MEDICAL MUTUAL®

Drug Policy

Policy:	Transmucosal Fentanyl Products Actiq (oral transmucosal fentanyl citrate) Fentora (fentanyl buccal tablet) Generic fentanyl buccal tablet Generic oral transmucosal fentanyl citrate Lazanda (fentanyl nasal spray) Subsys (fentanyl sublingual spray)	Annual Review Date: 07/20/2023 Last Revised Date: 07/20/2023

OVERVIEW

Actiq (generics), Fentora, and Subsys are immediate-release oral transmucosal formulations of fentanyl citrate. Lazanda is a nasal spray intended for intranasal transmucosal administration. The transmucosal fentanyl products are indicated only for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Patients considered opioid tolerant are those who are taking at least 60 mg of oral morphine daily, at least 25 mcg of transdermal fentanyl/hour, at least 30 mg of oxycodone daily, at least 8 mg oral hydromorphone daily, at least 25 mg oral oxymorphone daily, or an equianalgesic dose of another opioid for a week or longer. The appropriate dosing and safety of Actiq (generics) in opioid tolerant children with breakthrough cancer pain have not been established in those below 16 years of age. The safety and efficacy of Fentora, Subsys, and Lazanda have not been established in pediatric patients below 18 years of age.

Because of the risk for misuse, abuse, addiction, and overdose, the transmucosal fentanyl products are available only through a restricted program required by the Food and Drug Administration, called a Risk Evaluation and Mitigation Strategy (REMS). Under the Transmucosal Immediate-Release Fentanyl (TIRF) REMS Access program, outpatients, healthcare professionals who prescribe to outpatients, pharmacies, and distributors must enroll in the program.

POLICY STATEMENT

This policy involves the use of transmucosal fentanyl products. Prior authorization is recommended for pharmacy benefit coverage of transmucosal fentanyl products. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with transmucosal fentanyl products as well as the monitoring required for adverse events and long-term efficacy, initial approval requires transmucosal fentanyl products be prescribed by or in consultation with a physician who specializes in the condition being treated. All

approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of transmucosal fentanyl products is recommended in those who meet the following criteria:

1. **Breakthrough Pain in Patients with Cancer**
   Criteria. *Patient must meet the following criteria*
   - **A.** The patient meets ONE of the following:
     - **a.** The patient is unable to swallow, has dysphagia, esophagitis, mucositis, or uncontrollable nausea/vomiting; OR
     - **b.** The patient is unable to take two other short-acting narcotics (for example: immediate-release formulations of oxycodone, morphine sulfate, hydromorphone, etc.) secondary to allergy or severe adverse events; AND
   - **B.** The prescriber verifies no concurrent substance abuse treatments are being prescribed (examples include but are not limited to: Suboxone, Vivitrol, oral naloxone, buprenorphine); AND
   - **C.** The patient will be using or continuing use of an oral or transdermal long-acting narcotic (for example: Duragesic, OxyContin, morphine extended-release) or the patient is on intravenous, subcutaneous, or spinal (intrathecal, epidural) narcotics (for example: morphine sulfate, hydromorphone, fentanyl citrate) for around-the-clock pain coverage; AND
   - **D.** The patient is not opioid naïve (is opioid-tolerant, taking an opioid for one week or longer); AND
   - **E.** The requested product is prescribed by or in consultation with an oncologist or pain management specialist; AND
   - **F.** For Actiq and generic fentanyl citrate, the patient must be at least 16 years of age OR for all other transmucosal fentanyl products, the patient must be at least 18 years of age

Initial Approval/ Extended Approval.
A) *Initial Approval:* 3 months
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL
transmucosal fentanyl products has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Acute and/or Postoperative Pain** including surgery/post-surgery, trauma/post-trauma, acute medical illness (acute abdominal pain, pelvic pain, muscle spasm): Actiq (generics), Abstral, Fentora, Lazanda, and Subsys are contraindicated for use in the management of acute or postoperative pain. A case series reported the efficacious outpatient use (75% reduction in pain intensity at 2 hours; n = 18) of Actiq for the management of treating an acute, refractory migraine headache in 20 patients. Actiq was used as a rescue medication for management of a moderate to severe migraine after ineffective treatment with the patients' usual antimigraine therapy. All of these patients were

managed by a headache clinic and had undergone a full evaluation of their medical history, vital signs, and physical and neurological examinations. In addition, all 20 patients had been previously treated with multiple other therapies (e.g., 5-hydroxytryptamine [5-HT]$_1$ receptor agonists, ergots, antiemetics, prescription and over-the-counter analgesics, and anti-inflammatory drugs) and all had previously received outpatient opioid therapies in an attempt to manage their migraine pain. All patients were also known responders to use of parenteral opioid therapy. Side effects reported included nausea (n = 3), vomiting (n = 1), somnolence (n = 2), itching (n = 1), and dry mouth (n = 1). Controlled research is needed to fully determine the role of Actiq for the management of acute, refractory migraine.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Actiq® oral transmucosal [prescribing information]. Parsippany, NJ: Teva; March 2021.
2. Fentora® buccal tablet [prescribing information]. Parsippany, NJ: Teva; March 2021.
3. Subsys® sublingual spray [prescribing information]. Northbrook, IL: West Therapeutic Development; March 2021.
4. Lazanda® nasal spray [prescribing information]. Northbrook, IL: West Therapeutic Development; March 2021.
5. Shaiova L, Lapin J, Manco LS, et al. Tolerability and effects of two formulations of oral transmucosal fentanyl citrate (OTFC; ACTIQ) in patients with radiation-induced oral mucositis. *Support Care Cancer*. 2004;12:268-273.
6. U.S. Food and Drug Administration. (2014, December) Transmucosal immediate release fentanyl (TIRF) risk evaluation and mitigation strategy (REMS). Retrieved from: http://www.fda.gov/downloads/Drugs/DrugSafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm289730.pdf.
7. Fentanyl citrate. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 5 July 2022. Accessed on 19 July 2022.
8. Oral Transmucosal Fentanyl Citrate (OTFC) [prescribing information]. Parsippany, NJ: Teva; March 2021.
9. Fentanyl citrate. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 18 July 2023. Accessed on 20 July 2023.