



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 9/21/2017
LAST REVIEW DATE: 5/19/2022
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**TRANSMUCOSAL IMMEDIATE RELEASE FENTANYL FORMULATIONS:
ABSTRAL® (fentanyl citrate) sublingual disintegrating tablet
ACTIQ® (fentanyl citrate) transmucosal lozenge
Fentanyl citrate transmucosal lozenge
Fentanyl citrate buccal tablet
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.

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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.

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All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

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, generic fentanyl transmucosal lozenge, Fentora, generic fentanyl buccal tablet, Lazanda, or Subsys are considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
 1. Individual is **ONE** of the following:
 - a. 18 years of age or older for Abstral, Fentora, generic fentanyl buccal tablet, Lazanda or Subsys
 - b. 16 years of age or older for Actiq or generic fentanyl transmucosal lozenge
 2. A confirmed diagnosis of a **current active cancer**
 3. Individual is experiencing **breakthrough cancer-related pain**
 4. Member is currently on fentanyl transdermal patches with no side effects
 5. For **Abstral, Actiq, Fentora, generic fentanyl buccal tablet, Lazanda and Subsys** requests: failure, contraindication per FDA label, or intolerance to generic fentanyl citrate oral transmucosal lozenge
 6. There is **NO** concomitant use with benzodiazepines such as 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** 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

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- **Criteria for continuation of coverage (renewal request):** Abstral, Actiq, generic fentanyl transmucosal lozenge, Fentora, generic fentanyl buccal tablet, 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 has not developed 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 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

- **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 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**

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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.

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.

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- 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 ^Δ	
		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	
Used for bone pain	GABA agonists	Clonazepam	0.5 mg at bedtime	0.5-3 mg daily	
		Osteoclast inhibitors	Pamidronate	–	60-90 mg monthly, IV
			Zoledronic acid	–	4 mg monthly, IV
Used for bone pain	Osteoclast inhibitors	Denosumab	–	120 mg monthly, subcutaneously	
		Anticholinergic drugs	Glycopyrrolate	0.1 mg daily	0.1-0.2 mg three times daily, subcutaneously
			Somatostatin analogue	Octreotide	Varies

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:

CDC Recommendations for Opioid Prescribing for Chronic Pain:

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

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

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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://pharmacympm.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/>

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- 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](http://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		

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Resources:

Abstral (fentanyl citrate) disintegrating tablet product information, revised by Sentyln Therapeutics, Inc. 10-2019. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 16, 2022.

Actiq (fentanyl citrate) lozenge product information, revised by Cephalon, Inc. 03-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 16, 2022.

Fentanyl citrate lozenge product information, revised by SpecGx LLC. 02-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 16, 2022.

Fentora (fentanyl citrate) buccal tablet product information, revised by Cephalon, Inc. 03-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 16, 2022.

Fentanyl citrate buccal tablet product information, revised by Mayne Pharma 03-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 16, 2022.

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.

Subsys (fentanyl) sublingual spray product information, revised by Insys Therapeutics, Inc. 04-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 16, 2022.

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>. Topic last updated November 20, 2020. Accessed February 18, 2022.

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>. Topic last updated December 16, 2021. Accessed February 18, 2022.

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>. Topic last updated January 21, 2022. Accessed February 18, 2022.

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.