Cigna National Formulary Coverage Policy

Drug Quantity Management – Per Days
Opioids – Fentanyl Transmucosal Products

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Product Identifier(s)

Effective 1/1/23 to 2/6/23: 111458

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

Drugs Affected

- Actiq® (fentanyl citrate oral transmucosal lozenge – generic)
- Fentora® (fentanyl buccal tablet – generic)
- Lazanda® (fentanyl nasal spray)
- Subsys® (fentanyl sublingual spray)

This Drug Quantity Management program has been developed to promote dose consolidation, prevent stockpiling/waste, and address potential order entry error of transmucosal fentanyl products. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration.

Drug Quantity Limits
The initial quantity limit supplies a sufficient quantity for each of the transmucosal immediate-release fentanyl (TIRF) products to be utilized for up to **three** breakthrough pain episodes per day. The intent is for prescribers to maximize the long-acting pain medication that will control the chronic pain and minimize breakthrough pain

episodes. Additional quantities, up to a maximum of **four** breakthrough pain episodes per day, are available through coverage review.

A quantity of **oral** transmucosal fentanyl products of 90 units (tablets [buccal], lozenges, and/or single spray units) will be covered per 30 days without prior authorization. Subsys sublingual spray is supplied in a carton containing 30 single spray units, therefore a quantity of three cartons is equal to 90 units. A quantity of Lazanda nasal spray of 23 bottles (one bottle contains eight sprays after priming) will be covered per 30 days without prior authorization. These quantities are adequate for at least three episodes of breakthrough pain per day. For coverage of additional quantities, prior authorization is required. The quantity limit for the oral products and sublingual spray, is specific to the individual drugs or any combination of them.

Product	Strength and Form	Maximum Quantity per 30 Days
Actiq® (fentanyl citrate oral transmucosal lozenge, generic)	200 mcg lozenges	90 units
	400 mcg lozenges	
	600 mcg lozenges	
	800 mcg lozenges	
	1,200 mcg lozenges	
	1,600 mcg lozenges	
Fentora® (fentanyl buccal tablet, generic)	100 mcg buccal tablets	90 units
	200 mcg buccal tablets	
	400 mcg buccal tablets	
	600 mcg buccal tablets	
	800 mcg buccal tablets	
Subsys® (fentanyl sublingual spray)	100 mcg spray units	90 units (3 cartons)
	200 mcg spray units	
	400 mcg spray units	
	600 mcg spray units	
	800 mcg spray units	
	1,200 mcg spray units (packaged 2 x 600 mcg spray units in a single blister pack)*	
	1,600 mcg spray units (packaged as 2 x 800 mcg spray units in a single blister pack)*	
Lazanda® (fentanyl sublingual spray)	100 mcg/100 mcL spray (8 sprays/5.3 mL bottle)	23 bottles/30 days
	300 mcg/100 mcL spray (8 sprays/5.3 mL bottle)	23 bottles/30 days†
	400 mcg/100 mcL spray (8 sprays/5.3 mL bottle)	23 bottles/30 days†

*180 spray units is equivalent to 6 cartons of Subsys; enough for three breakthrough pain episodes/day. Subsys 1,200 mcg and Subsys 1,600 mcg strengths are supplied in packages of "30" (30 units of either 600 mcg or 800 mcg spray units). These packages of 30 only supply 15 doses since an individual must use two spray units of the lower strengths to achieve the higher, prescribed dose. The Express Scripts system does a conversion to ensure that these NDCs made up of 600 mcg and 800 mcg strengths accumulate correctly toward the above limit. That is, the individual is able to use three doses per day of 1,200 mcg or 1,600 mcg when these strengths are prescribed. † Lazanda doses are: 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, or 800 mcg. The limit accommodates three daily breakthrough pain episodes using the 200 mcg dose (two 100 mcg sprays) or maximum 800 mcg dose (two 400 mcg sprays).

Criteria

Cigna covers quantities of the transmucosal fentanyl products as medically necessary if the individual is using the product for breakthrough cancer pain and meets one of the following criteria:

Fentanyl Lozenges (Actiq, generic)

1. If the individual requires a quantity greater than 90 units during the initial titration phase (first 30 days of therapy), approve a one-time override of up to 120 units in a 30-day period.
Note: An override is not recommended for more than 120 units in a 30-day period; labeling notes that if an individual experiences more than four breakthrough pain episodes per day, then the dose of the long-acting opioid should be readjusted.

2. If the individual is experiencing more than three breakthrough pain episodes per day, approve up to 120 units per 30-day period.
Note: An override is not recommended for more than 120 units in a 30-day period; labeling notes that if an individual experiences more than four breakthrough pain episodes per day, then the dose of the long-acting opioid should be readjusted.

3. If the individual is taking a dose that does not correspond to a commercially-available dosage form, approve a quantity sufficient that allows treatment of up to four breakthrough pain episodes per day per 30-day supply.
Note: This total number of units includes all forms of transmucosal fentanyl being used.

4. For individuals who are receiving a dose greater than 1,600 mcg per breakthrough pain episode, approve a quantity sufficient that allows treatment of up to four breakthrough pain episodes per day per 30-day supply.
Note: This total number of units includes all forms of transmucosal fentanyl being used.

Fentanyl Buccal Tablet (Fentora, generic)

1. If the individual requires a quantity greater than 90 units during the initial titration phase (first 30 days of therapy), approve a one-time override of up to 120 units in a 30-day period.
Note: An override is not recommended for more than 120 units in a 30-day period; labeling notes that if an individual experiences more than four breakthrough pain episodes per day, then the dose of the long-acting opioid should be readjusted.

2. If the individual is experiencing more than three breakthrough pain episodes per day, approve up to 120 units per 30-day period.
Note: An override is not recommended for more than 120 tablets in a 30-day period; labeling notes that if an individual experiences more than four breakthrough pain episodes per day, then the dose of the long-acting opioid should be readjusted.

3. If the individual is taking a dose that does not correspond to a commercially-available dosage form, approve a quantity sufficient that allows treatment of up to four breakthrough pain episodes per day per 30-day supply.
Note: This total number of units includes all forms of transmucosal fentanyl being used.

4. If the individual is receiving a dose greater than 800 mcg per breakthrough pain episode, approve a quantity sufficient that allows treatment of up to four breakthrough pain episodes per day per 30-day supply.
Note: This total number of units includes all forms of transmucosal fentanyl being used.

Subsys

1. If the individual requires a greater quantity during the initial titration phase (first 30 days of therapy), approve a one-time override for up to 120 units in a 30-day period.
Note: An override is not recommended for more than 120 units in a 30-day period; labeling notes that if an individual experiences more than four breakthrough pain episodes per day, then the dose of the long-acting opioid should be readjusted.

2. If the individual is experiencing more than three breakthrough pain episodes per day, approve up to 120 units per 30-day period.
   Note: An override is not recommended for more than 120 units in a 30-day period; labeling notes that if an individual experiences more than four breakthrough pain episodes per day, then the dose of the long-acting opioid should be readjusted.

3. If the individual is taking a dose that does not correspond to a commercially-available dosage form, approve a quantity sufficient that allows treatment of up to four breakthrough pain episodes per day per 30-day period.
   Note: This total number of units includes all forms of transmucosal fentanyl being used.

4. If the individual is receiving a dose greater than 1,600 mcg per breakthrough pain episode, approve a quantity sufficient that allows treatment of up to four breakthrough pain episodes per day per 30-day period.
   Note: This total number of units includes all forms of transmucosal fentanyl being used.

Lazanda

1. If the individual requires a greater quantity during the initial titration phase (first 30 days of therapy), approve a one-time override of 30 bottles in a 30-day period.
   Note: An override is not recommended for more than 30 bottles in a 30-day period; labeling notes that if an individual experiences more than four breakthrough pain episodes per day, then the dose of the long-acting opioid should be readjusted.

2. If the individual is experiencing more than three breakthrough pain episodes per day, approve up to 30 bottles per 30-day period.
   Note: An override is not recommended for more than 30 bottles since the package labeling for these transmucosal fentanyl products notes that if individuals experience up to four breakthrough pain episodes per day, then the dose of long-acting opioid should be adjusted.

3. If the individual is taking a dose that does not correspond to a commercially-available dosage form, approve, a quantity sufficient that allows treatment of up to four breakthrough pain episodes per day per 30-day period.
   Note: This total number of units includes all forms of transmucosal fentanyl being used.

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

Overview

The transmucosal fentanyl drugs are indicated only for the management of **breakthrough pain in patients with cancer** who are already receiving and tolerant to opioid therapy for their underlying persistent cancer pain.[1-4]

Actiq (generic), Fentora (generic), and Subsys are immediate-release oral transmucosal formulations of fentanyl citrate.[1-3] Lazanda is a nasal spray intended for intranasal transmucosal administration.[4] The transmucosal fentanyl drugs are contraindicated in the management of acute or postoperative pain and in patients with known intolerance or hypersensitivity to any components of the product. In addition, the transmucosal fentanyl drugs must not be used in patients who are not opioid tolerant (contraindicated). The products are approved for use only in the care of cancer patients and only by healthcare professionals (oncologists and pain specialists) who are knowledgeable of and skilled in the use of Schedule II opioids to treat cancer pain.[1-4] Because of the risk of misuse, abuse, addiction, 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 TIRF REMS ACCESS program, outpatients, prescribers who prescribe to outpatients, pharmacies, and distributors must enroll in the program.

Dosing

Fentanyl Transmucosal Lozenge (Actiq, generic)

The initial dose of fentanyl transmucosal lozenges for breakthrough cancer pain is 200 mcg.[1] Patients should only be prescribed an initial titration supply of six 200 mcg fentanyl transmucosal lozenges; these should be used prior to increasing to a higher dose. Patients may re-dose one time within a single episode of breakthrough cancer pain, if needed. Re-dosing may start 15 minutes after the previous unit has been completed (30 minutes after the start of the previous lozenge). During the titration phase no more than two lozenges should be taken for each individual breakthrough cancer pain episode. A patient must wait ≥ 4 hours before treating another episode of breakthrough pain with fentanyl transmucosal lozenges. If treatment of several consecutive breakthrough cancer pain episodes requires more than one fentanyl transmucosal lozenge per episode, a dose increase to the next higher available strength should be considered. With each new dose of fentanyl transmucosal lozenges, the package labeling recommends that six units of the titration dose be prescribed. Each new dose of fentanyl transmucosal lozenges should be evaluated over several episodes of breakthrough cancer pain (generally 1 to 2 days) before adjusting the dose again. Once a successful dose has been found (i.e., an average episode is treated with a single lozenge), patients should limit consumption to four or fewer lozenges per day. Generally, the dose should be increased when the current dose fails to adequately treat the breakthrough pain episode for several consecutive episodes. If the patient experiences greater than four breakthrough pain episodes per day, then the dose of the long-acting opioid used for persistent cancer pain should be re-evaluated.

Fentanyl Buccal Tablet (Fentora, generic)

In patients not currently taking another TIRF product, the initial dose of fentanyl buccal tablet is 100 mcg.[2] Dosing may be repeated one-time only during a single episode of breakthrough pain, if needed. Re-dosing may occur 30 minutes after the start of administration of the first dose and the same dosage strength should be used. A patient must wait ≥ 4 hours before treating another episode of breakthrough pain with fentanyl buccal tablet. Generally, the dose of fentanyl buccal tablet should be increased when the patient requires more than one dose per breakthrough pain episode for several consecutive episodes. Titration should be initiated using 100 mcg tablets. Patients in need of > 100 mcg should use two 100 mcg tablets (one tablet on each side of the mouth). If this dose is not successful, two 100 mcg tablets may be placed on each side of the mouth (total of four 100 mcg tablets). For doses > 400 mg, titrate using multiples of 200 mcg. During titration, patients should only have one strength of Fentanyl buccal tablet available at any one time. Once a successful dose has been established, if the patient experiences greater than four breakthrough pain episodes per day, the dose of the maintenance opioid should be re-evaluated.

Subsys

Due to differences in pharmacokinetic properties and individual variability, patients should not be switched on a mcg per mcg basis from any other fentanyl product to Subsys.[3] Product labeling contains dose conversion information for patients currently taking fentanyl transmucosal lozenge (Actiq, generic). If the patient is not currently taking fentanyl transmucosal lozenge (Actiq, generic), the initial dose of Subsys is 100 mcg. If adequate analgesia is obtained within 30 minutes of administration of the 100 mcg single spray, subsequent episodes of breakthrough pain should be treated with this dose. If adequate analgesia is not achieved after 30 minutes of the first 100 mcg dose, patients may take one additional dose of the same strength for that episode. The dose should be escalated in a step-wise manner over consecutive episodes of breakthrough pain until adequate analgesia with tolerable adverse effects is achieved. If there is a need to titrate to higher doses, the corresponding strength of sublingual spray should be prescribed (that is, 200 mcg, 400 mcg, 600 mcg, 800 mcg, OR two of the 600 mcg sprays [1,200 mcg] or two of the 800 mcg sprays [1,600 mcg]). Patients must wait ≥ 4 hours before treating another episode of breakthrough cancer pain with Subsys. Once titrated, Subsys should be administered as one spray under the tongue and dose consolidation should be utilized (e.g., if a patient's titrated dose is 200 mcg, the 200 mcg strength should be utilized instead of using two sprays of the 100 mcg strength). Patients may not use more than two sprays per episode of breakthrough cancer pain. The safety and efficacy of doses > 1,600 mcg or more than two sprays per episode have not been evaluated in clinical studies. There are no clinical data to support the use of a combination of dose strengths to treat an episode. It is advised that patients only have one strength of Subsys available at any time to reduce the risk of overdose. Use of Subsys should be limited to four or fewer doses per day once a successful dose is found. If more than four episodes of breakthrough pain are experienced per day, the dose of the long-acting opioid should be re-evaluated.

Lazanda
Due to differences in pharmacokinetic properties and individual variability, patients should not be switched on a mcg per mcg basis from any other fentanyl product to Lazanda.[4] Lazanda must be primed prior to initial use. Treatment of all patients (including those switching from another fentanyl product) should begin with one 100 mcg spray of Lazanda (one spray in one nostril). If adequate analgesia is obtained within 30 minutes of administration of the 100 mcg single spray, subsequent episodes of breakthrough pain should be treated with this dose. If adequate analgesia is not achieved with the first 100 mcg dose, the dose should be escalated in a stepwise manner to 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg per dose over consecutive episodes of breakthrough pain until adequate analgesia with tolerable adverse effects is achieved. Lazanda should be administered as one spray in one nostril, one spray in each nostril, or up to two sprays per nostril (alternating each spray between nostrils). Patients must wait ≥ 2 hours before treating another episode of breakthrough cancer pain with Lazanda. The patient may require a different immediate-release medication for rescue during titration with inadequate pain relief. The safety and efficacy of doses > 800 mcg (one 400 mcg spray in each nostril) have not been evaluated in clinical studies. There are no clinical data to support the use of a combination of dose strengths to treat an episode. If more than four episodes of breakthrough pain are experienced per day, the dose of the long-acting opioid should be re-evaluated. Lazanda should be limited to treating four or fewer episodes of breakthrough pain per day.

Availability
Fentanyl transmucosal lozenges (Actiq, generic) are available in six dosage strengths: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,200 mcg and 1,600 mcg.[1]

Fentanyl buccal tablets (Fentora, generic) are available in five dosage strengths: 100 mcg, 200 mcg, 400 mcg, 600 mcg, and 800 mcg.[2]

Subsys sublingual spray is available in seven dosage strengths: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,200 mcg, and 1,600 mcg.[3] Each Subsys carton contains 30 individual blister packages containing single spray unit dose systems of Subsys. The 1,200 mcg and 1,600 mcg are supplied as two 600 mcg or two 800 mcg units in one package, respectively. After use, each unit dose system should be disposed of immediately.

Lazanda nasal spray is available in three dosage strengths: 100 mcg/100 mcL, 300 mcg/100 mcL and 400 mcg/100 mcL mcg.[4] One spray contains 100 mcL. Lazanda bottles contain 5.3 mL prior to priming and 5 mL or eight sprays after priming. Patients should dispose of a Lazanda bottle if they have used eight sprays, if it has been ≥ 5 days since the last time they used the bottle of Lazanda, or it has been ≥ 14 days since the bottle was primed.

References

1. Actiq® oral transmucosal [prescribing information]. Parsnippany, NJ: Teva Pharmaceuticals; March 2021.
2. Fentora® buccal tablet [prescribing information]. Parsippany, NJ: Teva Pharmaceuticals; 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.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	Abstral removed from the policy (obsolete). Generic to Fentora was added to the policy. **Fentanyl Lozenges (Actiq, generic).** For patients receiving a dose greater than 1,600 mcg per breakthrough pain episode, criteria requiring the patient has a history of using 1,600 mcg per day were removed. **Fentanyl Buccal Tablet (Fentora, generic).** For patients receiving a dose greater than 800 mcg per breakthrough pain episode, criteria requiring the patient has a history of using 800 mcg per day were removed. **Subsys.** For patients receiving a dose greater than 1,600 mcg per breakthrough pain episode, criteria requiring the patient has a history of using 1,600 mcg per day were removed. Exclusions for acute and/or postoperative pain including surgery/post-surgery, trauma/post-trauma, acute medical illness (e.g., acute abdominal pain, pelvic pain, muscle spasm, acute migraine); pre-anesthesia (preoperative anxiolysis and sedation and/or supplement to anesthesia); and breakthrough non-cancer chronic pain were removed from the policy. The policy only approves for breakthrough cancer pain, therefore these exclusions are not needed.	05/04/2022