OBJECTIVE
The intent of the Buprenorphine and Buprenorphine/Naloxone for Opioid Dependence Prior Authorization (PA) program is to ensure appropriate selection of patients for treatment of opioid dependence in appropriate quantities according to product labeling and/or clinical guidelines and/or clinical studies. These products will not be covered for the treatment of pain. Claims for opioids during buprenorphine or buprenorphine/naloxone therapy will only be covered with prior authorization and only in the event of acute pain/surgery not to exceed 5 day course of treatment.

TARGET DRUGS
buprenorphine
buprenorphine/naloxone
Bunavail™ (buprenorphine/naloxone)
Suboxone® (buprenorphine/naloxone)
Zubsolv® (buprenorphine/naloxone)

PROGRAM QUANTITY LIMIT

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit per 90 Days - Subutex Quantity Limit per Day - Suboxone, Zubsolv</th>
</tr>
</thead>
<tbody>
<tr>
<td>buprenorphine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 mg sublingual tablet</td>
<td>65200010100760</td>
<td>M, N, O, or Y</td>
<td>5 tablets/90 days</td>
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<tr>
<td>8 mg sublingual tablet</td>
<td>65200010100780</td>
<td>M, N, O, or Y</td>
<td>5 tablets/90 days</td>
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<tr>
<td>Bunavail (buprenorphine/naloxone)</td>
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<tr>
<td>2.1 mg/0.3 mg buccal film</td>
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<tr>
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<td>6.3 mg/1 mg buccal film</td>
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<td>M, N, O, or Y</td>
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<td>Suboxone (buprenorphine/naloxone)</td>
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<td>1 film/day</td>
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<td>Dosage</td>
<td>DEA Number</td>
<td>Prescriber Requirements</td>
<td>Coverage Days</td>
</tr>
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<tr>
<td><strong>Buprenorphine</strong></td>
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<td></td>
</tr>
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<td>2 films/day</td>
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<td>12 mg/3 mg sublingual film</td>
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<td>1 film/day</td>
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<td><strong>Zubsolv (buprenorphine/naloxone)</strong></td>
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<td></td>
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<td>1.4 mg/0.36 mg sublingual tablet</td>
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<td>65200010200760</td>
<td>M, N, O, or Y</td>
<td>1 tablet/day</td>
</tr>
</tbody>
</table>

**a** - Available as a generic and included in the quantity limit program.

**b** – Brand Suboxone tablets discontinued by manufacturer but may still be available.

**c** – Brand Subutex no longer available.

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**

**Initial Evaluation for Induction and Stabilization**

**Please provide clinical notes to support information below.**

**Buprenorphine or Bunavail/Suboxone/Zubsolv (buprenorphine/naloxone)** will be approved when ALL of the following are met:

1. The patient has an active diagnosis of opioid dependence supported by clinical notes submitted by the prescriber
   **AND**
2. The prescriber meets the qualification certification criteria in the Drug Addiction Treatment Act (DATA) of 2000 and has been issued a unique DEA identification number by the DEA, indicating that he or she is a qualified physician under the DATA to prescribe buprenorphine, Bunavail, Suboxone, buprenorphine/naloxone, or Zubsolv, and does not exceed maximum number of allowable patients under their care, to be verified upon submission
   **AND**
3. The patient is 16 years of age or older
   **AND**
4. ONE of the following:
   a. The patient is not currently taking an opioid agent, including tramadol and tapentadol, to be verified in claims history
      **OR**
   b. The patient will discontinue use with the opioid agent prior to/with the initiation of buprenorphine/naloxone
   **AND**
5. ONE of the following supported by clinical notes submitted by the prescriber:
   a. The patient is currently enrolled in an ongoing outpatient drug addiction treatment program/counseling (appointment dates)
      **OR**
   b. The patient has agreed to enroll in an ongoing outpatient drug addiction treatment program/counseling within the initial approval timeframe of 2 months
   **AND**
6. The prescriber has submitted an initial treatment plan which includes ALL of the following:
a. Medication history review
   AND
b. Current urine drug screen (within the past 30 days, not required to be clean)
   AND
c. Prescriber maintains current informed consent signed by the prescriber and the patient
   AND
7. ONE of the following:
   a. The patient is not currently taking other addictive medications (e.g. muscle relaxants, benzodiazepines, sedative/hypnotics, non-prescription drugs of abuse or alcohol)
   OR
   b. The prescriber has submitted documentation indicating benefits of treatment/use of the listed prescription agents outweighs risk associated with concomitant buprenorphine product use
   AND
8. The patient is receiving only one buprenorphine or buprenorphine/naloxone agent (including implantable buprenorphine)
   AND
9. ONE of the following:
   a. The quantity requested is less than or equal to the program quantity limit
   OR
   b. The quantity (dose) requested is within FDA-approved labeling (e.g. Suboxone 24 mg) and the prescriber has submitted documentation in support of therapy stating the need for a higher dose which has been reviewed and approved by the Clinical Review pharmacist
   OR
   c. For buprenorphine only: The patient is a pregnant woman or has a documented intolerance, FDA labeled contraindication, or hypersensitivity to naloxone or naltrexone

**Length of Approval:**

- **Buprenorphine:** allow for a single course of induction treatment within the quantity limit OR as requested and approved, based on submitted information for 2 months to allow for induction and stabilization.
- **Bunavail, Suboxone, buprenorphine/naloxone, Zubsolv:** 2 months for induction and stabilization.

**Prior Authorization for Opioid Use During Buprenorphine or Bunavail/Suboxone/Zubsolv (buprenorphine/naloxone) therapy** will be approved when the following are met:

1. The prescriber has submitted documentation supporting concurrent use of an opioid and the requested buprenorphine product due to one of the following:
   a. Dental procedure with dates
   b. Surgery with dates
   c. Acute injury with dates

**Length of Approval:** 5 days

Acceptable rationale and supporting documentation for concurrent buprenorphine/buprenorphine-naloxone and opioid use include clinical notes indicating treatment of acute pain with surgery, acute injury or dental procedure dates. The patient
must remain enrolled in ongoing outpatient drug addiction treatment program/counseling if appropriate as established in original treatment plan.

Renewal Evaluation for Maintenance Therapy

Buprenorphine or Bunavail/Suboxone/Zubsolv (buprenorphine/naloxone) will be approved when ALL of the following are met:

1. The prescriber has verified the patient has been through induction and stabilization therapy and is seeking approval for maintenance therapy

2. The patient has a confirmed diagnosis of active opioid dependence supported by clinical notes submitted by the prescriber, to be verified upon submission

3. The prescriber meets the qualification certification criteria in the Drug Addiction Treatment Act (DATA) of 2000 and has been issued a unique DEA identification number by the DEA, indicating that he or she is a qualified physician under the DATA to prescribe buprenorphine, Bunavail, Suboxone, buprenorphine/naloxone, or Zubsolv, and does not exceed maximum number of allowable patients under their care, to be verified upon submission

4. The patient is not currently taking an opioid agent, including tramadol and tapentadol, to be verified in claims history

5. ONE of the following:
   a. The patient is currently enrolled in an ongoing outpatient drug addiction treatment program/counseling supported by clinical notes submitted by the prescriber with visit dates

   OR

   b. The patient has completed 6 months or more of outpatient drug addiction treatment/counseling and the prescriber provides rationale as to why the patient no longer needs to continue

   AND

6. ONE of the following:
   a. The patient is not currently taking other addictive medications (e.g. muscle relaxants, benzodiazepines, sedative/hypnotics, non-prescription drugs of abuse or alcohol) to be verified in claims history

   OR

   b. The prescriber has submitted documentation indicating benefits of treatment/use of the listed prescription agents outweighs risk associated with concomitant buprenorphine use

   AND

7. The prescriber has submitted a current treatment plan which includes ALL of the following:
   a. Medication history review

   AND

   b. Frequency of urine drug screening, including most recent drug screen indicating patient is free from illicit drug use

   AND

   c. Prescriber maintains current informed consent signed by the prescriber and the patient

   AND

   d. Anticipated duration of therapy and plan for dose taper OR documentation of barriers to drug taper if patient is not a candidate for dose taper at this time
AND
8. The patient continues to be compliant with all elements of the treatment plan required at that time (including but not limited to recovery-oriented activities, psychotherapy, and/or other psychosocial modalities) as supported by evidence in clinical notes
AND
9. The prescriber has reviewed the patient’s records in the state’s prescription drug monitoring program (PDMP) as attestation that, to the best of the providers knowledge, the patient is not diverting the requested medication
AND
10. ONE of the following:
   a. The patient is receiving only one buprenorphine or buprenorphine/naloxone agent (including implantable buprenorphine) and strength unless undergoing dose taper
      OR
   b. The prescriber has submitted documentation in support of therapy with more than one agent or strength which has been reviewed and approved by the Clinical Review pharmacist
AND
11. ONE of the following:
   a. The quantity requested is less than or equal to the program quantity limit
      OR
   b. The quantity (dose) requested is within FDA-approved labeling (e.g. Suboxone 24 mg) and the prescriber has submitted documentation in support of therapy stating a need for a higher dose which has been reviewed and approved by the Clinical Review pharmacist
      OR
   c. For buprenorphine only: The patient is a pregnant woman or has a documented intolerance, FDA labeled contraindication, or hypersensitivity to naloxone or naltrexone

Length of Approval: 6 months or duration of pregnancy if less than 6 months to term
FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Agent</th>
<th>Treatment of opioid dependence and induction; should be used as part of a complete treatment plan to include counseling and psychosocial support.</th>
<th>Maintenance treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support</th>
</tr>
</thead>
<tbody>
<tr>
<td>buprenorphine sublingual tablet&lt;sup&gt;ac&lt;/sup&gt;</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td><strong>Bunavail™</strong>&lt;sup&gt;a&lt;/sup&gt; (buprenorphine/naloxone buccal film)</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Suboxone®</strong>&lt;sup&gt;b&lt;/sup&gt; (buprenorphine/naloxone sublingual tablet)&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td><strong>Suboxone®</strong>&lt;sup&gt;c&lt;/sup&gt; (buprenorphine/naloxone sublingual film)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Zubsolv®</strong> (buprenorphine/naloxone sublingual tablet)</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

<sup>a</sup> – Generic available.
<sup>b</sup> – Brand Suboxone tablets discontinued by manufacturer but may still be available.
<sup>c</sup> – Brand Subutex no longer available.

Under the Drug Addiction Treatment Act of 2000 (DATA) codified at 21 U.S.C. 823(g), prescription use of this product in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, and have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence.

**Dosing**<sup>1-3,15-17</sup>

**For the prevention of undue symptoms of opiate agonist withdrawal during induction of opiate agonist dependence treatment**

NOTE: For induction treatment, single-agent buprenorphine is preferred.

For patients dependent on short-acting opioid products who are in opioid withdrawal, single agent buprenorphine or Suboxone (buprenorphine/naloxone) may be used for induction.

For patients dependent on methadone or long-acting opioid products, single-agent buprenorphine is recommended.

Single agent buprenorphine induction is initiated with 8 mg sublingually on day 1, buprenorphine 16 mg sublingually on day 2, and then the patient should begin maintenance treatment. Dosage titration over 2 days rather than 3—4 days appears to result in greater treatment success.

Single-agent buprenorphine should be limited to a maximum of 5 days, except in pregnant women and patients with a documented allergy to naloxone or naltrexone. These patients should be allowed treatment with single-agent buprenorphine beyond 5 days.<sup>4</sup>
When determining treatment initiation, consider the opioid’s duration of action, time since last opioid use, and degree of opioid dependence. Administer first dose of buprenorphine at least 4 hours after the last used opioid or preferably when early signs of opioid withdrawal appear. Use of buprenorphine/naloxone during induction may result in more withdrawal symptoms than if single-agent buprenorphine is used.

Suboxone induction is initiated with a recommended dose of up to 8 mg /2 mg on day one. Clinicians should start with an initial dose of 2 mg/ 0.5 mg or 4 mg/1 mg buprenorphine/naloxone and may titrate upwards in 2 or 4 mg increments of buprenorphine, at approximately 2-hour intervals, under supervision, to 8 mg/2 mg buprenorphine/naloxone based on the control of acute withdrawal symptoms. On day 2, a single daily dose of up to 16 mg/4 mg Suboxone sublingual film is recommended.

Zubsolv induction is initiated with a recommended dose of up to 5.7 mg/1.4 mg on day one. This is administered sublingually in divided doses under supervision. Clinicians should start with an initial dose of 1.4 mg/0.36 mg ZUBSOLV sublingual tablet. The remainder of the day 1 dose of up to 4.2 mg/1.08 mg should be divided into doses of 1 to 2 tablets of 1.4 mg/0.36 mg at 1.5 to 2 hour intervals. Some patients (e.g., those with recent exposure to buprenorphine) may tolerate up to 3 x 1.4 mg/0.36 mg ZUBSOLV sublingual tablets as a single, second dose. On Day 2, a single daily dose of up to 11.4 mg/2.9 mg ZUBSOLV sublingual tablet is recommended. All doses should be based on clinical need to control acute withdrawal symptoms and administered under supervision.

Medication should be prescribed in consideration of the frequency of visits. Provision of multiple refills is not advised early in treatment or without appropriate patient follow-up visits.

Prior to induction, consideration should be given to the type of opioid dependence (i.e., long-or short-acting opioid products), the time since last opioid use, and the degree or level of opioid dependence. To avoid precipitating an opioid withdrawal syndrome, the first dose of buprenorphine/naloxone should be started only when objective signs of moderate withdrawal appear.

For maintenance treatment of opiate agonist dependence

**NOTE:** Buprenorphine/naloxone is preferred over single-agent buprenorphine for maintenance treatment, especially when drug administration will not be supervised. Only use single-agent buprenorphine for unsupervised administration in those patients who cannot tolerate buprenorphine/naloxone.

A target dose of buprenorphine for Suboxone sublingual film or tablets is 16 mg once daily is suggested; however, doses ranging from 4—24 mg/day buprenorphine for Suboxone film or tablets may be required. Titrate dosage in increments of 2—4 mg/day to a dose that holds the patient in treatment and suppresses opiate withdrawal symptoms. Higher dosages (12—16 mg/day) have been associated with reduced opiate craving and fewer opiate-positive urine tests.

A target dose of buprenorphine for Zubsolv is 11.4 mg once daily is suggested; however, doses for Zubsolv SL tablets ranging from 2.8-17.1 mg/day may be required. The dosage of Zubsolv should be progressively adjusted in increments/decrements of 1.4 -or 2.8 mg buprenorphine to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms.
A target dose of buprenorphine for Bunavial buccal film is 8.4 mg once daily is suggested. However, doses ranging from 2.1-12.6 mg/day buprenorphine for Bunavial may be required. Dosage should be titrated in increments of 2.1 mg buprenorphine per day to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms.

Buprenorphine and buprenorphine/naloxone is indicated for daily administration; however, efficacy has been demonstrated when the same total weekly dose is divided and given in 3 doses (i.e., dosing 3 times/week). Duration of treatment and the best method for drug discontinuation have not been determined; both abrupt discontinuation and dose tapering have been used. Withdrawal symptoms may occur upon discontinuation of buprenorphine/naloxone.

**Switching Between Products**

Buprenorphine and buprenorphine/naloxone (Suboxone) sublingual tablets

Buprenorphine dosing for buprenorphine tablets and Suboxone is considered interchangeable

8 mg buprenorphine in buprenorphine tablets is equivalent to 5.7 mg buprenorphine (1.4 mg naloxone) dose within Zubsolv

Switching between buprenorphine/naloxone (Suboxone) sublingual tablets and buprenorphine/naloxone (Suboxone) sublingual film

Start on same dosage as the previously administered product. However, dosage adjustments may be necessary when switching between products. Because of the potentially greater relative bioavailability of sublingual film compared to sublingual tablet, patients switching from sublingual tablet to sublingual film should be monitored for overmedication. Patients switching from sublingual film to sublingual tablet should be monitored for withdrawal or other indications of under-dosing.

<table>
<thead>
<tr>
<th>Suboxone Sublingual Tablet Dose</th>
<th>Corresponding Zubsolv Sublingual Tablet Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mg/0.5 mg buprenorphine/naloxone</td>
<td>1.4 mg/0.36 mg buprenorphine/naloxone</td>
</tr>
<tr>
<td>8 mg/2 mg buprenorphine/naloxone</td>
<td>5.7 mg/1.4 mg buprenorphine/naloxone</td>
</tr>
<tr>
<td>12 mg/3 mg buprenorphine/naloxone</td>
<td>8.6 mg/2.1 mg buprenorphine/naloxone</td>
</tr>
<tr>
<td>16 mg/4 mg buprenorphine/naloxone</td>
<td>11.4 mg/2.9 mg buprenorphine/naloxone</td>
</tr>
</tbody>
</table>

Switching between Suboxone sublingual tablets and film and Bunavial buccal film.

The difference in bioavailability of Bunavial compared to Suboxone sublingual tablet requires a different dosage strength to be administered to the patient. Patients should be started on the following corresponding dosage as defined below:

<table>
<thead>
<tr>
<th>Suboxone Sublingual Tablet Dosage Strength</th>
<th>Corresponding Bunavial Buccal Film Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/1 mg buprenorphine/naloxone</td>
<td>2.1/0.3 mg buprenorphine/naloxone</td>
</tr>
<tr>
<td>8/2 mg buprenorphine/naloxone</td>
<td>4.2/0.7 mg buprenorphine/naloxone</td>
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<tr>
<td>12/3 mg buprenorphine/naloxone</td>
<td>6.3/1 mg buprenorphine/naloxone</td>
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</tbody>
</table>

**Maximum Dosage Limit**
For buprenorphine tablets and Suboxone or buprenorphine/naloxone tablets: 24 mg/day sublingually of the buprenorphine component.

For Zubsolv: 17.1 mg/day sublingually of the buprenorphine component. Dosages higher than these have not been demonstrated to provide any clinical advantage.

For Bunavail: 12.6 mg/day buccal of the buprenorphine component. Dosages higher than this have not been demonstrated to provide any clinical advantage.

CLINICAL RATIONALE
In October 2000, treatment of opioid dependence was transformed by Congressional approval of the Drug Addiction Treatment Act (DATA 2000). Under DATA 2000, qualified physicians may obtain a waiver allowing them to prescribe and/or dispense approved Schedule III-V medications for the treatment of opioid dependence. Previously, this type of treatment was available only in federally approved Opioid Treatment Programs (methadone clinics). Suboxone and Subutex (buprenorphine tablets) were the first narcotic drugs available under the Drug Abuse Treatment Act (DATA) of 2000 for treatment of opiate dependence that can be prescribed in a doctor's office. Only qualified doctors with the necessary DEA (Drug Enforcement Agency) identification number are able to start in-office treatment and provide prescriptions for ongoing medication.1-3,5

Efficacy
Buprenorphine is a semisynthetic mixed opiate agonist-antagonist. As a partial mu-receptor agonist, buprenorphine exhibits a ceiling to its pharmacological effects; thus, the danger of overdose, abuse liability, and toxicity from buprenorphine may be less than with full opioid agonists. Naloxone is a full opiate antagonist.1,2 Since buprenorphine may be given outside of an opiate-treatment clinic, a formulation with naloxone (Suboxone, at a ratio of 4:1 buprenorphine: naloxone) was developed in an effort to dissuade patients from grinding up the Suboxone tablet and using as part of a combination of opiates that the user would inject. In this formulation, the naloxone component produces no clinical effect when administered sublingually; however, when dissolved in water and injected, the full opiate antagonist effect of naloxone occurs. As a result, the buprenorphine with naloxone combination product is preferred for maintenance therapy in patients with unsupervised drug administration.1,2

Comparisons of buprenorphine to full opioid agonists such as methadone and hydromorphone suggest that sublingual buprenorphine produces typical opioid agonist effects which are limited by a ceiling effect.1-3 In opioid-experienced subjects who were not physically dependent, acute sublingual doses of buprenorphine/naloxone (Suboxone) tablets produced opioid agonist effects which reached a maximum between doses of 8/2 mg and 16/4 mg buprenorphine/naloxone (Suboxone). Opioid agonist ceiling-effects were also observed in a double-blind, parallel group, dose-ranging comparison of single doses of buprenorphine sublingual solution (1, 2, 4, 8, 16, or 32 mg), placebo and a full agonist control at various doses. The treatments were given in ascending dose order at intervals of at least one week to 16 opioid-experienced subjects who were not physically dependent. Both active drugs produced typical opioid agonist effects. For all measures for which the drugs produced an effect, buprenorphine produced a dose-related response. However, in each case, there was a dose that produced no further effect. In contrast, the highest dose of the full agonist control always produced the greatest effects.1-3

According to the Substance Abuse and Mental Health Services Administration (SAMHSA),5 dosing can vary between 2mg/0.5mg (buprenorphine/naloxone) to 8mg/2mg (Suboxone)
on the first and second day of induction, and up to 32mg/8mg during maintenance period. Dosing depends on the stabilization of withdrawal symptoms. An article by Fareed et al suggests that flexible dosing up to 32 mg buprenorphine (as Suboxone) per day has increased benefit for patients who do not respond with lower doses. The authors suggest that doses greater than 32 mg may be ineffective due to a ceiling effect.

Buprenorphine is indicated for daily administration; however, administering the total weekly dose over three days (roughly every other day) may be effective in decreasing opioid dependence. In one study, comparable reductions in illicit opioid usage were found with three treatments for opioid dependence: buprenorphine, methadone, and levomethadyl acetate. The dosages were individually optimized within a range of 16—48 mg three times a week for buprenorphine, 60—100 mg daily for methadone, and 75—161 mg three times a week for levomethadyl acetate.

Buprenorphine and buprenorphine/naloxone placebo controlled randomized trials have demonstrated that buprenorphine/naloxone is safe and reduces the use of opiates and the craving for opiates among opiate-addicted persons who receive these medications in an office-based setting. There is limited evidence comparing buprenorphine with methadone, but completion of withdrawal appears to be more likely with buprenorphine and withdrawal symptoms may resolve more quickly with buprenorphine. In pivotal trials, buprenorphine and buprenorphine/naloxone was used in combination with psychosocial counseling.

The US National Institute on Drug Abuse considers buprenorphine and buprenorphine/naloxone as a first line option for office based management of opiate dependency.

The Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction issued by the US Dept of Health and Human Services recommends the following:

"The consensus panel recommends that the buprenorphine/naloxone combination be used for induction treatment (and for stabilization and maintenance) for most patients. However, pregnant women who are determined to be appropriate candidates for buprenorphine treatment should be inducted and maintained on buprenorphine monotherapy. In addition, patients who desire to change from long-acting opioids (e.g., methadone) to buprenorphine should be inducted using buprenorphine monotherapy."

"Patients and their physicians together need to reach agreement on the goals of treatment and develop a treatment plan based on the patient’s particular problems and needs. During the stabilization phase, patients receiving maintenance treatment should be seen on at least a weekly basis. Once a stable buprenorphine dose is reached and toxicologic samples are free of illicit opioids, the physician may determine that less frequent visits (biweekly or longer, up to 30 days) are acceptable. During opioid addiction treatment with buprenorphine, toxicology tests for relevant illicit drugs should be administered at least monthly."

The American Society of Addiction Medicine National Practice Guideline For the Use of Medications in the Treatment of Addiction Involving Opioid Use recommends the following:

- Buprenorphine mono-product is a reasonable and recommended alternative to methadone for pregnant women.
- Methadone is recommended for patients who may benefit from daily dosing and supervision in an opioid treatment program (OTP), or for patients for whom buprenorphine for the treatment of opioid use disorder has been used unsuccessfully in an OTP or office based opioid treatment (OBOT) setting.

**Safety**
A review of the safety profile of the combined buprenorphine/naloxone product was conducted for the US National Institute on Drug Abuse. The Institute supported the use of buprenorphine, alone or together with naloxone, as the first-line option for office-based management of opiate dependence. This support was based on three observations:\(^9\)

- reduced likelihood of diversion of the combination product for diversion to illicit parenteral misuse
- established utility of the mono product for the treatment of opiate dependence
- preferable safety profile of a partial mu-opiate receptor agonist such as buprenorphine compared with that of a full mu-opiate receptor agonist

Although methadone has been used as the standard of care for the treatment and maintenance of opioid dependence, the association with QT interval elongation with methadone has caused concern. Neither buprenorphine or buprenorphine/naloxone appear to be associated with QT interval prolongation.\(^10\) A meta-analysis of 13 randomized controlled trials concluded buprenorphine is an effective intervention for use in the maintenance treatment of heroin dependence, and is as effective as methadone at adequate dosages.\(^11\)

Despite measures to prevent abuse with buprenorphine, diversion and abuse of buprenorphine/naloxone have steadily increased from 2005 through 2009.\(^12,13\) The number of emergency department visits due to abuse/misuse with buprenorphine as one of the drugs listed increased monotonically from 5025 in 2006 to 17,546 in 2009 (\(R^2 = .98\), an additional 4403 visits per year, \(p = .01\)).\(^12\)

Continuation or modification of pharmacotherapy should be based on the physician's evaluation of treatment outcomes and objectives such as:\(^1,3,5,15-17\)

1. Absence of medication toxicity
2. Absence of medical or behavioral adverse effects
3. Responsible handling of medications by the patient
4. Patient’s compliance with all elements of the treatment plan (including recovery-oriented activities, psychotherapy, and/or other psychosocial modalities)
5. Abstinence from illicit drug use (including problematic alcohol and/or benzodiazepine use)

If treatment goals are not being achieved, the physician should re-evaluate the appropriateness of continuing the current treatment.\(^3\)

REFERENCES


**Additional Information**

Client states that have a fully operational prescription drug monitoring program (PDMP) as of October 2012 are Alabama, Florida, Illinois, Kansas, Minnesota, New Jersey, New Mexico, North Carolina, North Dakota, Oklahoma, Texas, and Wyoming. Montana and Nebraska have enacted PDMP legislation, but the program is not yet operational (as of October 2012). Please visit [http://www.deadiversion.usdoj.gov/faq/rx_monitor.htm](http://www.deadiversion.usdoj.gov/faq/rx_monitor.htm) or [http://www.pmpalliance.org/pdf/pmp_status_map_2012.pdf](http://www.pmpalliance.org/pdf/pmp_status_map_2012.pdf) for the most up to date information.