Clinical Policy: Buprenorphine (Subutex)

Reference Number: ERX.NPA.08
Effective Date: 09.01.17
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Buprenorphine (Subutex®) is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor.

FDA Approved Indication(s)
Subutex is indicated for the treatment of opioid dependence and is preferred for induction.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Subutex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Opioid Dependence (must meet all)**:**

1. Diagnosis of opioid dependence;
2. Member meets one of the following conditions (a, b, or c):
   a. Member is pregnant;
   b. Member has experienced clinically significant adverse effect(s) or contraindication(s) to buprenorphine/naloxone (e.g., Suboxone®);
   c. Request is for induction therapy (treatment duration of ≤ 5 days);
3. Dose does not exceed 24 mg (3 tablets) per day.

Approval duration:
Induction therapy: 5 days
Maintenance therapy: Duration of request or 12 months, whichever is less

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Opioid Dependence Induction Therapy

1. Re-authorization for continuation of treatment beyond initial induction therapy is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

B. Opioid Dependence Maintenance Therapy (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;*
   **Note: Subutex will not be renewed for pregnancy unless there is documentation supporting that member is pregnant again.*
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 a diagnosis of acute pain;
4. If request is for a dose increase, new dose does not exceed 24 mg (3 tablets) per day.

Approval duration: Duration of request or 12 months, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. 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 – ERX.PA.01 or evidence of coverage documents;

B. Pain management.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
buprenorphine-naloxone (Suboxone®)	**Opiate agonist dependence** • DAY 1 DOSING: First induction dose buprenorphine; naloxone 2 mg/0.5 mg or 4 mg/1 mg SL film; may titrate in 2 or 4 mg increments of buprenorphine, at approximately 2-hour increments, under supervision, up to a total dose of buprenorphine/naloxone 8 mg/2 mg SL film. • DAY 2 DOSING: A single daily dose of buprenorphine; naloxone up to 16 mg/4 mg SL film is recommended. • DAY 3 DOSING AND BEYOND: Progressively adjust dose in increments or decrements of 2 mg/0.5 mg or 4 mg/1 mg to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms.	24/6 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): history of hypersensitivity to buprenorphine
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Opioid dependence	Induction Adults: 8 mg sublingually (SL) on Day 1 and 16 mg SL on Day 2; then start maintenance treatment.	24 mg/day

Indication	Dosing Regimen	Maximum Dose
	Maintenance The maintenance dose is generally in the range of 4 mg to 24 mg per day depending on the individual patient. The recommended target dose is 16 mg. Doses higher than 24 mg have not been demonstrated to provide any clinical advantage. The dosage of buprenorphine should be progressively adjusted in increments/decrements of 2 mg or 4 mg to a level that holds the patient in treatment and suppresses opioid withdrawal signs and symptoms.	

VI. Product Availability

Sublingual tablets: 2 mg, 8 mg

VII. References

1. Buprenorphine Prescribing Information. Eatontown, NJ: Hikma Pharmaceuticals USA Inc.; August 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed November 23, 2021.
2. Center for Substance Abuse Treatment. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2004. (Treatment Improvement Protocol (TIP) Series, No. 40.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK64245/. Accessed December 2, 2020.
3. Center for Substance Abuse Treatment. Medications for opioid use disorder. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2020. (Treatment Improvement Protocol (TIP) Series, No. 63) Available from: https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Document/PEP20-02-01-006. Accessed December 2, 2020.
4. Center for Substance Abuse Treatment. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. DHHS Publication No. (SMA) 05-4048. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2005. Available at: https://www.ncbi.nlm.nih.gov/books/NBK64164/pdf/Bookshelf_NBK64164.pdf. Accessed December 3, 2020.
5. Center for Substance Abuse Treatment. Detoxification and Substance Abuse Treatment. Treatment Improvement Protocol (TIP) Series, No. 45. HHS Publication No. (SMA) 15-4131. Rockville, MD: Center for Substance Abuse Treatment, 2006. Available at: https://www.samhsa.gov/search-samhsa/featured/tip-45. Accessed December 3, 2020.
6. American Society of Addiction Medicine (ASAM). National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. Available at: https://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf. Accessed December 3, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Removed XDEA number (DATA2000 waiver) as a requirement since prescription use of this product is limited under the Drug Addiction Treatment Act. Removed criteria related to participation in drug abuse counseling and urine drugs screens (e.g., submission of at least 2 negative random urine drug screens) to shift the responsibility of appropriate monitoring and use to the prescriber. Removed "member is allergic to naloxone" as an approval condition for Subutex since it's covered by "member has experienced clinically significant adverse effects or has contraindication(s) to buprenorphine/naloxone". Removed requirement related to adherence to therapy on re-auth and added requirement for positive response to therapy.	11.09.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: no significant changes; added clarification that re-auth will not be permitted for those who were initially approved for induction treatment unless other initial criteria (e.g., pregnancy) is met; reference reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.26.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	12.02.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.23.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.