BELBUCA™ (buprenorphine) buccal film

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Belbuca (buprenorphine) buccal film is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. They should be reserved for use in patients for whom alternative treatment options (such as, non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Belbuca (buprenorphine) buccal film is not indicated as an as-needed (prn) analgesic.

There are many other long-acting generically available opioid analgesics, including Morphine ER, Hydromorphone ER, Oxycodeone ER, Oxymorphone ER, Methadone, and Fentanyl transdermal patches.

All opioids are similarly effective for pain relief as determined by years of clinical experience, systematic reviews, and clinical practice guidelines. There is no evidence that supports superiority of one product (brand or generic) over another product (brand or generic). There is also no evidence to support superiority of a long acting opioid agent over a short acting opioid agent. There is no evidence in efficacy between scheduled dosing of a sustained
BELBUCA™ (buprenorphine) buccal film (cont.)

release opioid over as needed dosing of an immediate release opioid. There is no reliable evidence that any one opioid is safer than another, including abuse-deterrent formulations, long-acting opioids compared to short-acting opioids, Schedule 3 Controlled Substances (Belbuca) compared to Schedule 2 Controlled Substances (Fentanyl, Morphine, others), or use of partial-versus pure opioid agonists. Clinical guidelines recognize the use of long-acting opioids for management of chronic pain in specific circumstances but do not recommend one medication or dosage form.

Evidence on long-term opioid therapy for chronic pain is very limited but suggests an increased risk of serious harms that are dose-dependent. Long-term opioids for chronic pain are associated with increased risk of abuse, overdose, fracture, and myocardial infarction versus not currently being prescribed opioids. All long-acting opioid analgesics have a boxed warning for addiction, abuse, misuse, life-threatening respiratory depression, accidental exposure, and neonatal opioid withdrawal syndrome.

Belbuca is a buccal dissolving film tablet that provides transmucosal delivery of buprenorphine.

**Definitions:**

**Opioid Risk Assessment Tool:**

<table>
<thead>
<tr>
<th>Score each that applies</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family history of substance abuse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Rx drugs</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td><strong>Personal history of substance abuse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Rx drugs</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Age between 16-45 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of preadolescent sexual abuse</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>Psychological disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADD, OCD, Bipolar, Schizophrenia</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Assessment of risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk for abuse</td>
<td>≤ 3</td>
<td></td>
</tr>
<tr>
<td>Moderate risk for abuse</td>
<td>4-7</td>
<td></td>
</tr>
<tr>
<td>High risk for abuse</td>
<td>≥ 8</td>
<td></td>
</tr>
<tr>
<td><strong>Definitions of risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low = unlikely to abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate = as likely will as will not abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High = likely to abuse</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
BELBUCA™ (buprenorphine) buccal film (cont.)

Drug related events:

**Ineffective / failure**
Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

**Adverse Drug Event:** Allergic reaction / Hypersensitivity / Intolerance
Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

**Allergic reaction / hypersensitivity** – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

**Intolerance** – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

**Contraindication**
Use of a drug that is not recommended by the manufacturer or FDA labelling

Use of any drug in the face of a contraindication is outside of the FDA and manufacturer's labelled recommendation and is considered investigational or experimental

**Non-adherence**
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record
BELBUCA™ (buprenorphine) buccal film (cont.)

Precertification:

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states’ Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Criteria:

See “Resources” section for FDA-approved dosage.

- Precertification for Belbuca (buprenorphine) buccal film requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms will be returned.

- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Belbuca (buprenorphine) is considered medically necessary when ALL of the following criteria are met:
  1. Individual is 18 years of age or older
  2. Individual has medical record documentation of a confirmed diagnosis of pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate
  3. Used in conjunction with a comprehensive pain management regimen that includes (where clinically appropriate):
     - Acetaminophen (APAP)
     - Non-steroidal anti-inflammatory drug (NSAID)
     - Gastrointestinal ulcer protection
     - Adjuvant pain medication:
       - Muscle relaxant
       - Antidepressant
       - Antiepileptic
  4. Individual’s opioid abuse potential, based on the Opioid Risk Assessment Tool (see Definitions section) is ONE of the following:
BELBUCA™ (buprenorphine) buccal film (cont.)

- Low risk for opioid abuse AND the individual has failed, or experienced a significant adverse drug event from, or has a contraindication to Butrans (buprenorphine) transdermal system AND 3 of the following:
  - Morphine sustained release (brand or generic)
  - Avinza ER capsules
  - Kadian ER capsules
  - Nucynta ER tablets
  - Oxycontin tablets
  - Fentanyl transdermal
- Moderate risk for opioid abuse AND individual is on a Controlled Substance 2 opioid that will be discontinued AND individual has failed, or experienced a significant adverse drug event from, or has a contraindication to Butrans (buprenorphine) transdermal system AND there will be transition to Belbuca
- High risk for opioid abuse AND there is concern for opioid abuse or diversion from use of opioids in Controlled Substance 2 category AND the individual has failed, or experienced a significant adverse drug event from, or has a contraindication to Butrans (buprenorphine) transdermal system

5. Absence of ALL of the following contraindications:
   - Significant respiratory depression
   - Acute or severe bronchial asthma
   - Known or suspected gastrointestinal obstruction, including paralytic ileus
   - Hypersensitivity to buprenorphine or any components of the formulation

6. Absence of ALL of the following exclusions:
   - Individuals with Long QT Syndrome
   - Family history of Long QT Syndrome
   - Simultaneous use with Class IA antiarrhythmic medications
   - Simultaneous use with Class III antiarrhythmic medications
   - Simultaneous use with other medications that prolong the QT interval
   - Individuals with circulatory shock
   - Individuals with impaired consciousness or coma
   - Simultaneous use of mixed agonist/antagonist and partial agonist opioid analgesics (Butorphanol, Nalbuphene, Pentazocine)
   - Simultaneous use with a pure opioid agonist
   - Woman of child bearing age who is pregnant
   - Woman breastfeeding an infant or child

- Belbuca (buprenorphine) for all other indications not previously listed is considered experimental or investigational based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

This includes but is not limited to the following:

- Opiate addiction syndrome
- Management of acute pain or in patients who require opioid analgesia for a short period of time
- Management of post-operative pain, including use after outpatient or day surgeries
- Management of mild pain
- Management of intermittent pain (such as use on an as-needed (prn) basis)

Resources:


BELBUCA™ (buprenorphine) buccal film (cont.)

FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
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<tbody>
<tr>
<td>BELBUCA buccal film contains buprenorphine, a partial opioid agonist. Belbuca is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate.</td>
<td>• To be prescribed only by health care providers knowledgeable in use of potent opioids for management of chronic pain.</td>
</tr>
<tr>
<td>Limitations of Use:</td>
<td>• For opioid-naïve patients, initiate therapy with 75 mcg Belbuca once daily or every 12 hours, as tolerated, for at least 4 days before increasing dose to 150 mcg every 12 hours.</td>
</tr>
<tr>
<td>• Because of the risk of addiction, abuse, and misuse with opioids, even at the recommended doses, and because of the greater risks of overdose and death with long-acting opioid formulations, reserve Belbuca for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.</td>
<td>• Conversion from other opioids to Belbuca: taper current daily opioid dose to 30 mg oral morphine sulfate equivalents (MSE) or less prior to initiating therapy with Belbuca.</td>
</tr>
<tr>
<td>• Belbuca is not indicated as an as-needed (prn) analgesic.</td>
<td>• For patients taking less than 30 mg oral MSE, initiate therapy with 75 mcg once daily or every 12 hours</td>
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<td></td>
<td>• For patients taking between 30 mg and 89 mg oral MSE, initiate therapy with 150 mcg Belbuca every 12 hours following analgesic taper.</td>
</tr>
<tr>
<td></td>
<td>• For patients taking between 90 mg and 160 mg oral MSE, initiate therapy with 300 mcg Belbuca every 12 hours following analgesic taper.</td>
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<td></td>
<td>• For patients taking greater than 160 mg oral MSE, consider alternate analgesic.</td>
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<tr>
<td></td>
<td>• Belbuca doses of 600 mcg, 750 mcg, and 900 mcg are only for use following titration from lower doses of Belbuca.</td>
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<td></td>
<td>• Do not abruptly discontinue Belbuca in a physically dependent patient.</td>
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<td></td>
<td>• For patients with severe hepatic impairment: Reduce the starting and incremental dose by half that of patients with normal liver function.</td>
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<tr>
<td></td>
<td>• For patients with oral mucositis: Reduce the starting and incremental dose by half that of patients without mucositis.</td>
</tr>
</tbody>
</table>