BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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TRANSMUCOSAL IMMEDIATE RELEASE FENTANYL FORMULATIONS: ABSTRAL® (fentanyl citrate) sublingual tablet ACTIQ® (fentanyl citrate) transmucosal lozenge FENTORA® (fentanyl citrate) buccal tablet LAZANDA® (fentanyl citrate) nasal spray SUBSYS® (fentanyl) sublingual spray

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.

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.

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Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **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 or forms without the chart notes will be returned.**

Criteria:

- **Criteria for initial therapy:** Abstral, Actiq, Fentora, Lazanda, or Subsys is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual is
    a. 18 years of age or older for Abstral, Fentora, Lazanda or Subsys
    b. 16 years of age or older for Actiq
2. Documentation of a **current** confirmed diagnosis of cancer
3. Individual is experiencing **breakthrough** cancer-related pain
4. Member is currently on fentanyl transdermal patches with no side effects
5. For **Abstral, Fentora, Lazanda and Subsys** requests: Failure, contraindication, or intolerance to:
    a. generic fentanyl citrate oral transmucosal lozenge **(Actiq)**
6. There is **NO** concomitant use with benzodiazepines-ex. clonazepam, lorazepam, diazepam etc. **OR** there is a plan to taper use and to coordinate care among all prescribers
7. There is documentation that coordination of care will be performed between different prescribers for **ALL** controlled substances
8. There are **NO** contraindications.
    a. Contraindications include:
        i. Use in the emergency department
        ii. Known or suspected gastrointestinal obstruction, including paralytic ileus
        iii. Hypersensitivity to Fentanyl or other component of the product
        iv. Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
        v. Opioid non-tolerant patients
        vi. Management of acute or postoperative pain including headache/migraines dental pain
        vii. Significant respiratory depression

Initial approval duration:
Abstral, Actiq (or generic), Fentora, Lazanda, or Subsys will be approved at the requested dosage for 12 months for pain related to cancer

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- **Criteria for continuation of coverage (renewal request):** Abstral, Actiq, Fentora, Lazanda, or Subsys is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's cancer related pain is controlled with these products

  2. There is documentation that coordination of care is being performed between different prescribers for **ALL** controlled substances

  3. The condition has not progressed or worsened while on therapy and no development of severe side effects like:
     a. Apnea, dyspnea, epistaxis, hemoptysis, hyperventilation, hypoxia, upper respiratory infection etc.
     b. Confusion/speech disturbance
     c. Dehydration
     d. Atrial fibrillation/arrhythmia/chest pain
     e. Ascites

  4. There is **NO** concomitant use with benzodiazepines-ex. clonazepam, lorazepam, diazepam etc. **OR** there is a plan to taper use and to coordinate care among all prescribers

  Renewal duration:
  - Abstral, Actiq (or generic), Fentora, Lazanda, or Subsys will be approved at the requested dosage for 12 months for pain related to cancer

- **Patients should be tapered off or lower the dosage if any of the following apply: See "Definitions" section for Tapering guidelines**
  - There is a history of risky, harmful, non-medical or inappropriate use of these and other substances that might be unhealthy, hazardous or a problem (i.e.; multiple providers, multiple pharmacy or multiple controlled substances)
  - The patient makes no progress toward therapeutic goals

- **For all patients receiving more than 200 mg morphine or equivalent per 24 hours: See "Definitions" section for Tapering guidelines**
  - Taper patient to a lower dosage
  - Provide a Naloxone prescription to avoid side effects
  - Initiate/augment non-opioid treatments
  - Provide BH/Case management support to help with the taper

Description:

Opioid therapy is the first-line approach for moderate or severe pain in populations with active cancer. However, the comprehensive management of pain in patients with cancer also requires expertise in the use of the nonopioid analgesics, such as acetaminophen (paracetamol), non-steroidal anti-inflammatory agents (NSAIDs), and a group of drugs referred to as "adjuvant" analgesics or coanalgesics. The term "adjuvant analgesics" has been used to describe drugs that are marketed for indications other than pain, but are potentially useful as analgesics when

added to opioid therapy in patients with chronic pain syndromes. In more recent years, some of these drugs have acquired approved indications for pain.
Stepwise approach to management of cancer pain that includes both opioid and nonopioid drugs has been codified in the World Health Organization's (WHO) "analgesic ladder" approach to cancer pain management (figure 1) [1]:

World Health Organization (WHO) analgesic ladder:

- Step 1, which represents mild to moderate cancer-related pain, suggests the use of acetaminophen or an NSAID, possibly combined with an adjuvant drug to provide additional analgesia, treat a side effect, or manage a coexisting symptom.

- For patients with moderate to severe pain, and those who do not achieve adequate relief with acetaminophen or an NSAID alone, treatment with a step 2 opioid (conventionally used for moderate pain) or a step 3 opioid (conventionally used for severe pain) is appropriate. On both steps 2 and 3, the use of an acetaminophen or an NSAID should be considered, as well as other drugs (adjuvants) to enhance analgesia or treat side effects

Therapeutic dose ranges for commonly used adjuvant analgesics:

Category based on conventional use	Class	Drugs	Usual starting dose	Usual effective dose range*
Multipurpose analgesics	Corticosteroids	Dexamethasone	Varies	1-2 mg twice daily, orally or IV
		Prednisone	Varies	5-10 mg twice daily
	Antidepressants	Desipramine	10-25 mg at bedtime	50-150 mg at bedtime
		Duloxetine	20-30 mg daily	60-120 mg daily¶
		Bupropion	75 mg twice daily	300-450 mg daily$^{\Delta}$
		Venlafaxine, sustained release	75 mg once daily	150-225 mg daily
		Nortriptyline	10 to 25 mg at bedtime	50 to 150 mg at bedtime
	Alpha-2 adrenergic agonists	Tizanidine	1-2 mg at bedtime	2-8 mg twice daily
Used for neuropathic pain	Anticonvulsants	Gabapentin	100-300 mg twice daily	300-1200 mg three times daily
		Pregabalin	25-75 mg twice daily	150-300 mg twice daily
	GABA agonists	Clonazepam	0.5 mg at bedtime	0.5-3 mg daily
Used for bone pain	Osteoclast inhibitors	Pamidronate	–	60-90 mg monthly, IV
		Zoledronic acid	–	4 mg monthly, IV
		Denosumab	–	120 mg monthly, subcutaneously
Used for bowel obstruction	Anticholinergic drugs	Glycopyrrolate	0.1 mg daily	0.1-0.2 mg three times daily, subcutaneously
	Somatostatin analogue	Octreotide	Varies	0.1-0.3 mg twice daily, subcutaneously

GABA: gamma amino butyric acid.

* All dosages shown are for adult patients, oral administration, unless otherwise noted.

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¶ Randomized trials conducted in patients with diabetic peripheral neuropathy suggest no additional efficacy from

120 mg daily versus 60 mg daily.

Δ Bupropion doses ≥150 mg should be sustained release.

Transmucosal immediate release (oral and nasal) formulations of the opioid analgesic fentanyl are indicated only for the management of breakthrough cancer pain in individuals, who are already receiving around-the-clock opioid pain medication for cancer pain and who are tolerant to opioid therapy for their persistent cancer pain.

Substantial differences exist in the pharmacokinetic profiles of each product formulation that result in clinically important differences in extent of absorption of fentanyl. The formulations are not interchangeable on a mcg for mcg basis. There are no dose conversion directions available on any other fentanyl product; this includes oral, transdermal, or parenteral formulations.

Use of transmucosal immediate release (oral and nasal) formulations of fentanyl is subject to a Risk Evaluation and Mitigation Strategies (REMS) program that requires provider, patient, and dispensing pharmacy be enrolled into the program. Only providers and Pharmacies enrolled into the REMS may prescribe and dispense the drug, respectively, to individuals who are also in the program. A REMS program attempts to manage known or potentially serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) for some drugs to ensure that the benefits of a drug outweigh its risks.

Providers, pharmacies, and individual patients must be enrolled in the shared Transmucosal Immediate-release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Access Program in order to prescribe, dispense, and receive TIRF products. The TIRF REMS web site can be accessed at: www.TIRFREMSaccess.com

Definitions:

CDC Recommendations for Opioid Prescribing for Chronic Pain:

A. Determining when to initiate or continue opioids for chronic pain

1. Opioids are not first-line or routine therapy for chronic pain
2. Establish and measure goals for pain and function
3. Discuss benefits and risks and availability of non-opioid therapies with patient

B. Opioid selection, dosage, duration, follow-up, and discontinuation

1. Use immediate-release opioids when starting
2. Start low and go slow - Use caution at any dose and avoid increasing to high dosages
3. When opioids are needed for acute pain, prescribe no more than needed
    - Do NOT prescribe ER/LA opioids for acute pain
4. Follow-up and re-evaluate risk of harm; reduce dose or taper and discontinue if opioids cause harm or are not helping

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C. Assessing risk and addressing harms of opioid use

1. Evaluate risk factors for opioid-related harms
2. Check CSPMP for high dosages and prescriptions from other providers at the beginning of the treatment and at least quarterly while on the opioid treatment
3. Use urine drug testing to identify prescribed substances and undisclosed use
4. Avoid concurrent benzodiazepine and opioid prescribing
5. Arrange treatment for opioid use disorder if needed

Prescriber Education:

- Guidelines for Prescribing Opioids for Chronic Pain
  https://www.cdc.gov/drugoverdose/pdf/TurnTheTide_PocketGuide-a.pdf
  http://www.agencymeddirectors.wa.gov/Files/FY16-288SummaryAMDGOpioidGuideline_FINAL.pdf
  https://www.cdc.gov/drugoverdose/pdf/Guidelines_Factsheet-a.pdf

- Checklist for prescribing opioids for chronic pain
  https://www.cdc.gov/drugoverdose/pdf/PDO_Checklist-a.pdf

- Tapering Opioids for Chronic Pain
  https://www.cdc.gov/drugoverdose/pdf/Clinical_Pocket_Guide_Tapering-a.pdf

- Non-Opioid Treatments
  https://www.cdc.gov/drugoverdose/pdf/nonopioid_treatments-a.pdf

- Assessing Benefits and Harms of Opioid
  https://www.cdc.gov/drugoverdose/pdf/Assessing_Benefits_Harms_of_Opioid_Therapy-a.pdf

- Calculating Total Daily Dose of Opioids for Safer Dosage
  https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

- Checking Controlled Substances Prescription Monitoring Program (CSPMP)
  https://arizona.pmpaware.net/login
  https://pharmacypmp.az.gov/

- Educational Webinar Series for Prescribers
  https://www.cdc.gov/drugoverdose/pdf/COCA-webinar-series-allslides-a.pdf
  https://www.cdc.gov/drugoverdose/prescribing/trainings.html
  http://www.coperems.org/

- CDC Guideline for Prescribing Opioids for Chronic Pain
  https://www.cdc.gov/drugoverdose/prescribing/clinical-tools.html

- Washington State Opioid Taper Plan Calculator
  www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf

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- Tapering Long-Term Opioid Therapy in Chronic Non-Cancer Pain
  www.mayoclinicproceedings.org/article/S0025-6196(15)00303-1/fulltext

- UpToDate
  https://www-uptodate-com.mwu.idm.oclc.org/contents/overview-of-the-treatment-of-chronic-non-cancer-pain?source=search_result&search=non-cancer%20pain&selectedTitle=1~150

Opioid Risk Assessment Tool:

Score each that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Rx drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Rx drugs	5	5
Age between 16-45 years	1	1
History of preadolescent sexual abuse	3	0
Psychological disorders		
ADD,OCD, Bipolar, Schizophrenia	2	2
Depression	1	1
Total score		
Assessment of risk		
Low risk for abuse	≤ 3	
Moderate risk for abuse	4-7	
High risk for abuse	≥ 8	
Definitions of risk		
Low = unlikely to abuse Moderate = as likely will as will not abuse High = likely to abuse		

Resources:

Abstral. Package Insert. Revised 10/2019 by manufacturer. Reviewed 06-09-2020.

Actiq. Package Insert. Revised 10/2019 by manufacturer. Reviewed 06-09-2020.

Fentora. Package Insert. Revised 10/2019 by manufacturer. Reviewed 06-09-2020.

Lazanda. Package Insert. Revised 2/2020 by manufacturer. Reviewed 06-09-2020.

Subsys. Packet Insert. Revised 2/2020 by manufacturer. Reviewed 02-25-2017, 07-19-2018, 06-09-2020.

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Transmucosal immediate release fentanyl (TIRF) Risk Evaluation and Mitigation Strategy 12-2014.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.