Clinical Policy: Buprenorphine/Naloxone (Bunavail, Cassipa, Suboxone, Zubsolv)

Reference Number: CP.PMN.81
Effective Date: 09.01.17
Last Review Date: 02.23
Line of Business: Commercial, HIM, Medicaid Revision Log

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

Description

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

FDA Approved Indication(s)

Bunavail, Cassipa, Suboxone, and Zubsolv 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, Cassipa, Suboxone, and Zubsolv 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. Member must use generic buprenorphine/naloxone sublingual tablets or film;
3. Dose does not exceed:
   a. Bunavail: 12.6 mg/2.1 mg per day;
   b. Cassipa: 16 mg/4 mg per day;
   c. Suboxone: 24 mg/6 mg per day;
   d. Zubsolv: 17.2 mg/4.2 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Opioid Dependence (must meet all):

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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:
   a. Bunavail: 12.6 mg/2.1 mg per day;
   b. Cassipa: 16 mg/4 mg per day;
   c. Suboxone: 24 mg/6 mg per day;
   d. Zubsolv: 17.2 mg/4.2 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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, HIM.PA.154 for health insurance marketplace, CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

SL: sublingual

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
buprenorphine/ naloxone sublingual (SL) tablets	Maintenance: 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	24 mg/6 mg per day
buprenorphine/ naloxone SL film	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 mg/6 mg per 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): hypersensitivity to buprenorphine or naloxone
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
buprenorphine/ naloxone (Suboxone) SL or buccal dissolving film	Induction: Titrate to 8 mg/2 mg SL on Day 1 and 16 mg/4 mg SL on Day 2; then start maintenance treatment Maintenance: 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	24 mg/6 mg per day
buprenorphine/ naloxone (Bunavail) buccal film	Maintenance: 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	12.6 mg/2.1 mg per day
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 a level that maintains treatment and suppresses opioid withdrawal symptoms; usual range: 2.9 mg/0.71 mg to 17.2 mg/4.2 mg per day	17.2 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

Drug Name	Availability
buprenorphine/naloxone (Suboxone)	Sublingual film: buprenorphine/naloxone 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg

Drug Name	Availability
buprenorphine/naloxone (Bunavail)	Buccal film: buprenorphine/naloxone 2.1 mg/0.3 mg; 4.2 mg/0.7 mg, 6.3 mg/1 mg
buprenorphine/naloxone (Zubsolv)	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
buprenorphine/naloxone (Cassipa)	Sublingual film: buprenorphine/naloxone 16 mg/4 mg

VII. References

1. Bunavail Prescribing Information. Raleigh, NC: BioDelivery Sciences International, Inc.; March 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/205637s021lbl.pdf. Accessed November 16, 2022.
2. Cassipa Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; June 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208042s005s007lbl.pdf. Accessed November 16, 2022.
3. Suboxone Sublingual Film Prescribing Information. North Chesterfield, VA: Indivior Inc.; June 2022. Available at: https://www.suboxone.com/. Accessed November 16, 2022.
4. Zubsolv Prescribing Information. Morristown, NJ: Orexo US, Inc.; June 2022. Available at: https://www.zubsolv.com/. Accessed November 16, 2022.
5. 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 November 16, 2022.
6. 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 November 16, 2022.
7. 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/. Accessed November 16, 2022.
8. 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: Available at: https://store.samhsa.gov/product/TIP-45-Detoxification-and-Substance-Abuse-Treatment/SMA15-4131. Accessed November 16, 2022.
9. Kampman K and Jarvis M. American society of addiction medicine (ASAM): national practice guideline for the use of medications in the treatment of addiction involving opioid use. *J Addict Med.* 2015 Oct; 9(5):358-367. Available at: hhttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC4605275/. Accessed November 16, 2022.

10. Cunningham C, Edlund MJ, Gordon AJ et al. The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update. Available from: https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline. Accessed November 16, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: no significant change from previously approved policy; references reviewed and updated.	10.23.18	02.19
1Q 2020 annual review: no significant changes; RT4: added new dosage form Cassipa to the policy; references reviewed and updated.	11.26.19	02.20
Revised product preferencing language to reflect current formulary status of the various buprenorphine/naloxone products.	02.26.20	
1Q 2021 annual review: no significant changes; policies combined for Medicaid and HIM lines of business; commercial: updated redirection to generic SL tablets only (and not to generic SL film, which requires PA); HIM: added NF Zubsolv and generalized the existing redirection to Suboxone SL tabs to apply to all agents on the policy; retired HIM.PA.35; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	12.02.20	02.21
Per March SDC modified redirection to also allow use of generic buprenorphine/naloxone sublingual film; modified redirection language from 'documentation supports inability to use' to 'member must use'; added Commercial line of business (CP.CPA.299 to retire).	03.09.21	05.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.23.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.16.22	02.23

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 practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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