Clinical Policy: Fentanyl IR (Abstral, Actiq, Fentora, Lazanda, Subsys)

Reference Number: PA.CP.PMN.127
Effective Date: 10.17.18
Last Review Date: 10.17.18

Revision Log

Description
The following are potent opioid agonist products requiring prior authorization: oral transmucosal fentanyl citrate (Actiq®, Fentora®), fentanyl sublingual (Abstral®), fentanyl nasal spray (Lazanda™), fentanyl sublingual spray (Subsys™).

_____

****For Health Insurance Marketplace (HIM),** Abstral, Fentora, Lazanda, and Subsys are non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)
Transmucosal immediate release fentanyl products are indicated for the management of breakthrough pain in cancer patients (≥16 years old for Actiq and ≥ 18 years old for Fentora, Lazanda, Subsys and Abstral) who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

Patients considered opioid tolerant are those who are taking, for one week or longer, around-the-clock medicine consisting of at least 60 mg of oral morphine per day, at least 25 mcg of transdermal fentanyl per hour, at least 30 mg of oral oxycodone per day, at least 8 mg of oral hydromorphone per day, at least 25 mg oral oxymorphone per day, at least 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid daily for a week or longer. Patients must remain on around-the-clock opioids while taking Actiq, Fentora, Abstral, Lazanda, Subsys.

Limitation(s) of use:
- Not for use in opioid non-tolerant patients.
- Not for use in the management of acute or postoperative pain, including headache/migraine, dental pain, or in the emergency room.
- As a part of the Transmucosal Immediate Release Fentanyl Risk Evaluation and Mitigation Strategy (TIRF REMS) Access program, potent opioid agonist products may be dispensed only to outpatients enrolled in the program. For inpatient administration (e.g., hospitals, hospices, and long-term care facilities that prescribe for inpatient use), patient and prescriber enrollment is not required.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Actiq, Fentora, Abstral, Lazanda, and Subsys are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cancer Pain (must meet all)**:**
1. Diagnosis of cancer pain;
2. Prescribed for the management of breakthrough pain;
3. Member is on fentanyl transdermal patches or another long-acting opioid taken around the clock;
4. Age ≥ 16 years (for Actiq requests) OR age ≥ 18 years (for Abstral, Fentora, Lazanda, or Subsys requests);
5. Failure of a trial of two formulary short-acting opioid analgesics unless all are contraindicated or clinically significant adverse effects are experienced;
6. For Abstral, Fentora, Lazanda and Subsys requests: Failure of a trial of generic fentanyl citrate oral transmucosal lozenge (Actiq) unless contraindicated or clinically significant adverse effects are experienced;

Approval duration: 6 months

B. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 and PA.LTSS.PHARM.12 (Short Acting Narcotic Analgesics).

II. Continued Therapy

A. Cancer Pain (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy as evidenced by reduction in breakthrough pain, no significant toxicity;

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 and PA.LTSS.PHARM.12(Short Acting Narcotic Analgesics).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – refer to PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
REMS: Risk Evaluation and Mitigation Strategy
TIRF: transmucosal immediate-release fentanyl

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be formulary agents for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Various (morphine sulfate immediate-release)	10 mg – 30 mg PO Q 4 H PRN Individualize dosage based on extent of pre-existing opioid tolerance	Varies
Roxicodone® (oxycodone immediate-release)	5 mg - 15 mg PO Q 4 to 6 H PRN Individualize dosage based on extent of pre-existing opioid tolerance	Varies
Dilaudid® (hydromorphone immediate-release)	2 mg – 4 mg PO Q 3 to 4 H PRN Individualize dosage based on extent of pre-existing opioid tolerance	Varies
Opana® (oxymorphone immediate-release)	5 mg – 20 mg PO Q 4 to 6 H PRN Individualize dosage based on extent of pre-existing opioid tolerance	Varies
Fentanyl transdermal patches (Duragesic®)	Apply one patch topically every 72 hours	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: General Information

- Because of the potential risk for misuse, abuse, and overdose, the fentanyl sublingual and transmucosal products listed below are only available through restricted distribution programs. Under the TIRF REMS program, only prescribers, pharmacies, and patients registered with TIRF REMS are able to prescribe, dispense, and receive these products. Additional information is available at: www.tirfremsaccess.com/TirfUISplashWeb/index.html or by calling 1-866-822-1483.
- These products are not interchangeable and must not be used in opioid non-tolerant patients because life-threatening hypoventilation could occur at any dose in patients not taking chronic opiates. Substantial differences exist in the pharmacokinetic profiles of these drugs that result in clinically important differences in the extent of absorption of fentanyl. As a result of these differences, the substitution of these products may result in fatal overdose. Patients considered opioid tolerant are those who are taking around the clock medicine consisting of at least 60 mg morphine/day, at least 25 mcg transdermal fentanyl/hour, at least 30 mg of oxycodone daily, at least 8 mg oral hydromorphone daily, or an equianalgesic dose of another opioid for a week or longer.
- Fentanyl absorption with different formulations of transmucosal delivery systems can be substantially different. When Abstral is prescribed, patients should not be converted on a

mcg per mcg basis from any other transmucosal fentanyl product. Patients beginning treatment with Abstral must begin with titration from 100 mcg dose.

- The initial dose of Fentora, Abstral, and Subsys is always 100 mcg with the only exception being patients already using Actiq. Patients switching from Actiq to Fentora, Abstral, or Subsys should be initiated as shown:

Actiq dose (mcg)	Fentora dose (mcg)	Abstral dose (mcg)	Subsys dose (mcg)
200	100	100	100
400	100	200	100
600	200	200	200
800	200	200	200
1200	400	200	400
1600	400	400	400

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Oral transmucosal fentanyl citrate (Actiq)	Initiate dosing with 200 mcg PO and if breakthrough episode is not relieved in 30 minutes, patients may take only 1 additional dose using the same strength and must wait at least 4 hours before taking another dose. Individually titrate to a dose that provides adequate analgesia using single dosage unit per breakthrough cancer pain episode and minimizes side effects. Initial prescription recommendation for maximum of 6 units; No more than 4 doses per day; separate by at least 4 hours.	Varies Use of more than 3 lozenges/buccal films/tablets per day indicates the need to increase the dose of fentanyl transdermal patches
Oral transmucosal fentanyl citrate (Fentora)	Initiate dosing with 100 mcg PO and if breakthrough episode is not relieved in 30 minutes, patients may take only 1 additional dose using the same strength and must wait at least 4 hours before taking another dose. Maximum: 4 tablets simultaneously	Varies Use of more than 3 lozenges/buccal films/tablets per day indicates the need to increase the dose of fentanyl transdermal patches
Fentanyl sublingual (Abstral)	Begin titration of all patients with an initial dose of Abstral of 100 mcg SL. Due to differences in the pharmacokinetic properties and individual variability, even patients switching from other fentanyl containing products to Abstral must start with the 100 mcg dose. Abstral is not equivalent on a mcg per mcg basis with all other fentanyl products; therefore, do not switch patients on a mcg per mcg basis from	Varies Use of more than 3 lozenges/buccal films/tablets per day indicates the need to increase the dose of fentanyl transdermal patches

Drug Name	Dosing Regimen	Maximum Dose
	any other fentanyl product. The safety and efficacy of doses higher than 800 mcg have not been evaluated. Maximum two doses for each each episode of breakthrough pain. Patients must wait at least 2 hours before treating another episode.	
Fentanyl nasal spray (Lazanda)	Initial dose of Lazanda for all patients is 100 mcg into one nostril. Individually titrate to an effective dose, from 100 mcg to 200 mcg to 400 mcg, and up to a maximum of 800 mcg, that provides adequate analgesia with tolerable side effects. Dose is a single spray into one nostril or a single spray into each nostril (2 sprays). Maximum dose is a single spray into one nostril or single spray into each nostril per episode; no more than four doses per 24 hours. Wait at least 2 hours before treating another episode of breakthrough pain with Lazanda.	Varies Maximum 96 sprays (12 bottles) per 30 days – Use of more indicates the need to increase the dose of fentanyl transdermal patches
Fentanyl sublingual spray (Subsys)	Initial dose of Subsys: 100 mcg SL. Individually titrate to a tolerable dose that provides adequate analgesia using a single Subsys dose per breakthrough cancer pain episode. No more than two doses can be taken per breakthrough pain episode. Wait at least 4 hours before treating another episode of breakthrough pain with Subsys. Limit consumption to four or fewer doses per day once successful dose is found.	Varies Use of more indicates the need to increase the dose of fentanyl transdermal patches

VI. Product Availability

Drug Name	Availability
Oral transmucosal fentanyl citrate (Actiq)	Lozenges: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, 1600 mcg 30 lozenges per package
Oral transmucosal fentanyl citrate (Fentora)	Buccal tablet: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg Package of 7 blister cards containing 4 tablets in each card
Fentanyl sublingual (Abstral)	Sublingual tablets: 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, 800 mcg (32 tablets per package).
Fentanyl nasal spray (Lazanda)	Metered dose nasal spray: 100 mcg, 300 mcg, 400 mcg per spray Each bottle contains 8 sprays
Fentanyl sublingual spray (Subsys)	Single spray units: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, 1600 mcg per spray

VII. References

1. Actiq [Prescribing Information] North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2016. Available at www.actiq.com. Accessed February 21, 2018.
2. Fentora [Prescribing Information] North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2016. Available at www.fentora.com. Accessed February 21, 2018.
3. Abstral [Prescribing Information] Hunt Valley, MD: Pharmaceutics International, Inc.; December 2016. Available at www.abstral.com. Accessed February 21, 2018.
4. Lazanda [Prescribing Information] Newark, CA: Depomed, Inc.; March 2017. Available at www.lazanda.com. Accessed February 21, 2018.
5. Subsys [Prescribing Information] Chandler, AZ: Insys Therapeutics, Inc.; December 2016. Available at www.subsys.com. Accessed February 21, 2018.
6. Aronoff GM, Brennan MJ, Pritchard DD, et al. Evidence-based oral transmucosal fentanyl citrate (OTFC) dosing guidelines. Pain Medicine. 2005;6(4):305-14.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 21, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy Created	10/18	