2-inch needle provided, or acute hepatitis.

Relative contraindications that require caution when administering medication-assisted treatment for opioid use disorder include (SAMHSA, 2015b):

- Methadone only — Elderly and debilitated patients, head injury, increased intracranial pressure, known sensitivity to central nervous system depressants, comorbid conditions or concomitant medications that may predispose to dysrhythmia or reduced ventilatory drive. Depending on the patient’s risk profile, an electrocardiogram may be indicated prior to initiation of methadone, at 30 days, and yearly thereafter (Chou, 2014; Martin, 2011).
- Buprenorphine only — Polysubstance use, severe hepatic impairment, compromised respiratory function, head injury, transfer from methadone, or prior to opioid withdrawal.
- Extended-release naltrexone only — Active liver disease, moderate to severe renal impairment, women of childbearing age, thrombocytopenia, or any coagulation disorder (e.g., hemophilia, severe hepatic failure).

In pregnant women, initiating treatment with naltrexone should be avoided. If a woman becomes pregnant while receiving naltrexone, it may be discontinued if the risk of relapse is low. If relapse occurs, methadone or buprenorphine may be appropriate. If she still chooses to be on naltrexone, she must be informed of the risks of treatment (ACOG, 2017).

**Alternative covered services:**

- Alpha-2-adrenergic agonists (e.g., clonidine) or muscle relaxants (e.g., methocarbamol) for withdrawal.
- Psychosocial treatment.
- Social services.

**Background**

Opioids are a class of drugs that are chemically related and interact with opioid receptors on neurons in the body and brain producing euphoria and pain relief (National Institute on Drug Abuse [NIDA], 2015). They include illegal opioids (e.g., heroin) and natural and synthetic prescription narcotics, such as oxycodone, hydrocodone, codeine, morphine, fentanyl, and many others.

Since 2000, the death rate from drug overdoses involving opioids (opioid pain relievers and heroin) has increased 200 percent (Rudd, 2016). The sharp increase in the supply of heroin and illicitly manufactured fentanyl are likely contributors, particularly as access to prescription opioids narrows. Compounding the problem is the widespread abuse and misuse (nonmedical use) of prescription opioids (Compton, 2016; SAMHSA, 2017). In 2016, 11.8 million Americans aged 12 or older misused opioids, the vast majority of which were prescription pain relievers (SAMHSA, 2017). Nonmedical prescription opioid use is greater among 18- to 64-year-old individuals, whites, Native Americans, and individuals with lower socioeconomic status (Saha, 2016).

**Opioid use disorder:**

Opioid use disorder is a chronic medical condition characterized by a pattern of repeated, compulsive use of a range of drugs of the opioid class that causes clinically and functionally significant impairment and distress. Diagnostic criteria incorporate the degree of severity and clinical characteristics that manifest within a 12-month period based on patient history and clinical examination (APA, 2013; Appendix).
Significant challenges to treating opioid use disorder include co-occurring mental illness or other substance uses, the most common being alcohol, amphetamines, benzodiazepines and other prescription sedatives, cocaine, and marijuana in varying patterns of consumption and dosages (SAMHSA, 2005). Despite expanding treatment options for opioid abuse, there remains significant under-treatment of adolescents and adults with a co-occurring mental illness and substance use disorder (SAMHSA, 2017). Contributors to under-treatment reflect biases in philosophy of care, limited access to prescribers, a lack of training among prescribers and counselors, financing and licensing policies that inhibit use of certain medications, and perceptions that the cost of the medications is excessive (Hartung, 2014; Burns, 2016).

Several national initiatives call for expanding prevention efforts to address the opioid crisis. These efforts include increasing provider training and education on the safe prescribing of opioids, monitoring through statewide Prescription Drug Monitoring Programs, use of naloxone, and access to medication-assisted treatment and recovery services (National Academies of Sciences Engineering Medicine [NASEM], 2017).

**Medication-assisted treatment:**

Medication-assisted treatment is the use of specific FDA-approved medications in combination with counseling and behavioral therapies to treat opioid use disorder (SAMHSA, 2015a; SAMHSA, 2005). Medication-assisted treatment works by interacting with some of the same receptors in the brain that are triggered by the abused drug, thereby substituting the opioid with a safer drug. It improves withdrawal symptoms and reduces cravings, and many risk factors of the drug-abusing lifestyle can be mitigated.

Medically supervised withdrawal uses tapering doses to wean patients off addictive substances and manage withdrawal. Maintenance programs involve a phased approach of stabilization, medication maintenance, and ongoing rehabilitation that may or may not emphasize complete detoxification as a treatment objective. Since relapse after abstinence is common among opioid abusers, ongoing medication-assisted treatment may be the safest and best approach for opioid rehabilitation.

The FDA has approved three pharmacotherapies for the medication-assisted treatment of opioid dependence.

- **Methadone hydrochloride (methadone)** is a synthetic µ-opioid agonist and the most common opioid substitution treatment (FDA, 2017a). It binds to and activates the opioid receptors to provide pain relief and euphoria. Its effects come on more slowly and last longer, which helps prevent withdrawal. Methadone is available as an injection and in oral pill, liquid, and wafer forms taken daily (SAMHSA, 2015c). As a Schedule II drug, methadone may be dispensed only on an outpatient basis through opioid treatment programs that are certified and regulated by the federal Drug Enforcement Agency and SAMHSA. In some locations, dispensing may also be subject to county or municipal regulations.
• **Buprenorphine hydrochloride** (buprenorphine) is a partial agonist at the µ-opioid receptor and an antagonist at the κ-opioid receptor (FDA, 2017b). Buprenorphine is a Schedule III drug available in various dosing regimens in sublingual tablet, buccal film, injection, transdermal, and implant forms as monotherapy, and in combination with naloxone hydrochloride as an extended-release tablet. Buprenorphine implants are limited to two rounds (one year) for those who have demonstrated clinical stability from previous oral regimens of the drug; access to buprenorphine implants is restricted to providers participating in a Risk Evaluation Mitigation Strategy program (FDA, 2017b). Buprenorphine prescribing privileges extend beyond outpatient treatment programs to office-based treatment by physicians, physician assistants, and nurse practitioners who meet certain qualifying requirements, but without the requirement of counseling or other treatment services (ASAM, 2016).

• **Naltrexone hydrochloride** (naltrexone) is a µ-opioid antagonist that binds to opioid receptors but prevents activation by agonist compounds. The FDA approved naltrexone for the prevention of relapse to opioid dependence following opioid detoxification and for alcohol dependence; it is available as a 50 mg oral tablet taken daily and as monthly extended-release intramuscular injection (FDA, 2017c). Other forms of naltrexone have been approved for use in obesity management, opioid-induced constipation, and chronic pain management. Its subcutaneous implantable form is not yet FDA-approved. Naltrexone can be prescribed by any clinician with the authority to prescribe any medication (ASAM, 2016).

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on November 28, 2017. Search terms were: “Opioid-Related Disorders” (MeSH), “Opiate Substitution Treatment” (MeSH), “Narcotic Antagonists” (MeSH), and free text terms “methadone,” “buprenorphine,” and “naltrexone.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.

- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Due to the high volume of literature on this topic, searches were restricted to articles published within the past five years.

**Findings**

We identified multiple systematic reviews, meta-analyses, and evidence-based guidelines for this policy. The evidence is sufficient to support the use of agonist- and antagonist-based medication-assisted treatment for medically supervised withdrawal and maintenance of opioid use disorder. The quality and quantity of the evidence is higher for studies of non-pregnant adults than for studies of adolescents or pregnant women. One major limitation to the evidence base is the exclusion of patients with concurrent disorders, which may result in overestimating the true effectiveness of medication-assisted treatment in this population (Dennis, 2015).

Compared to non-medication based therapies (e.g., abstinence-based), medication-assisted treatment is associated with increased treatment retention and social function, and reduced illicit opiate use, mortality, craving, and infection risk (Gowing, 2017a and 2017b; Itzoe, 2017; Sordo, 2017; Nielsen, 2016; Noormohammadi, 2016; Mattick, 2014; Minozzi, 2014a and 2014b; Minozzi, 2013; Amato, 2013; Gowing, 2011). Methadone, buprenorphine, and naltrexone are generally safe when used as directed for treatment of dependence on prescription and illicit opioids. The choice of medication should be based on safety and efficacy, availability of medications, patient preferences, risk of dropout, treatment setting, and treatment goals (Srivastava, 2017; SAMHSA, 2005).

The newest forms of delivery are subcutaneous implants. Implants come with their own risks such as surgical site irritation, possible movement, and protrusion of implant out of skin (Itzoe, 2017). Buprenorphine implants are generally safe and effective in persons who have demonstrated clinical stability from previous oral regimens of the drug. Prescription is limited to two six-month rounds (one total year), and prescribers have additional training requirements. There is insufficient evidence to support naltrexone subcutaneous implants as maintenance treatment for opioid dependency, and the FDA has not approved the use of these implants outside of clinical trials (Larney, 2014).

**Expanding access to medication-assisted treatment:**

Few psychiatric or medical diagnoses should rule out admission to an opioid treatment program or access to opioid pharmacotherapy; inclusion rather than exclusion should be the guiding principle (SAMHSA, 2005). Several professional organizations encourage more research and updating regulations and professional guidelines to expand access to comprehensive, evidence-based medication-assisted
treatment (Crowley, 2017; ACOG, 2017; Srivastava, 2017; AAP, 2016). Central to this is the integration of medication-assisted treatment in primary care.

Several models of care exist for adaptation across different health care settings. Common components include (Korthuis, 2017): pharmacotherapy with buprenorphine or naltrexone; provider and community education; coordination/integration of opioid use disorder with other medical/psychological needs; and psychosocial services/interventions. The roles of primary care providers, counseling, and medication supervision continue to evolve, as there is a need to balance the availability of safe and efficacious new treatment options with reducing barriers to access (NASEM, 2017; Saulle, 2017).

Special considerations for adolescents:

In this population, opioid use is increasing, particularly among younger adolescents, but relatively few treatment options are available. For patients under age 18, federal and state requirements and FDA approvals need to be met (Kampman, 2015). An increasing body of evidence suggests buprenorphine, methadone, and naltrexone are effective and can be easily combined with psychosocial treatments, but only buprenorphine is FDA-approved for medication-assisted treatment of patients younger than age 18, and the safety and effectiveness of buprenorphine hydrochloride sublingual tablets in patients younger than age 16 have not been established (SAMHSA, 2015b).

The AAP (2016) states that buprenorphine should be made available to younger adolescents with severe opioid use disorders based on new evidence from randomized controlled trials (RCTs). SAMHSA (2015b) recommends referring young patients to an addiction specialist or program with experience in treating adolescents as the best course of action. There is a lack of consensus among guidelines on the value of naltrexone, as very little research has been conducted in this population, despite increased dispensing of naltrexone over time (Hadland, 2017). Oral naltrexone may be effective for those who report a shorter duration of opioid use, but the safety, efficacy, and pharmacokinetics of extended-release injectable naltrexone have not been established in this population.

Special considerations for pregnant and breast feeding women, and neonates:

Methadone and buprenorphine are not FDA-approved for use in this population, but medication-assisted treatment with either monotherapy is recommended best practice instead of withdrawal or abstinence, as abrupt discontinuation of opioid use during pregnancy can result in premature labor, fetal distress, and miscarriage (ACOG, 2017; SAMHSA, 2016; Kampman, 2015; SAMHSA, 2004). Methadone is generally preferred, but buprenorphine monotherapy may produce equivalent maternal and fetal outcomes (ACOG, 2017; Noormohammadi, 2016; Minozzi, 2013).

Intrauterine exposure to medication-assisted treatment can present challenges to the fetus that can lead to neonatal opioid withdrawal syndrome (ACOG, 2017). The risk from medication-assisted treatment must be balanced against the risk of untreated opioid addiction during pregnancy. Neonatal
opioid withdrawal syndrome can be effectively managed, but may be life-threatening if not recognized and treated.

Mothers on either methadone or buprenorphine monotherapy, but not naltrexone, are encouraged to breast feed as long as they are stable on their opioid agonists, not using illicit drugs, and have no other contraindications, such as human immunodeficiency virus (HIV) infection (ACOG, 2017; Kampman, 2015; SAMHSA, 2004). Women should be counseled about the need to suspend breast feeding in the event of a relapse. If a pregnant woman still chooses to be on naltrexone, she must be informed of the risks of treatment.

Additional considerations for pregnant women include (ACOG, 2017):
- Patients considered for treatment with buprenorphine instead of methadone need to be able to self-administer the drug safely and maintain adherence to their treatment regimen.
- If the pregnant woman is already on methadone, she should not transition to buprenorphine because of the significant risk of precipitated withdrawal. There is not a similar risk of withdrawal when transitioning from buprenorphine to methadone.
- The potential risk of unrecognized, adverse long-term outcomes with buprenorphine use, which is inherent with use of any relatively new medications during pregnancy, should always be taken into consideration.
- To date, there are no clinical data on the use of the buprenorphine implant in pregnant women.
- Initiating treatment with naltrexone should be avoided, as less is known about its effects on maternal and fetal outcomes. If a woman becomes pregnant while receiving naltrexone, it may be discontinued if the risk of relapse is low. If relapse occurs, methadone or buprenorphine may be appropriate.
- Access to adequate postpartum psychosocial support services, including substance use disorder treatment and relapse prevention programs, should be made available.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gowing (2017a)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Cochrane review</td>
<td>Systematic review of nine RCTs and prospective cohort studies comparing an opioid antagonist (naltrexone or naloxone) plus clonidine or lofexidine to treatment based on clonidine or lofexidine, primarily in heroin users.</td>
</tr>
<tr>
<td></td>
<td>Overall quality: very low with high risk of bias and too heterogeneous for meta-analysis.</td>
</tr>
<tr>
<td></td>
<td>Insufficient evidence of superiority of opioid antagonists plus alpha-2-adrenergic agonist to withdrawal with an adrenergic agonist for reducing duration of withdrawal or facilitating transfer to naltrexone treatment.</td>
</tr>
<tr>
<td>Gowing (2017b)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Cochrane review</td>
<td></td>
</tr>
<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------</td>
</tr>
</tbody>
</table>
| Buprenorphine for managing opioid withdrawal | • Systematic review and meta-analysis of 27 RCTs involving 3,048 participants, mostly male. The main comparators were: clonidine or lofexidine (14 studies); buprenorphine vs. methadone (six studies); and different rates of buprenorphine dose reduction (seven studies).
• Overall quality: low to moderate.
• Buprenorphine is more effective than clonidine or lofexidine for managing opioid withdrawal in terms of severity of withdrawal, duration of withdrawal treatment, and the likelihood of treatment completion.
• Limited data suggest buprenorphine and methadone are equally effective; the pattern of withdrawal experienced may differ and withdrawal symptoms may resolve more quickly with buprenorphine.
• Inconclusive evidence of relative effectiveness of different rates of buprenorphine dose tapering; multiple factors may affect the response to the rate of dose taper, e.g., transition to subsequent relapse prevention treatment with naltrexone.
• Gender differences could not be determined. |
| Itzoe (2017) | Key points:
• Best available evidence from two RCTs and several observational studies of Probuphine® (Braeburn Pharmaceuticals, Princeton, NJ).
• Delivers steady-state levels of buprenorphine over the course of six months.
• May improve the quality of life, improve patient adherence, avoid accidental overdose or purposeful medication diversion, and circumvent behaviors that might perpetuate the cycle of addiction.
• Implanted in an outpatient setting, avoiding a hospital stay.
• Common adverse side effects include headache, depression, constipation, nausea, vomiting, back pain, mouth pain, and injection site irritation.
• Serious but rare complications include: nerve or blood vessel injury, bleeding, pain, swelling, and infection at the insertion site; arm numbness or weakness; implant migration; and protrusion or expulsion of implant out of the skin. |
| Saulle (2017) | Key points:
• Systematic review and meta-analysis of four RCTs and two prospective observational cohort studies (7,999 total participants) comparing supervised to unsupervised opioid substitution treatment.
• Overall quality: very low to low with moderate risk of bias.
• No statistically significant differences in retention at any duration, abstinence at the end of treatment (self-reported drug use), medication diversion, or incidence of adverse effects.
• Limited data on severity of dependence but showed no difference.
• Insufficient evidence for effect on mortality rates.
• No studies reported pain symptoms, drug craving, aberrant opioid-related behaviors, days of unsanctioned opioid use and overdose. |
<p>| Sordo (2017) | Key points: |</p>
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| Mortality risk during and after opioid substitution treatment | • Systematic review and meta-analysis of 19 eligible cohorts, following 122,885 people treated with methadone over 1.3 to 13.9 years and 15,831 people treated with buprenorphine over 1.1 to 4.5 years.  
• Overall quality: low with high risk of bias and confounding.  
• Retention in methadone maintenance is associated with substantial reductions in the risk for all cause and overdose mortality.  
• Buprenorphine maintenance is probably also effective in reducing mortality, but quantification of averted deaths requires further study.  
• Mortality risk in the first four weeks of methadone maintenance is high but appears to decrease substantially during this period, with stabilization at around six deaths/1,000 person-years in the remaining time in treatment. Not observed with buprenorphine.  
• The mortality risk in the four weeks immediately after cessation of either treatment is high and could exceed 30 deaths/1,000 person years. |
| Srivastava (2017) | Key points:  
• For all patient groups, recommend methadone or buprenorphine-naloxone treatment over abstinence-based treatment (level I evidence from multiple large RCTs and systematic reviews).  
• Recommend methadone over buprenorphine-naloxone for:  
  - Patients at higher risk of treatment dropout, (e.g., injection opioid users [level I evidence] including youth and pregnant women [level III evidence from cohort and case-control studies]).  
  - If withdrawal symptoms, cravings, or opioid use persist despite an optimal buprenorphine-naloxone dose (level II evidence from one or two cohort and case-control studies).  
• Recommend buprenorphine-naloxone for:  
  - Socially stable prescription oral opioid users, particularly if their work or family commitments make it difficult for them to attend the pharmacy daily.  
  - Individuals with a medical or psychiatric condition requiring regular primary care (level IV evidence from consensus).  
  - Individuals whose jobs require higher levels of cognitive functioning or psychomotor performance (level III evidence).  
  - Patients at high risk of methadone toxicity, e.g., elderly, persons on high doses of benzodiazepines or other sedating drugs, heavy drinkers, or a lower level of opioid tolerance.  
  - Patients at high risk of prolonged QT interval (level III evidence). |
| Nielsen (2016) | Key points:  
• There was low-to-moderate-quality evidence supporting the use of maintenance agonist pharmacotherapy for pharmaceutical opioid dependence.  
• Methadone or buprenorphine appeared equally effective.  
• Maintenance treatment with buprenorphine appeared more effective than detoxification or psychological treatments.  
• Due to the overall low-to-moderate-quality of the evidence and small sample sizes, there is the possibility that the further research may change these findings. |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| Naltrexone subcutaneous implants maintenance therapy | - Systematic review and meta-analysis of five RCTs (576 patients) and four non-randomized studies (8,358 patients).  
- Overall quality: very low to moderate.  
- For suppressing opioid use, naltrexone was superior to placebo implants and equivalent to methadone maintenance therapy.  
- Limited evidence of safety and efficacy of naltrexone implants; use should be limited to clinical trials until better quality data are available. |
| Mattick (2014) Cochrane review Buprenorphine vs. methadone maintenance therapy or placebo | **Key points:**  
- Systematic review and meta-analysis of 31 RCTs with 5,430 participants.  
- Overall quality: moderate-to-high.  
- Buprenorphine is effective in retaining people in treatment at any dose >2 mg and suppressing illicit opioid use at doses ≥16 mg compared to placebo.  
- Buprenorphine and methadone are equally effective at fixed medium or high doses.  
- Methadone at flexible doses is superior to buprenorphine for treatment retention and equally effective at suppressing illicit opioid use.  
- Fixed doses are rarely used in clinical practice, so the flexible dose results are more relevant to patient care. |
| Minozzi (2014a) Cochrane review Detoxification treatments for adolescents | **Key points:**  
- Systematic review of two trials with 190 participants.  
- Overall quality: low to moderate.  
- Buprenorphine versus clonidine: No difference in dropout or acceptability of treatment. More participants on buprenorphine initiated naltrexone treatment.  
- Buprenorphine with naloxone versus buprenorphine detoxification: Maintenance treatment had lower dropout rate and opiate use at follow-up.  
- Results are limited and inconclusive. Neither considered the efficacy of methadone. |
| Minozzi (2014b) Cochrane review Maintenance treatments for adolescents | **Key points:**  
- Systematic review of two trials:  
  - Methadone vs. levo-alpha-acetylmethadol for 16 weeks maintenance followed by detoxification (one study, 35 patients).  
  - Buprenorphine vs. buprenorphine-naloxone followed by detoxification with buprenorphine (one study, 154 patients).  
- Overall quality: low.  
- Buprenorphine was more effective than detoxification for treatment retention but not for reducing the number of patients with a positive urine test at the end of the study.  
- Maintenance programs were associated with lower self-reported opioid use and higher enrollment in other addiction treatment programs at 12-month follow-up, although both groups reported a high level of opioid use.  
- RCTs are needed. |
| Amato (2013) Cochrane review | **Key points:**  
- Systematic review of 23 RCTs with 2,467 patients comparing methadone to adrenergic agonists (11 studies), other opioid agonists (eight studies), anxiolytic (two studies), and paiduyangsheng (one study). |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| Methadone at tapered doses for opioid detoxification | • Overall quality: moderate. Limited by wide variation in assessment of outcome measures, which impaired the application of meta-analysis.  
• No clinical difference between treatments in treatment completion, abstinence at follow-up, or degree of discomfort for withdrawal symptoms and adverse events.  
• Comparing methadone with placebo (two studies): more severe withdrawal and more dropouts in the placebo group.  
• Slow tapering with temporary substitution of long-acting opioids, can reduce withdrawal severity. The majority of patients relapsed to heroin use. |
| Minozzi (2013) Cochrane review | Key points:  
• Systematic review of four RCTs: three compared methadone to buprenorphine and one compared methadone to oral slow-release morphine.  
• Overall quality: low to moderate.  
• Methadone versus buprenorphine: treatment retention was superior with methadone, but less severe neonatal abstinence syndrome with buprenorphine.  
• No significant differences between methadone and buprenorphine or slow-release morphine to conclude superiority of one treatment to another for all relevant outcomes.  
• RCTs are needed. |
| Gowing (2011) Cochrane review | Key points:  
• Systematic review of 38 non-experimental studies with 12,400 patients.  
• Overall quality: low with high risk of bias. No RCTs found.  
• Both oral methadone and buprenorphine maintenance therapy for injecting opioid users reduce drug-related behaviors associated with a high risk of HIV transmission, but has less effect on sex-related risk behaviors. |
| Minozzi (2011) Cochrane review | Key points:  
• Systematic review and meta-analysis of 13 RCTs (1,158 patients).  
• Overall quality: moderate. Risk of bias was low or unclear in most studies.  
• Naltrexone vs. placebo or no pharmacological treatments:  
  – No statistically significant difference in abstinence, abstinence at follow-up, treatment retention, or side effects.  
  – Naltrexone had more favorable re-incarceration rates (two studies).  
  – Naltrexone had more favorable retention and abstinence rates in patients who were forced to adherence.  
• Naltrexone vs. psychotherapy: no statistically significant differences (one study).  
• Naltrexone + psychotherapy vs. benzodiazepines + psychotherapy: no significant difference in outcomes (one study).  
• Naltrexone + psychotherapy vs. buprenorphine + psychotherapy: no significant differences in retention, abstinence, or side effects (one study).  
• Overall treatment retention rate was low (28%).  
• Insufficient evidence of superiority of oral naltrexone to no therapy or other medications. |
Professional society guidelines/other:


Substance Abuse and Mental Health Services Administration (SAMHSA) publications:


Peer-reviewed references:

42 CFR 8. Certification of Opioid Treatment Programs.


CMS National Coverage Determinations (NCDs):

NCD 130.7 Withdrawal Treatments for Narcotic Addictions. CMS website.
https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=59&ncdver=1&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SAD%7cEd&PolicyType=Final&s=All&KeyWord=addiction&KeyWordLookUp=Doc&KeyWordSearchType=Or&q=false&bc=IAAAABAAAAAAA%3d%3d&. Accessed December 8, 2017.

Local Coverage Determinations (LCDs):

NO LCDs identified as of the writing of this policy.

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>90791</td>
<td>Psychiatric diagnostic evaluation</td>
<td></td>
</tr>
<tr>
<td>90792</td>
<td>Psychiatric diagnostic evaluation with medical services</td>
<td></td>
</tr>
<tr>
<td>90785</td>
<td>Interactive complexity</td>
<td>Add on code for 90791-90792</td>
</tr>
<tr>
<td>90863</td>
<td>Pharmacologic management, including prescription and review of medication, when performed psychotherapy services</td>
<td></td>
</tr>
<tr>
<td>99212 – 99215</td>
<td>Office or other outpatient visit for the evaluation and management of an established patient</td>
<td>Code Range</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>F11.10-F11.99</td>
<td>Opioid related disorders</td>
<td>Code Range</td>
</tr>
<tr>
<td>HCPCS Level II Code</td>
<td>Description</td>
<td>Comments</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>H0020</td>
<td>Alcohol and/or drug services; methadone administration and/or service</td>
<td></td>
</tr>
<tr>
<td>H0033</td>
<td>Oral medication administration, direct observation</td>
<td></td>
</tr>
<tr>
<td>J0570</td>
<td>Buprenorphine implant, 74.2 mg</td>
<td></td>
</tr>
<tr>
<td>J0571 – J0575</td>
<td>Buprenorphine or Buprenorphine/naloxone, oral</td>
<td>Code Range</td>
</tr>
<tr>
<td>S0109</td>
<td>Methadone, 5 mg, oral</td>
<td></td>
</tr>
</tbody>
</table>

**Appendix**

**DSM-5 Diagnosis Criteria for Opioid Use Disorder.**

Severity is defined as:
- Mild (2–3 symptoms).
- Moderate: (4–5 symptoms).
- Severe: (6 or more symptoms).

Opioid use disorder requires at least two of the following criteria be met within a 12-month period:
1. Opioids are often taken in larger amounts or over a longer period of time than intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving or a strong desire to use opioids.
5. Recurrent opioid use resulting in failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.
10. Tolerance*, as defined by either of the following:
   (a) Need for markedly increased amounts of opioids to achieve intoxication or desired effect.
   (b) Markedly diminished effect with continued use of the same amount of an opioid.
11. Withdrawal*, as manifested by either of the following:
   (a) Characteristic opioid withdrawal syndrome.
   (b) Same (or a closely related) substance is taken to relieve or avoid withdrawal.
   (c) Symptoms.
* Patients who are prescribed medications such as opioids may exhibit these two criteria (withdrawal and tolerance), but would not necessarily be considered to have a substance use disorder.