BlueCross BlueShield
Federal Employee Program

SUBOXONE DRUG CLASS

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

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

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Brixadi, Bunavail, Cassipa, 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 (1-7).

Regulatory Status

FDA-approved indication: Buprenorphine and buprenorphine with naloxone is indicated for maintenance treatment of opioid dependence. (1-7).

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).

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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 (6).

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 (7).

Sublocade is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of transmucosal buprenorphine product or who are already being treated with buprenorphine (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 (5, 7).

Warnings and precautions for buprenorphine include (1-7):

- 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.

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- 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.

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 (1-7).

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 (8).

Safety and effectiveness in patients under the age 18 has not been established (1-7).

Summary

Brixadi, Bunavail, Cassipa, 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

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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 (1-7).

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

References

1. Suboxone sublingual film [package insert]. Richmond, VA: Indivior Inc.; December 2023.
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3. Buprenorphine HCL sublingual tablet [package insert]. Columbus, OH, West-Ward Pharmaceuticals Corp.; November 2019.
4. Bunavail buccal film [package insert]. Raleigh, NC: BioDelivery Sciences International Inc.; June 2022.
5. Sublocade [package insert]. North Chesterfield, VA: Indivior Inc.; February 2025.
6. Cassipa [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2023.
7. Brixadi [package insert]. Cockeysville, MD. Pharmaceutics International, inc.; December 2023.
8. Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). Drug Safety and Availability: U.S. Food & Drug Administration. September 19, 2018.