Fentanyl Oral Transmucosal and Nasal Opioid Analgesics

Policy # 00213
Original Effective Date: 12/20/2006
Current Effective Date: 07/10/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider brand and generic fentanyl oral or nasal opioid analgesics for the treatment of breakthrough cancer pain in patients with malignancies already receiving opioid therapy to be **eligible for coverage**.**

Patient Selection Criteria

The use of brand and generic fentanyl oral or nasal opioid analgesics will be considered for coverage eligibility when the following criteria are met:

- Patients with malignancies experiencing breakthrough cancer pain who are already receiving opioid therapy; AND
- Patient must be opioid tolerant; AND
- Requested drug is oral transmucosal fentanyl citrate (e.g., Actiq®, generic)‡:
  - Patient must be 16 years of age or older; AND
  - If the request is for the brand product: Patient has tried and failed (e.g., intolerance or inadequate response) generic oral transmucosal fentanyl citrate unless there is clinical evidence or patient history that suggests the use of the generic equivalent will be ineffective or cause an adverse reaction to the patient; OR
    *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested drug is a fentanyl citrate buccal film or tablet (Onsolis®, Fentora®)‡ , sublingual product (Abstral®, Subsys®)‡, or nasal spray (Lazanda®)‡:
  - Patient must be 18 years of age or older.

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of brand Actiq when the member has NOT tried and failed the generic equivalent oral transmucosal fentanyl citrate to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of brand and generic fentanyl oral or nasal opioid analgesics when patient selection criteria are not met (with the exception of the criterion denoted as **not medically necessary****) to be **investigational.***

Background/Overview

Breakthrough pain characteristically has a rapid onset with moderate to severe intensity but brief duration. Pain of such intense severity but short duration is difficult to treat because currently available oral agents administered at the onset of a breakthrough pain episode may require 30-45 minutes to be absorbed and produce an analgesic effect.

Patients considered opioid tolerant are those who are taking at least 60mg of oral morphine per day, or at least 25 mcg of transdermal fentanyl/hour, or at least 30 mg of oxycodone daily, or at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.

Actiq delivers pain relief via a single–use medicated lozenge that is attached to a handle. It dissolves as the patient moves the unit along the inside of the cheek.

Fentanyl buccal tablet (Fentora) is a sugar-free tablet that is placed along the inside of the cheek. These medications utilize the oral transmucosal system to treat breakthrough cancer pain.

Onsolis (fentanyl buccal soluble film) is an oral transmucosal form of the potent opioid analgesic, fentanyl citrate, intended for application to the buccal mucosa. Onsolis uses the BioErodible MucoAdhesive (BEMA™)‡ bilayer delivery technology which is comprised of water-soluble

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polymeric films. Onsolis consists of a pink bioadhesive layer bonded onto a white inactive layer. The active ingredient, fentanyl citrate, is incorporated into the bioadhesive layer, which adheres to the moist buccal mucosa. The amount of fentanyl delivered transmucosally is proportional to the film surface area. It is believed that the inactive layer isolates the bioadhesive layer from the saliva, which may optimize delivery of fentanyl across the buccal mucosa.

Subsys (fentanyl sublingual spray) is a potent opioid analgesic intended for sublingual mucosal administration. Subsys is formulated to be sprayed underneath the tongue to allow for absorption of fentanyl across the sublingual mucosa.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

The FDA approves Actiq, Fentora, Onsolis, Lazanda, Abstral and Subsys for the management of breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to opioid therapy. Because fentanyl is a schedule II narcotic, the FDA recommends that the product be packaged and marketed to minimize the opportunity for diversion, abuse or access to children.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The goals of cancer pain therapy are to find the right dose of around-the-clock medications to control persistent pain and the right dose of supplemental medication to relieve breakthrough pain. Treatment of breakthrough pain requires an effective analgesic that has a rapid onset of analgesia, a short duration of effect and a route of administration that is appropriate for the patient's condition.

Fentanyl is a pure opioid agonist whose principal therapeutic action is analgesia. The pharmacological effects of opioid agonists include anxiolysis, euphoria, feelings of relaxation, respiratory depression, constipation, miosis, cough suppression and analgesia.

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Actiq, Fentora and Onsolis are intended to be used in the care of cancer patients and only by oncologists and pain specialists who are knowledgeable of and skilled in the use of schedule II opioids to treat cancer pain.

The absorption of the transmucosal dosage form is a combination of an initial rapid absorption from the buccal mucosa and a more prolonged absorption of swallowed fentanyl from the gastrointestinal tract. Approximately 25% of the total dose of transmucosal fentanyl is rapidly absorbed from the buccal mucosa and becomes systemically available. The remaining 75% of the total dose is swallowed with the saliva and then is slowly absorbed from the gastrointestinal tract.

Studies on the relationship of age to the effects of transmucosal fentanyl have not been performed in the pediatric population. Transmucosal fentanyl contains a medicine in an amount that can be fatal to children. No difference was noted in the safety profile of the patients group over 65 years of age as compared to younger patients in clinical trials. The older population did titrate to a slightly lower dose.

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Policy History

Original Effective Date: 12/20/2006
Current Effective Date: 07/10/2023

12/13/2006	Medical Director review
12/20/2006	Medical Policy Committee approval
12/12/2007	Medical Director review
12/19/2007	Medical Policy Committee approval. No change to coverage eligibility.
12/03/2008	Medical Director review
12/17/2008	Medical Policy Committee approval. Added note to coverage section from FDA regarding age restrictions for use of Actiq and Fentora.

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11/12/2009	Medical Director review
11/18/2009	Medical Policy Committee approval. No change to coverage eligibility. Onsolis added to policy.
11/04/2010	Medical Policy Committee review
11/16/2010	Medical Policy Implementation Committee approval. No change to coverage eligibility.
03/01/2011	Added a note for the use of Abstral in the coverage section.
11/03/2011	Medical Policy Committee review
11/16/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/02/2012	Medical Policy Committee review
02/15/2012	Medical Policy Implementation Committee approval. New nasal spray added to policy.
06/14/2012	Medical Policy Committee review
06/20/2012	Medical Policy Implementation Committee approval. Added the drug Subsys for use with age restrictions to the *Note* following the criteria in the coverage section.
03/04/2013	Coding update
06/06/2013	Medical Policy Committee review
06/25/2013	Medical Policy Implementation Committee approval. No change to coverage.
06/05/2014	Medical Policy Committee review
06/18/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/04/2015	Medical Policy Committee review
06/17/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/02/2016	Medical Policy Committee review
06/20/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/01/2017	Medical Policy Committee review
06/21/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/07/2018	Medical Policy Committee review
06/20/2018	Medical Policy Implementation Committee approval. New policy, Coverage changes, or Coverage eligibility unchanged.

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06/06/2019	Medical Policy Committee review
06/19/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. Added generic Actiq to the policy reflecting use of the generic product first. Clarified that this policy includes generic products as well, where available.
06/03/2021	Medical Policy Committee review
06/09/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/02/2022	Medical Policy Committee review
06/08/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/01/2023	Medical Policy Committee review
06/14/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 06/2024

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or

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3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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