VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Opioids – Fentanyl Transmucosal Drugs

- Abstral® (fentanyl sublingual tablet – Novartis/ProStrakan)
- Actiq® (oral transmucosal fentanyl citrate – Cephalon, generics)
- Fentora® (fentanyl buccal tablet – Cephalon, authorized generic)
- Lazanda® (fentanyl nasal spray – Depomed)
- Subsys® (fentanyl sublingual spray – Insys)

TAC APPROVAL DATE: 10/3/2018

OVERVIEW

Actiq (generics), Abstral, Fentora, and Subsys are immediate-release oral transmucosal formulations of fentanyl citrate.[1-5] Lazanda is a nasal spray intended for intranasal transmucosal administration.[6] 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.[1-6] 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.[1,3] The safety and efficacy of Abstral, Fentora, Subsys, and Lazanda have not been established in pediatric patients below 18 years of age.[2,4-6]

The transmucosal fentanyl products are contraindicated in the management of acute or postoperative pain and in patients with known intolerance or hypersensitivity to any of its components or the drug fentanyl.[1-6] In addition, these products must not be used in opioid non-tolerant patients (contraindicated). The transmucosal fentanyl products are approved for use only in the care of cancer patients and only by healthcare professionals[1-5] (oncologists and pain specialists)[2-3,6] who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain. Because of the risk of misuse, abuse, addition, and overdose, these products are available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Transmucosal Immediate-Release Fentanyl (TIRF) REMS ACCESS program. Under the TIFR REMS ACCESS program, outpatients, prescribers who prescribe to outpatients, pharmacies, and distributors must enroll in the program.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of fentanyl transmucosal drugs. All approvals are provided for the duration noted below.

Automation: If the patient has a prescription for a cancer medication (see Appendix A) within a 180-day period, the claim will adjudicate. When available, the ICD-9/ICD-10 codes for cancer will be used as part of automation to allow approval of the requested medication (see Appendix B).

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of fentanyl transmucosal drugs is recommended for those who meet one of the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Breakthrough Pain in Patients with Cancer:** Approve for 1 year if the patient meets the following criteria (**A and B**):
   A) Patient meets ONE of the following conditions (i or ii):
      i. Patient is unable to swallow, has dysphagia, esophagitis, mucositis,[7] or uncontrollable nausea/vomiting (In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion); OR
      ii. Patient is unable to take two other short-acting narcotics (e.g., oxycodone, morphine sulfate, hydromorphone, etc.) secondary to allergy or severe adverse events (In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion); AND
   B) Patient is on or will be on an oral or transdermal long-acting narcotic (e.g., Duragesic, OxyContin, morphine extended-release), or the patient is on intravenous, subcutaneous, or spinal (intrathecal, epidural) narcotics (e.g., morphine sulfate, hydromorphone, fentanyl citrate).

   Actiq (generics), Abstral, Fentora, Lazanda, and Subsys are indicated 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.[1-6]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Fentanyl transmucosal drugs have 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. Rationale for non-coverage for these specific conditions is provided below. (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.[1-6] 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.[8] 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.

REFERENCES

1. Actiq® oral transmucosal [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2016.
2. Fentora® buccal tablet [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2016.
3. Oral Transmucosal Fentanyl Citrate (OTFC) [prescribing information]. Chestnut Ridge, NY: Par Pharmaceuticals; March 2017.
4. Abstral® sublingual tablets [prescribing information]. Solana Beach, CA: Sentynl Therapeutics, Inc.; December 2016.
5. Subsys® sublingual spray [prescribing information]. Chandler, AZ: Insys Therapeutics, Inc.; December 2016.
6. Lazanda® nasal spray [prescribing information]. Newark, CA: Depomed, Inc.; March 2017.
7. 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.
8. Landy SH. Oral transmucosal fentanyl citrate for the treatment of migraine headache pain in outpatients: a case series. *Headache.* 2004;44(8):762-766.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes.	09/14/2016
Annual revision	No change to criteria.	09/20/2017
Selected revision	Removal of criteria for the "Other Use with Supportive Evidence" of Breakthrough Chronic (Non-Cancer) Pain. This decision was made to be consistent with the Opioid Management solution and supported by external guidance. Automation is being changed to only look back for cancer medications and/or ICD-9/ICD-10 codes for cancer/hospice.	01/24/2018
Selected revision	Automation will only look back for cancer medications and/or ICD-9/ICD-10 codes for cancer (not hospice) in order to align the automation with criteria changes from 1/24/18.	02/07/2018
Annual revision	Removal of Onsolis which has been off the market for > 3 years. Removal of Condition Not Recommended for Approval of pre-anesthesia.	10/3/2018

TAC – Therapeutic Assessment Committee; PA – Prior authorization; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.

APPENDIX A

STC*	STC Description
0475	ANTINEOPLASTICS, MISCELLANEOUS
7235	ANTINEOPLASTICS ANTIBODY/ANTIBODY-DRUG COMPLEXES
0471	ANTINEOPLASTIC - ANTIMETABOLITES
C232	ANTINEOPLASTIC - MTOR KINASE INHIBITORS
9150	ANTINEOPLASTIC SYSTEMIC ENZYME INHIBITORS
0470	ANTINEOPLASTIC - ALKYLATING AGENTS
C593	ANTINEOPLASTIC - AROMATASE INHIBITORS
8585	ANTINEOPLAST HUM VEGF INHIBITOR RECOMB MC ANTIBODY
B759	ANTINEOPLAST, HISTONE DEACETYLASE (HDAC) INHIBITORS
6323	ANTINEOPLASTIC - ANTIANDROGENIC AGENTS
C532	ANTINEOPLASTIC - TOPOISOMERASE I INHIBITORS
G575	ANTINEOPLASTIC - MEK1 AND MEK2 KINASE INHIBITORS
F501	ANTINEOPLASTIC - VEGFR ANTAGONIST
G590	ANTINEOPLASTIC - ANTI-CD38 MONOCLONAL ANTIBODY
8254	ANTINEOPLASTIC LHRH(GNRH) AGONIST, PITUITARY SUPPR.
G607	ANTINEOPLASTIC - ANTI-SLAMF7 MONOCLONAL ANTIBODY
8569	ANTINEOPLASTIC EGF RECEPTOR BLOCKER MCLON ANTIBODY
E150	ANTINEOPLASTIC - HEDGEHOG PATHWAY INHIBITOR
8460	ANTINEOPLASTIC LHRH(GNRH) ANTAGONIST,PITUIT.SUPPRS
D560	ANTINEOPLASTIC - HALICHONDRIN B ANALOGS
G545	ANTINEOPLASTIC - IMMUNOTHERAPY, VIRUS-BASED AGENTS
C370	ANTINEOPLASTIC - EPOTHILONES AND ANALOGS
E039	ANTINEOPLASTIC - JANUS KINASE (JAK) INHIBITORS
F665	ANTINEOPLASTIC, ANTI-PROGRAMMED DEATH-1 (PD-1) MAB
H018	ANTINEOPLASTIC, PDGFR-ALPHA BLOCKER MC ANTIBODY
0472	ANTINEOPLASTIC - VINCA ALKALOIDS
7977	ANTINEOPLASTIC IMMUNOMODULATOR AGENTS
D426	ANTINEOPLASTIC - IMMUNOTHERAPY, THERAPEUTIC VAC
F495	ANTINEOPLASTIC - INTERLEUKIN-6(IL-6)INHIB,ANTIBODY
G802	ANTINEOPLASTIC- B CELL LYMPHOMA-2(BCL-2) INHIBITORS
E600	ANTINEOPLASTIC - VEGF-A,B AND PLGF INHIBITORS
0473	ANTIBIOTIC ANTINEOPLASTICS
D687	CYTOTOXIC T-LYMPHOCYTE ANTIGEN (CTLA-4) RMC ANTIBODY
G857	ANTI-PROGRAMMED CELL DEATH-LIGAND 1 (PD-L1) MAB
H214	ANTINEOPLASTIC COMB-KINASE AND AROMATASE INHIBIT
H289	ANTINEOPLASTIC-ISOCITRATE DEHYDROGENASE INHIBITORS
H309	ANTINEOPLASTIC – ANTIBIOTIC AND ANTIMETABOLITE
H317	ANTINEOPLASTIC – CD22 ANTIBODY-CYTOTOXIC ANTIBIOTIC
H324	ANTINEOPLASTIC- CD19 DIR. CAR-T CELL IMMUNOTHERAPY
H329	ANTINEOPLASTIC – CD33 ANTIBODY-CYTOTOXIC ANTIBIOTIC

* Excluding topical products

APPENDIX B

ICD-9 Codes	ICD-10 Codes
Cancer-related codes	
140.* to 209	C00.* to D09.*
230.* to 234	D3A.* to D48.*
235.* to 239	E34.0*
	Q85.0*

*Indicates the inclusion of subheadings.