Clinical Policy: Buprenorphine-Naloxone (Bunavail, Suboxone, Zubsolv, Cassipa)
Reference Number: CP.CPA.299
Effective Date: 03.01.18
Last Review Date: 02.19
Line of Business: Commercial

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Buprenorphine-naloxone (Bunavail®, Suboxone®, Zubsolv®, and Cassipa®) is a partial opioid agonist.

FDA Approved Indication(s)
Bunavail, Suboxone, Zubsolv, and Cassipa are indicated for the treatment of opioid dependence.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Bunavail, Suboxone, Zubsolv, and Cassipa are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Opioid Dependence (must meet all):
      1. Diagnosis of opioid dependence;
      2. Dose does not exceed:
         a. Bunavail: 12.6 mg/2.1 mg per day;
         b. Suboxone: 24 mg/6 mg per day;
         c. Zubsolv: 17.1 mg/4.2 mg per day;
         d. Cassipa: 16 mg/4 mg per day.

   Approval duration: 12 months

   B. Other diagnoses/indications
      1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

II. Continued Therapy
   A. Opioid Dependence (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. One of the following conditions is met (a or b):
         a. Member has NOT received an opioid analgesic since last approval;
b. Prescriber submits documentation acknowledging that the use of opioid during the last approval period was due to legitimate diagnosis of pain;

4. If request is for a dose increase, new dose does not exceed:
   a. Bunavail: 12.6 mg/2.1 mg per day;
   b. Suboxone: 24 mg/6 mg per day;
   c. Zubsolv: 17.1 mg/4.2 mg per day;
   d. Cassipa: 16 mg/4 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Pain management;
   B. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.CPA.09 for commercial or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   FDA: Food and Drug Administration

   Appendix B: Therapeutic Alternatives
   Not applicable

   Appendix C: Contraindications/Boxed Warnings
   • Contraindication(s): hypersensitivity to buprenorphine or naloxone
   • Boxed warning(s): none reported

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine-naloxone (Suboxone) sublingual (SL) or buccal dissolving film</td>
<td><strong>Induction:</strong> Titrate to 8 mg/2 mg SL on Day 1 and 16 mg/4 mg SL on Day 2; then start maintenance treatment <strong>Maintenance:</strong> Target dose: buprenorphine 16 mg/naloxone 4 mg once daily; dosage should be adjusted in increments or decrements of 2 mg/0.5 mg or 4 mg/1 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 4 mg/1 mg to 24 mg/6 mg per day</td>
<td>24 mg/6 mg per day</td>
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</table>
### CLINICAL POLICY

**Buprenorphine-Naloxone**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine-naloxone (Bunavail) buccal film</td>
<td><strong>Maintenance</strong>: Target dose: buprenorphine 8.4 mg/naloxone 1.4 mg once daily; dosage should be adjusted in increments or decrements of 2.1 mg/0.3 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 2.1 mg/0.3 mg to 12.6 mg/2.1 mg per day</td>
<td>12.6 mg/2.1 mg per day</td>
</tr>
<tr>
<td>Buprenorphine-naloxone SL tablet</td>
<td><strong>Maintenance</strong>: Target dose: buprenorphine 16 mg/naloxone 4 mg SL once daily; dosage should be adjusted in increments or decrements of 2 mg/0.5 mg or 4 mg/1 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 4 mg/1 mg to 24 mg/6 mg per day</td>
<td>24 mg/6 mg per day</td>
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</tbody>
</table>
| Buprenorphine-naloxone (Zubsolv) SL tablet     | **Induction**: Titrate to 5.7 mg/1.4 mg SL on Day 1 and 11.4 mg/2.9 mg SL on Day 2; then start maintenance treatment  
**Maintenance**: Target dose: buprenorphine 11.4 mg/naloxone 2.9 mg once daily; dosage should be adjusted in increments or decrements of 2.9 mg/0.71 mg to 17.2 mg/4.2 mg per day | 17.1 mg/4.2 mg per day                           |
| Buprenorphine-naloxone (Cassipa) SL film       | **Maintenance**: Target dose: buprenorphine 16 mg/naloxone 4 mg SL once daily; dosage should be titrated to target dose using another marketed product (Cassipa comes in a single dose and cannot be adjusted) | 16 mg/4 mg per day                               |

### VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine-naloxone (Suboxone)</td>
<td>Sublingual film: buprenorphine/naloxone 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg</td>
</tr>
<tr>
<td>Buprenorphine-naloxone (Bunavail)</td>
<td>Buccal film: buprenorphine/naloxone 2.1 mg/0.3 mg; 4.2 mg/0.7 mg, 6.3 mg/1 mg</td>
</tr>
<tr>
<td>Buprenorphine-naloxone</td>
<td>Sublingual tablet: buprenorphine/naloxone 2 mg/0.5 mg, 8 mg/2 mg</td>
</tr>
<tr>
<td>Buprenorphine-naloxone (Zubsolv)</td>
<td>Sublingual tablet: buprenorphine/naloxone 0.7 mg/0.18 mg, 1.4 mg/0.36 mg, 2.9 mg/0.71 mg, 5.7 mg/1.4 mg, 8.6 mg/2.1 mg, 11.4 mg/2.9 mg</td>
</tr>
<tr>
<td>Buprenorphine-naloxone (Cassipa)</td>
<td>Sublingual film: buprenorphine/naloxone 16 mg/4 mg</td>
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</table>
VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>New policy created</td>
<td>11.08.17</td>
<td>02.18</td>
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<tr>
<td>- Policy split from CP.CPA.276 Buprenorphine, Buprenorphine plus Naloxone (retired).</td>
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<td>- Initial: removed requirement that member is not using concurrent opioid medications (including tramadol).</td>
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<td>- Re-auth: added requirement related to absence/presence of opioid use since last approval;</td>
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<tr>
<td>- Modified initial/continued approval duration from LOB to 12 months due to potential for abuse.</td>
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<td>- Added pain management as a diagnosis for which coverage is not authorized.</td>
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<tr>
<td>- References reviewed and updated.</td>
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<tr>
<td>1Q 2019 annual review: no significant change from previously approved policy; references reviewed and updated.</td>
<td>10.23.18</td>
<td>02.19</td>
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<tr>
<td>RT4: added new dosage form Cassipa to the policy.</td>
<td>06.21.19</td>
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Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical
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The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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