BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

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

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Actiq, fentanyl transmucosal lozenge, Fentora, fentanyl buccal tablet, Lazanda, or Subsys is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual is **ONE** of the following:
    a. 18 years of age or older for Fentora, fentanyl buccal tablet, Lazanda or Subsys
    b. 16 years of age or older for Actiq or fentanyl transmucosal lozenge

2. Individual has a confirmed diagnosis of a **current active cancer**

3. Individual is experiencing **breakthrough cancer-related pain**

4. Individual is currently on fentanyl transdermal patch with no side effects

5. For **Actiq, Fentora, fentanyl buccal tablet, Lazanda and Subsys** requests: Failure, contraindication per FDA label, intolerance, or is not a candidate for fentanyl citrate transmucosal lozenge

6. There is documentation that coordination of care will be performed between different prescribers for **ALL** controlled substances

7. There is **NO** concomitant use with a benzodiazepine such as clonazepam, lorazepam, diazepam etc. **OR** there is a plan to taper use and to coordinate care among all prescribers

8. There are **NO** FDA-label contraindications such as:
    a. Use in the emergency department
    b. Known or suspected gastrointestinal obstruction, including paralytic ileus
    c. Hypersensitivity to Fentanyl or another component of the product
    d. Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
    e. Opioid non-tolerant patients
    f. Management of acute or postoperative pain including headache/migraines dental pain
    g. Significant respiratory depression

Initial approval duration: 12 months for pain related to cancer

- **Criteria for continuation of coverage (renewal request):** Actiq, fentanyl transmucosal lozenge, Fentora, fentanyl buccal tablet, Lazanda, or Subsys is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

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. Individual's condition has not progressed or worsened while on therapy and has not developed severe side effects such as:
    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 a benzodiazepine such as clonazepam, lorazepam, diazepam etc. **OR** there is a plan to taper use and to coordinate care among all prescribers

Renewal duration: 12 months for pain related to cancer

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- **Patients should be tapered off or dosage lowered 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 pharmacies, 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

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Transmucosal immediate release fentanyl formulations (sublingual tablets and spray, oral lozenges, buccal tablets, intranasal spray) 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 around the clock opioid therapy for their persistent cancer pain. They are not indicated for use in opioid non-tolerant patients, and they are not indicated for use in the management of acute or postoperative pain, including headache/migraine, dental pain, or in the emergency department.

Opioid-tolerant patients are defined as patients who are taking at least oral morphine 60 mg/day, or transdermal fentanyl 25 mcg/hour, or oral oxycodone 30 mg/day, or oral hydromorphone 8 mg/day, or oral oxymorphone 25 mg/day, or oral hydrocodone 60 mg/day, or equianalgesic dose of another opioid for at least 1 week.

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 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.

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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

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:

World Health Organization (WHO) analgesic ladder:

- **Step 1**, 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 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	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.
¶ 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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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

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:

A. 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

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

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

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

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

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

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

H. 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/

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

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

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

L. UpToDate
https://www-uptodate.com

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:

Actiq (fentanyl citrate) lozenge product information, revised by Cephalon, LLC. 11-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 16, 2023. **Discontinued 07-12-2023**

Fentanyl citrate lozenge product information, revised by Teva Pharmaceuticals USA, Inc. 01-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 13, 2024.

Fentora (fentanyl citrate) buccal tablet product information, revised by Cephalon, LLC. 12-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 13, 2024.

Fentanyl citrate buccal tablet product information, revised by Mayne Pharma 01-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 13, 2024.

Lazanda (fentanyl citrate) nasal spray product information, revised by West Therapeutic Development LLC 03-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 16, 2022. **Discontinued 12/20/2022**

Subsys (fentanyl) sublingual spray product information, revised by West Therapeutics Development, LLC. 03-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 16, 2023. **Discontinued 04-29-2021**

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R: CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. MMWR Recomm Rep. 2022;71(3):1. Epub 2022 Nov 4. Accessed April 17, 2023. Re-evaluated February 13, 2024.

Tauben D, Stacey BR. Approach to the management of chronic non-cancer pain in adults. In: UpToDate, Fishman S, Crowley M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2024. Topic last updated December 11, 2023. Accessed February 13, 2024.

Tauben D, Stacey BR. Pharmacologic management of chronic non-cancer pain in adults. In: UpToDate, Fishman S, Crowley M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2024. Topic last updated July 27, 2023. Accessed February 13, 2024.

Rosenquist R. Use of opioids in the management of chronic non-cancer pain. In: UpToDate, Aronson MD, Fishman S, Crowley M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2024. Topic last updated November 21, 2023. Accessed February 13, 2024.

Portenoy RK, Mehta Z, Ahmed E. Cancer pain management with opioids: Optimizing analgesia. In: UpToDate, Abraham J, Yushak M. (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2024. Topic last updated January 25, 2024. Accessed February 13, 2024.

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.