

Cigna National Preferred Formulary Coverage Policy



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Drug Quantity Management – Per Days Fentanyl Transmucosal Drugs Duration Limit

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Related Coverage Resources

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.

NPF Coverage Policy

Drugs Affected

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

Table 1. Quantity Level Limits¹⁻⁵

Medication Name and Strength	Per Days Quantity Level Limit
Abstral - 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, and 800 mcg	90 units per 30 days
Actiq, generics - 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, and 1600 mcg	
Fentora - 100 mcg, 200 mcg, 400 mcg, 600 mcg, and 800 mcg	

Subsys - 100 mcg, 200 mcg, 400 mcg, 600 mcg, and 800 mcg (90 spray units = 3 cartons) Subsys - 1200 mcg and 1600 mcg * <ul style="list-style-type: none"> • 1200 mcg = two of the 600 mcg sprays • 1600 mcg = two of the 800 mcg sprays (180 spray units = 6 cartons = 3 breakthrough pain episodes per day - see footnote)	
Lazanda - 100 mcg, 300 mcg and 400 mcg <ul style="list-style-type: none"> • Labeled doses are: 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg or 800 mcg • Limit accommodates 3 daily breakthrough pain episodes using 200 mcg dose (two 100 mcg sprays) or max 800 mcg dose (two 400 mcg sprays) 	23 bottles per 30 days (8 sprays/doses per bottle)

*Subsys 1200 mcg and Subsys 1600 mcg strengths have their own NDCs and come in packages of "30" (Thirty units of either 600 mcg or 800 mcg spray units). These packages of 30 actually only supply 15 doses since individuals must use two spray units of the lower strengths to achieve the higher, prescribed dose.

Oral Fentanyl Transmucosal Drugs

(tablets [buccal and sublingual], films, lozenges, and/or single spray units)

Maximum quantity per 30 days = 90 units

Nasal Fentanyl (Lazanda)

Maximum quantity per 30 days = 23 bottles

A quantity of oral transmucosal fentanyl products of 90 units (tablets [buccal and sublingual], films, 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, sublingual spray included, is specific to the individual drugs or any combination of them.

Examples:

- 90 units (lozenges) of generic Actiq 200 mcg would be covered in 30 days; OR
- 30 units (tablets) of Fentora 200 mcg plus 60 units (tablets) of Fentora 400 mcg per 30 days; OR
- 30 units (sprays) of Subsys 200 mcg plus 20 units (tablets) of Fentora 100 mcg per 30 days

Criteria

Cigna covers quantities as medically necessary when the following criteria are met:

All approvals are provided for 12 months in duration unless otherwise noted below. **(Note: 1.d. does not apply to Lazanda).**

1. Individuals with breakthrough cancer pain, AND (a, b, c, OR d)
 - a) A greater quantity is required during the initial titration phase (first 30 days of therapy).
Approve a one-time override for up to 120 units of Actiq (generics), Fentora, Abstral, or 120 single-use Subsys sublingual sprays in a 30-day period. Approve a **one-time** override for up to 30 bottles of Lazanda in a 30-day period. An override is not recommended for more than 120 units of Actiq (generics), Fentora, Abstral, or Subsys, or 30 bottles of Lazanda in a 30-day period since the package labeling for these transmucosal fentanyl products notes that if individuals experience more than 4 breakthrough pain episodes per day, then the dose of long-acting opioid should be adjusted.
 - b) For individuals experiencing more than 3 breakthrough pain episodes per day.
Approve for up to 120 units per 30-day period of Actiq (generics), Fentora, Abstral, or Subsys, or up to 30 bottles of Lazanda per 30-day period. An override is not recommended for more than 120 units in a 30-day period of Actiq (generics), Fentora, or Abstral, or 30 bottles of Lazanda since the package labeling for these transmucosal fentanyl products notes that if individuals experience more than 4 breakthrough pain episodes per day, then the dose of long-acting opioid should be adjusted.

- c) For individuals taking a dose that does not correspond to a commercially-available dosage form [that is, the dose requires multiple same strength units be used AND would otherwise require two (or more) strengths to be used]. For example, a dose of 1000 mcg requires 400 mcg plus 600 mcg, or 200 mcg plus 800 mcg.

Approve a quantity of units (all transmucosal fentanyl forms being used) that allows treatment of no more than 4 breakthrough pain episodes per day per 30 day supply.

Examples:

- For a 30 day period, an individual requires 15 days of Actiq (or generic) plus 15 days of Fentora.
 - 1000 mcg of Actiq (or generic) per breakthrough pain episode using a 400 mcg lozenge plus a 600 mcg lozenge of Actiq.
 - 500 mcg of Fentora per breakthrough pain episode using a 300 mcg tablet plus a 200 mcg tablet.
 - The maximum to be dispensed for the 30-day period would be a total of 240 units which includes 60 units of Actiq 400 mcg, 60 units of Actiq 600 mcg, 60 units of Fentora 300 mcg, and 60 units of Fentora 200 mcg.
- An individual on Subsys using two different dosage strengths per breakthrough pain episode.
 - 500 mcg of Subsys per episode using one 400 mcg spray plus one 100 mcg spray.
 - Four breakthrough pain episodes per day would require 240 single spray units per 30 days which includes 120 units of Subsys 400 mcg and 120 units of Subsys 100 mcg.
- An individual on Lazanda using both the 100 mcg and 400 mcg dosage strengths.
 - 500 mcg of Lazanda per episode using one 100 mcg spray in one nostril and one 400 mcg spray in the other nostril for each breakthrough pain episode (each bottle contains 8 sprays after priming).
 - Four breakthrough pain episodes per day would require 30 bottles per 30 days which includes 15 bottles of Lazanda 400 mcg and 15 bottles of Lazanda 100 mcg.
- An individual on Lazanda using both the 300 mcg and 400 mcg dosage strengths.
 - 700 mcg of Lazanda per episode using one 300 mcg spray in one nostril and one 400 mcg spray in the other nostril for each breakthrough pain episode (each bottle contains 8 sprays after priming).
 - Four breakthrough pain episodes per day would require 30 bottles per 30 days which includes 15 bottles of Lazanda 400 mcg and 15 bottles of Lazanda 300 mcg.

- d) For individuals who are receiving doses higher than the largest strengths available per breakthrough pain episode for the requested transmucosal fentanyl product (see table 2). **This exception does not apply to Lazanda.**

Authorize a quantity limit override if the individual has a prior history of using the largest strength available for the requested product. Approve a quantity sufficient for a 30 day supply, up to a quantity of units (all oral transmucosal fentanyl forms being used) that allows treatment of no more than 4 breakthrough pain episodes per day.

Example: For a 30 day period, an individual requires 15 days of Actiq (or generic) plus 15 days of Fentora.

- 1800 mcg of Actiq (or generic) per breakthrough pain episode using a 1600 mcg lozenge plus a 200 mcg lozenge of Actiq
- 1000 mcg of Fentora per breakthrough pain episode using a 800 mcg tablet plus a 200 mcg tablet
- The maximum to be dispensed for the 30-day period would be a total of 240 units comprised of 60 units of Actiq 1600 mcg, 60 units of Actiq 200 mcg, 60 units of Fentora 800 mcg, and 60 units of Fentora 200 mcg.

Table 2. Highest strengths of transmucosal fentanyl products

Medication Name	Highest available dosage strength
Abstral	Individual must have a prior history of using the Abstral 800 mcg dosage.

Actiq (generics)	Individual must have a prior history of using the Actiq (or generic) 1600 mcg dosage strength.
Fentora	Individual must have a prior history of using the Fentora 800 mcg dosage strength.
Subsys	Individual must have a prior history of using the Subsys 1600 mcg dosage strength.
Lazanda	No exceptions. The maximum dose of Lazanda is 800 mcg (one 400 mcg spray in each nostril).

Conditions Not Covered

Any other exception is considered not medically necessary, including the following:

1. No overrides are recommended for individuals with 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). Transmucosal fentanyl products are contraindicated for use in the management of acute or postoperative pain.
2. No overrides are recommended for pre-anesthesia (preoperative anxiolysis and sedation and/or supplement to anesthesia). This use is typically a one-time dose and there is a multitude of other narcotic options for use as a pre-anesthetic for adults and children.
3. No overrides are recommended for breakthrough non-cancer chronic pain. Transmucosal fentanyl products are not indicated for breakthrough non-cancer pain.

Background

Overview

The initial quantity limit supplies a sufficient quantity for each of the six 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.

Fentanyl is a pure opioid agonist (controlled substance in Schedule II of the Controlled Substances Act) that can produce drug dependence of the morphine type.¹⁻⁵ Actiq (generics), Fentora, Abstral, Subsys, and Lazanda, may be subject to misuse, abuse, and addiction. Actiq (generics), Fentora, and Abstral are immediate-release oral transmucosal formulations of fentanyl citrate.¹⁻⁵ Subsys is a sublingual transmucosal spray.⁴ Lazanda is a nasal spray intended for intranasal transmucosal administration.⁵ Transmucosal fentanyl products are indicated only for the management of breakthrough cancer pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.¹⁻⁵ Patients considered opioid tolerant are those who are taking around-the-clock medication consisting of at least 60 mg of oral morphine per day, at least 25 mcg of transdermal fentanyl/hour, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid for a week or longer.

Transmucosal fentanyl products are contraindicated in the management of acute or postoperative pain and in non-opioid tolerant patients.¹⁻⁵ These products are intended to be used 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. Actiq (generics), Fentora, Abstral, Subsys, and Lazanda are only available through a the Transmucosal Immediate-Release Fentanyl (TIRF) Risk Evaluation and Mitigation Strategy (REMS) Access Program due to the risk of misuse, abuse, addiction, and overdose. The appropriate dosing and safety of Actiq (generics) in opioid tolerant children with breakthrough cancer pain have not been established below the age of 16 years.^{1,3} The safety and efficacy of Abstral, Fentora, Subsys, and Lazanda have not been established in pediatric patients below the age of 18 years.^{2,4-5}

None of the transmucosal fentanyl products can be converted on a microgram to microgram basis from one product to another, but some, like Fentora contain conversion instructions within the product labeling for patients who have already started therapy with Actiq. For patients who are new to therapy, transmucosal fentanyl products should be individually titrated to a dose that provides adequate analgesia and minimizes side effects.¹⁻⁵

Actiq (generics)

Actiq buccal lozenges are available in six dosage strengths: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg and 1600 mcg.¹ For administration, Actiq (generics) should be placed in the patient's mouth between the cheek and lower gum; occasionally moving the drug matrix from one side of the mouth to the other using the handle.^{1, 3} Actiq (generics) should be sucked and not chewed. If it is chewed and swallowed, lower peak concentrations and lower bioavailability might result. Actiq (generics) should be consumed over a 15-minute period. Longer or shorter durations may produce less efficacy than that established in clinical studies. The initial dose of Actiq (generics) for the management of episodes of breakthrough cancer pain is always 200 mcg. The product labeling states that patients should only be prescribed an initial titration supply of six 200 mcg Actiq (or generic) units, and that these initial six units should be used up before increasing to a higher dose. Patients may redose one time within a single episode of breakthrough cancer pain, if needed. Redosing may start 15 minutes after the previous unit has been completed (30 minutes after the start of the previous unit). While patients are in the titration phase and consuming units which individually may be sub therapeutic, no more than two units should be taken for each individual breakthrough cancer pain episode. A patient must wait at least four hours before treating another episode of breakthrough pain with Actiq (generics). If treatment of several consecutive breakthrough cancer pain episodes requires more than one Actiq (or generic) per episode, then an increase in dose to the next higher available strength should be considered. At each new dose of Actiq (or generic), the package labeling recommends that six units of the titration dose be prescribed. Each new dose of Actiq (or generic) should be evaluated over several episodes of breakthrough cancer pain (generally 1-2 days) before adjusting the dose again. Once a successful dose has been found (i.e., an average episode is treated with a single Actiq [or generic] unit), patients should limit consumption to four or fewer units per day. Generally, the Actiq (or generic) 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.

Fentora

Fentora buccal tablets are available in five dosage strengths: 100 mcg, 200 mcg, 400 mcg, 600 mcg, and 800 mcg.² Fentora tablets are to be placed between the upper cheek and gum above a rear molar tooth and allowed to dissolve (usually takes approximately 14-25 minutes).² Alternatively, Fentora can be dissolved under the tongue. After 30 minutes, remnants of the tablet may be swallowed with a glass of water. Fentora tablets should not be sucked, chewed, or swallowed as this will reduce the effectiveness of the medication by lowering the plasma concentration. The tablets should not be split. If the patient is not currently taking another TIRF product, the initial dose of Fentora is always 100 mcg. Dosing may be repeated only once 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 at least four hours before treating another episode of breakthrough pain with Fentora. Generally, the dose of Fentora should be increased when patients require more than one dose per breakthrough pain episode for several consecutive episodes. Titration should be initiated using 100 mcg tablets. Patients in need of more than 100 mcg should use two 100 mcg tablets (one 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). Titrate above 400 mcg using multiples of 200 mcg. The product labeling states that during titration, patients should only have one strength of Fentora 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.

Abstral

Abstral sublingual tablet is available in six dosage strengths: 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, and 800 mcg.³ Abstral should be placed on the floor of the patient's mouth directly under the tongue immediately after removing from the blister unit.³ Abstral tablets should not be chewed, sucked, or swallowed. The tablets should completely dissolve in the sublingual cavity. Patients also should not eat or drink anything until the tablet has completely dissolved. Dose titration for all patients should begin with an initial dose of 100 mcg. If adequate analgesia is not achieved with the first 100 mcg Abstral dose, the dose may be increased in a stepwise manner over consecutive breakthrough pain episodes until adequate analgesia with tolerable side effects is achieved. The dose should be increased by 100 mcg multiples up to 400 mcg. If using the 400 mcg dose does not produce adequate analgesia, the next titration step is 600 mcg (three 200 mcg tablets or one 600 mcg tablet). If the 600 mcg dose does not produce adequate analgesia, the next titration step is 800 mcg. Once an appropriate

dose for pain management has been established, patients should use only one Abstral tablet of the appropriate strength per dose. Abstral should be limited to treating four or fewer episodes of breakthrough pain per day. During titration, patients use multiples of 100 mcg tablets and/or 200 mcg tablets for any single dose; however they should not use more than four tablets at one time. If adequate analgesia is not obtained 30 minutes after the use of Abstral, the patient may repeat the same dose of Abstral. No more than two doses of Abstral may be used to treat an episode of breakthrough pain. Patients must wait at least 2 hours before treating another breakthrough pain episode with Abstral. If more than four episodes of breakthrough pain are experienced per day, the dose of the long-acting opioid should be re-evaluated.

Subsys

Subsys sublingual spray is available in seven dosage strengths: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg and 1600 mcg.⁴ Each Subsys carton contains 30 individual blister packages containing single spray unit dose systems of Subsys and a supply of small white disposal bags for disposing of used Subsys units (30). Each unit dose system consists of a white actuator attached to a light purple vial holder. One separate carton accompanies each Subsys container which includes a disposal bottle (1), and one large disposal bag. For use, each blister package should be opened with a scissors immediately prior to product use. The contents of the unit should be carefully sprayed into the patient's mouth underneath the tongue. After use, each unit dose system should be disposed of immediately. This includes disposal of any unneeded unit dose systems remaining from a prescription as soon as they are no longer needed. 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. Product labeling does contain conversion information for those patients currently taking Actiq. If the patient is not currently taking Actiq, the initial dose of Subsys is always 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 only 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 (packaged as 1200 mcg) or two of the 800 mcg sprays (packaged as 1600 mcg) - *see footnote to Table 1). Patients must wait at least 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. For example, 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 2 sprays per episode of breakthrough cancer pain. The safety and efficacy of doses higher than 1600 mcg or more than two sprays per episode have not been evaluated in clinical studies. There is no clinical data to support the use of a combination of dose strengths to treat an episode and the package insert advises 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

Lazanda nasal spray is available in three dosage strengths, 100 mcg, 300 mcg and 400 mcg.⁵ Each bottle of Lazanda contains eight sprays after priming. Lazanda must be primed prior to initial use. To administer a dose, the nozzle must be inserted into the nose and then the finger grips pressed down firmly until a "click" is heard and the number in the counting window advances by one. The fine mist spray is not always felt on the nasal mucosal membrane and patients must rely on the audible click and the advancement of the dose counter to confirm a spray has been administered. Patients should dispose of a Lazanda bottle if they have used eight sprays, if it has been five days or more since the last time they used the bottle of Lazanda, or it has been 14 days or more since the bottle was primed. 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. 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 step-wise 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 at least two 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 higher than 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.

References

1. Actiq® oral transmucosal [prescribing information]. Frazer, PA: Cephalon, Inc.; October 2019.
2. Fentora® buccal tablet [prescribing information]. North Wales, PA: Teva Pharmaceuticals; October 2019.
3. Abstral® sublingual tablet [prescribing information]. Solana Beach, CA: Sentyln Therapeutics, Inc.; October 2019.
4. Subsys® sublingual spray [prescribing information]. Phoenix, AZ: Insys Therapeutics, Inc.; November 2019.
5. Lazanda® nasal spray [prescribing information]. Northbrook, IL: West Therapeutic Development, LLC; May 2019.

Last Revision Details

Annual Revision	Reviewed by Clinical Specialists. No changes to criteria.	01/31/2020
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