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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	September 12, 2014
Subject:	Suboxone Drug Class	**Page:**	1 of 10

Last Review Date: December 8, 2023

Suboxone Drug Class

Description

Bunavail, Cassipa*, Suboxone, Zubsolv (buprenorphine with naloxone sublingual tablets and film), Buprenorphine sublingual tablets, Probuphine (buprenorphine), Brixadi*, Sublocade (buprenorphine extended-release injection)

*This medication is included in this policy but is not available in the market as of yet

Background
Brixadi, Bunavail, Cassipa, Probuphine, Sublocade injection, Suboxone, Zubsolv, and buprenorphine sublingual tablets are Schedule III narcotics with a single indication, the maintenance treatment of opioid dependence. Buprenorphine is a partial pain receptor agonist at mu-opioid receptors unlike typical opioids of dependence, which are full agonists. Naloxone is an opioid receptor antagonist. The use of buprenorphine with or without naloxone should also be part of a comprehensive plan which includes counseling and psychosocial support. They should not be used for analgesia or in opioid naïve patients (1-8).

Regulatory Status
FDA-approved indication: Buprenorphine and buprenorphine with naloxone is indicated for maintenance treatment of opioid dependence. (1-8).

The recommended target dose of buprenorphine is 16 mg per day. Doses may range from 16 mg to 24 mg per day (3). The difference in bioavailability between Bunavail and Zubsolv compared to Suboxone sublingual tablet requires a different dosage strength to be administered to the patient. A Bunavail 4.2/0.7 mg buccal film or a Zubsolv 5.7/1.4 mg sublingual tablet provides equivalent buprenorphine exposure to a Suboxone 8/2 mg sublingual tablet. The recommended target dosage of Bunavail buccal film is 8.4/1.4 mg per day as a single daily dose. The maintenance dose of Bunavail buccal film is generally in the range of 2.1/0.3 mg buprenorphine/naloxone to 12.6/2.1 mg buprenorphine/naloxone per day depending on the individual patient. The maintenance dose of Zubsolv sublingual tablet is generally in the range of 2.8 mg/0.72 mg buprenorphine/naloxone to 17.2 mg/4.2 mg buprenorphine/naloxone per day depending on the individual patient. Due to these variations in bioavailability, the products are managed by package insert recommended quantity limit rather than MME (morphine milligram equivalence). Dosages higher than those described have not been demonstrated to provide any clinical advantage (1-4).

Cassipa should only be used after induction and stabilization of the patient, and when the patient has been titrated to a dose of 16 mg buprenorphine using another marketed product (7).

Probuphine is indicated for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine containing product (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent). Probuphine is not appropriate for new entrants to treatment and patients who have not achieved and sustained prolonged clinical stability, while being maintained on buprenorphine 8 mg per day or less of a Subutex or Suboxone sublingual tablet or generic equivalent. Probuphine implants should be used only in patients who are opioid tolerant (5).

Brixadi is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with buprenorphine (8).

Sublocade is indicated for the maintenance treatment of opioid dependence in patients who have initiated treatment with a transmucosal buprenorphine-containing product. Patients may only be transitioned to Sublocade after a minimum of 7 days of therapy (6).

Probuphine carries a boxed warning of the risks associated with insertion and removal, Probuphine is available only through a restricted program called the Probuphine REMS Program. All Healthcare Providers must successfully complete a live training program on the

insertion and removal procedures and become certified, prior to performing insertions or prescribing Probuphine implants (5).

Brixadi and Sublocade carry a boxed warning of serious harm or death that could result if administered intravenously. Both medications are available only through a restricted program called the Brixadi REMS Program and the Sublocade REMS Program. Healthcare settings and pharmacies that order and dispense Brixadi and Sublocade must be certified in this program and comply with the REMS requirements. Brixadi (weekly) should be administered in 7-day intervals while Brixadi (monthly) should be administered in 28-day intervals. Administer Sublocade monthly with a minimum of 26 days between doses (6, 8).

Warnings and precautions for buprenorphine include (1-8):

- Respiratory depression is the chief hazard of opioid agonists, including morphine sulfate, which if not immediately recognized and treated, may lead to respiratory arrest and death. Risk is increased in patients receiving concurrent benzodiazepines or other CNS depressants (including alcohol), patients with chronic obstructive pulmonary disease, orthostatic hypotension, increased intracranial pressure, biliary tract diseases, and seizure disorders. To reduce the risk of respiratory depression, proper dosing, titration, and monitoring are essential.

- All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

- Prolonged use of opioid agonists during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening.

- Patients should not consume alcohol or any products containing alcohol while taking.

Probuphine dosing consists of four implants inserted subdermally in the inner side of the upper arm. The implants are intended to be in place for 6 months of treatment. New implants may be inserted in the other arm that has not been previously used at the time of removal, if continued treatment is desired. If new implants are not inserted on the same day as the removal of implants, maintain patients on their previous dosage of transmucosal buprenorphine (i.e., the dose from which they were transferred to Probuphine treatment) prior to additional Probuphine treatment. After one insertion of Probuphine in each arm, most patients should be transitioned back to a transmucosal buprenorphine-containing product for continued treatment. There is no experience with inserting additional implants into other sites in the arm to recommend an

approach to a second insertion into a previously-used arm. Neither re-insertion into previously-used administration sites, nor into sites other than the upper arm, has been studied (5).

Buprenorphine has the potential for misuse, abuse, and diversion. Patient use should be monitored as part of a counseling and psychosocial support during treatment and precautions taken against potential abuse. As with other opioids, physical dependence, respiratory depression, and overdose may also occur; hence monitoring and frequent patient evaluation should be used as part of an overall treatment plan (1-8).

The FDA has determined that a REMS is necessary for all opioid analgesics intended for outpatient use to ensure that the benefits of these drugs continue to outweigh the risks. The Opioid Analgesic REMS is a strategy to reduce the risk of abuse, misuse, addiction, overdose, and deaths due to prescription opioid analgesics (9).

Safety and effectiveness in patients under the age 18 has not been established (1-8).

Related policies
Methadone

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Brixadi, Bunavail, Cassipa, Probuphine, Sublocade injection, Suboxone, Zubsolv, and buprenorphine sublingual tablets may be considered **medically necessary** if the conditions indicated below are met.

Brixadi, Bunavail, Cassipa, Probuphine, Sublocade injection, Suboxone, Zubsolv, and buprenorphine sublingual tablets are considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Opioid dependence

. **AND ALL** of the following:

1. Patient will **NOT** be receiving other opioids
    a. Patients currently on opioid therapy must be tapered off within 30 days
2. Patient will receive counseling and psychosocial support
3. Patient will be monitored during therapy for signs and symptoms of abuse / misuse as well as compliance and the potential diversion to others
4. Patient is **NOT** taking **exclusively** for pain control
5. **Cassipa only:** patient has been titrated to a dose of 16 mg buprenorphine using another marketed product
6. **Probuphine only:** patient has achieved and sustained prolonged clinical stability on a transmucosal buprenorphine product
    a. Patient is **NOT** on more than 8mg per day
    b. Patient will be monitored for implant migration, expulsion and nerve damage
    c. Prescriber must be certified in the Probuphine REMS program
7. **Brixadi only:** patient was initially treated with a single dose of a transmucosal buprenorphine product **OR** is already being treated with buprenorphine
8. **Sublocade only:** patient has achieved clinical stability on a buprenorphine product
    a. Patient must have had a minimum of 7 days prior treatment with a transmucosal buprenorphine-containing product

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Maintenance treatment of opioid dependence

AND ALL of the following:

1. Patient has shown no signs of opioid dependence-relapse

2. Patient will **NOT** be receiving other opioids during therapy
    a. If patient was approved previously with a taper of opioid therapy, confirmation that taper is complete and **NO** longer on opioid therapy
3. Monitoring of therapy and support will be continued
4. Patient is **NOT** taking **exclusively** for pain control

Policy Guidelines

Pre - PA Allowance

Age 18 years of age or older

Quantity

Medication	Strength	Quantity Limit per 90 days
Suboxone	2mg /0.5mg, 4mg /1mg	360 units per 90 days
Zubsolv	0.7mg /0.18mg, 1.4mg /0.36mg, 2.9mg /0.71mg	
Bunavail film	2.1mg /0.3mg	
Buprenorphine SL tablet	2mg	
Suboxone	8mg /2mg	270 units per 90 days
Zubsolv	5.7mg /1.4mg	
Bunavail film	4.2mg /0.7mg	
Buprenorphine SL tablet	8mg	
Suboxone	12mg /3mg	180 units per 90 days
Zubsolv	8.6mg /2.1mg	
Bunavail film	6.3mg /1mg	
Zubsolv	11.4mg/2.9mg	90 units per 90 days

***Utilizing the highest strengths available to achieve the dosage is recommended to minimize dosing errors and improve compliance

Prior - Approval Limits

Quantity

Strength	Quantity Limit per 90 days
2mg /0.5mg	360 dosage units per 90 days **OR**
4mg /1mg	360 dosage units per 90 days **OR**

8mg /2mg	270 dosage units per 90 days **OR**
12mg /3mg	180 dosage units per 90 days **OR**

Suboxone

Combination of strengths not to exceed: 24/6mg / day

Zubsolv tablet

Strength	Quantity Limit per 90 days
0.7mg /0.18mg	360 dosage units per 90 days **OR**
1.4mg /0.36mg	360 dosage units per 90 days **OR**
2.9mg /0.71mg	360 dosage units per 90 days **OR**
5.7mg /1.4mg	270 dosage units per 90 days **OR**
8.6mg /2.1mg	180 dosage units per 90 days **OR**
11.4mg /2.9mg	90 dosage units per 90 days **OR**

Combination of strengths not to exceed: 17.2mg/4.2mg / day

Bunavail film

Strength	Quantity Limit per 90 days
2.1mg /0.3mg	360 dosage units per 90 days **OR**
4.2mg /0.7mg	270 dosage units per 90 days **OR**
6.3mg /1mg	180 dosage units per 90 days **OR**

Combination of strengths not to exceed: 12.6/2mg /day

Buprenorphine SL tablet

Strength	Quantity Limit per 90 days
2mg	360 dosage units per 90 days **OR**
8mg	270 dosage units per 90 days **OR**

Combination of strengths not to exceed: 24mg/ day

Cassipa film

Strength	Quantity Limit per 90 days
16mg /4mg	90 dosage units per 90 days

Duration	**NO** Concurrent Opioid Therapy	12 months
	Concurrent Opioid Therapy	1 month

Probuphine implants

Strength	Quantity Limit per 180 days

74.2mg	4 implants per 180 days **OR**

Brixadi injection

Strength	Quantity Limit per 84 days
(Weekly) 8mg, 16mg, 24mg, 32mg	12 syringes per 84 days **OR**
(Monthly) 64mg, 96mg, 128mg	3 syringes per 84 days

Sublocade injection

Strength	Quantity Limit per 90 days
100mg	9 syringes per 90 days **OR**
300mg	3 syringes per 90 days

Duration 6 months

Prior – Approval *Renewal* Limits

Same as above

Exception
Quantity

Probuphine implants – one time renewal

Strength	Quantity Limit per 180 days
74.2mg	4 implants per 180 days – must be inserted into other arm

Rationale

Summary

Brixadi, Bunavail, Cassipa, Probuphine, Sublocade injection, Suboxone, Zubsolv, and buprenorphine sublingual tablets are Schedule III narcotics with a single indication, the maintenance treatment of opioid dependence. As of 2023, the requirement for a DATA waiver to prescribe these medications has been removed, and now all DEA registrants must be meet other training or certification requirements. Buprenorphine preparations have the potential for misuse, abuse, and diversion. Patient use should be monitored as part of counseling and psychosocial support during treatment and precautions taken against potential abuse. As with other opioids, physical dependence, respiratory depression, and overdose may also occur; hence monitoring and frequent patient evaluation should be used as part of an overall treatment

plan. Safety and effectiveness in pediatric patients under the age of 18 has not been established (1-8).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Brixadi, Bunavail, Cassipa, Probuphine, Sublocade injection, Suboxone, Zubsolv, and buprenorphine sublingual tablets while maintaining optimal therapeutic outcomes.

References

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4. Bunavail buccal film [package insert]. Raleigh, NC: BioDelivery Sciences International Inc.; October 2019.
5. Probuphine [package insert]. Princeton, NJ: Braeburn Pharmaceuticals, Inc.; October 2019.
6. Sublocade [package insert]. North Chesterfield, VA: Indivior Inc.; June 2022.
7. Cassipa [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2018.
8. Brixadi [package insert]. Cockeysville, MD. Pharmaceutics International, inc.; May 2023.
9. Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). Drug Safety and Availability: U.S. Food & Drug Administration. September 19, 2018.

Policy History

Date	Action
September 2014	New addition to PA
February 2015	Addition of Zubsolv 8.6mg /2.1mg and patient is not taking exclusively for pain control
June 2015	Annual editorial review and reference update. Addition of Zubsolv 11.4mg/ 2.9mg
September	Addition of Zubsolv 2.9mg / 0.71mg
March 2016	Annual editorial review and reference update Policy code changed from 5.02.32 to 5.70.32
June 2016	Addition of Probuphine to PA Removal of Bunavail from standard allowance

September 2016	Annual review Addition of patient will **NOT** be receiving other opioids if patients currently on opioid therapy must be tapered off within 30 days and the confirmation on renewal of no opioid therapy. Also, the addition of 1 month duration for patients on opioid therapy.
January 2017	Addition of Zubsolv 0.7mg / 0.18mg Addition of the age requirement in renewal section
March 2017	Annual review
June 2017	Removal of Bunavail requirement of the patient has to be currently on sublingual tablet and is changing therapy Addition of Bunavail to the Standard Allowance Increase in all of the Standard Allowances to max dosing limits
September 2017	Annual review
December 2017	Addition of Sublocade
March 2018	Annual editorial review and reference update
September 2018	Removal of Sublocade REMS requirement Addition of Cassipa
November 2018	Annual review and reference update
March 2019	Annual review
March 2020	Annual review and reference update
March 2021	Annual review and reference update
September 2022	Annual review and reference update
February 2023	Per FEP, removed requirement that prescriber be qualified by HHS (Health and Human Services) and registered with SAMHSA (Substance Abuse and Mental Health Services Administration) before prescribing for MAT
June 2023	Annual review
July 2023	Addition of Brixadi; Per FEP updated Regulatory section to explain use of quantity limits rather than MME for Mental Health Parity Act compliance
September 2023	Annual review
December 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.