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

Reference Number: IL.ERX.NPA.66
Effective Date: 06.01.21
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Line of Business: Illinois Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Fentanyl IR [immediate-release] (Abstral® sublingual tablets, Actiq® lozenges, Fentora® buccal tablets, Lazanda® nasal spray, Subsys® sublingual spray) is a pure opioid agonist.

FDA Approved Indication(s)
Abstral, Actiq, Fentora, Lazanda, and Subsys 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 around-the-clock medicine consisting of at least 60 mg of oral morphine daily, 25 mcg of transdermal fentanyl/hour, 30 mg of oral oxycodone daily, 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid daily for a week or longer. Patients must remain on around-the-clock opioids when taking fentanyl IR products.

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 or dental pain.
- As a part of the Transmucosal Immediate-Release Fentanyl REMS Access program, these fentanyl IR 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Abstral, Actiq, Fentora, 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. Age ≥ 16 years (for Actiq requests) OR age ≥ 18 years (for Abstral, Fentora, Lazanda, or Subsys requests);
4. Currently receiving fentanyl transdermal patches;
5. Failure of a trial of two formulary short-acting opioid analgesics, unless clinically significant adverse effects are experienced or all are contraindicated;
6. A treatment plan is required, including:
   a. Pain intensity (scales or ratings);
   b. Functional status (physical and psychosocial);

c. Patient`s goal of therapy (level of pain acceptable and/or functional status);
d. Current analgesic (opioid and adjuvant) regimen;
e. Current non-pharmacological treatment;
f. Opioid-related side effects;
g. Indications of medical misuse;
h. Action plan if analgesic failure occurs;

7. Request does not exceed health plan quantity limit, unless dose cannot be adjusted within quantity limit using other dosage strengths.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Cancer Pain (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Request does not exceed health plan quantity limit, unless dose cannot be adjusted within quantity limit using other dosage strengths.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 or evidence of coverage documents.

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 a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
codeine	Varies	N/A
hydrocodone/acetaminophen (Lortab®, Norco®, Vicodin®)		
hydromorphone (Dilaudid®)		
morphine		
oxycodone (Roxicodone®, Oxaydo®)		
oxycodone/acetaminophen (Percocet®)		
oxymorphone (Opana®)		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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.
**Not all-inclusive*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): opioid non-tolerant patients; management of acute or postoperative pain including headache/migraines dental pain, or use in the emergency department; significant respiratory depression; acute or severe bronchial asthma; gastrointestinal obstruction, including paralytic ileus; hypersensitivity to fentanyl or components of the fentanyl product
- Boxed warning(s): life-threatening respiratory depression; accidental ingestion; cytochrome P450 3A4 interactions; risk of medication errors; concomitant use with benzodiazepines or other CNS depressants; addiction, abuse, and misuse; Risk Evaluation and Mitigation Strategy (REMS) access program; neonatal opioid withdrawal syndrome

Appendix D: 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. Patients should not be converted on a mcg per mcg basis between any transmucosal fentanyl products.
- 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
1,200	400	200	400
1,600	400	400	400

V. Dosage and Administration

Drug Name*	Dosing Regimen	Maximum Dose**
Fentanyl IR (Abstral)	Only 1 tablet of the appropriate strength should be used per dose, with up to 2 doses (30 minutes apart) per episode; wait at least 2 hours before treating another episode *Initial*: always 100 mcg SL unless already on Actiq (refer to prescribing information for conversion)	2 doses per episode

Drug Name*	Dosing Regimen	Maximum Dose**
	Maintenance: titrate to an effective dose (note: doses > 800 mcg have not been evaluated in clinical studies)	
Fentanyl IR (Actiq)	Only 1 unit of the appropriate strength should be used per dose, with up to 2 doses (30 minutes apart) per episode; wait at least 4 hours before treating another episode *Initial*: always 200 mcg PO consumed over 15 minutes [providers should prescribe a supply of six 200 mcg units] *Maintenance*: titrate to an effective dose	2 doses per episode
Fentanyl IR (Fentora)	Only 1 tablet of the appropriate strength should be used per dose, with up to 2 doses (30 minutes apart) per episode; wait at least 4 hours before treating another episode *Initial*: always 100 mcg placed in buccal cavity unless already on Actiq (refer to prescribing information for conversion) *Maintenance*: titrate to an effective dose; may administer SL	2 doses per episode
Fentanyl IR (Lazanda)	Up to 2 doses (30 minutes apart) per episode; wait at least 2 hours before treating another episode *Initial*: always 100 mcg (1 spray) in one nostril *Maintenance*: titrate to an effective dose (note: doses > 800 mcg have not been evaluated in clinical studies); patients should limit consumption to 4 or fewer doses per day	2 doses per episode
Fentanyl IR (Subsys)	Up to 2 doses (30 minutes apart) per episode; wait at least 4 hours before treating another episode *Initial*: always 100 mcg (1 spray) SL unless already on Actiq (refer to prescribing information for conversion) *Maintenance*: titrate to an effective dose; patients should limit consumption to 4 or fewer doses per day	2 doses per episode

*These products are not equivalent on a mcg per mcg basis with other fentanyl products; therefore, patients should not be switched on a mcg per mcg basis from any other fentanyl product.
**If more than 4 episodes of breakthrough pain are experienced per day, the dose of the long-acting opioid used for persistent underlying cancer pain should be re-evaluated.

VI. Product Availability

Drug Name	Availability
Fentanyl IR (Abstral)	Sublingual tablets: 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, 800 mcg (32 tablets per package)
Fentanyl IR (Actiq)	Solid oral transmucosal lozenges: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,200 mcg, 1,600 mcg (30 lozenges per package)
Fentanyl IR (Fentora)	Buccal tablets: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg (28 tablets per package)
Fentanyl IR (Lazanda)	Nasal spray: 5 mL bottle containing 8 sprays (100 mcL of solution per spray, delivering either 100 mcg, 300 mcg, or 400 mcg fentanyl)
Fentanyl IR (Subsys)	Sublingual spray: 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,200 mcg, 1,600 mcg

VII. References

1. Abstral Prescribing Information. Hunt Valley, MD: Pharmaceutics International, Inc.; October 2019. Available at www.abstral.com. Accessed March 2, 2021.
2. Actiq Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2019. Available at www.actiq.com. Accessed March 2, 2021.
3. Fentora Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; October 2019. Available at www.fentora.com. Accessed March 2, 2021.

4. Lazanda Prescribing Information. North Brook, IL: West Therapeutic Development, LLC; October 2019. Available at www.lazanda.com. Accessed March 2, 2021.
5. Subsys Prescribing Information. Chandler, AZ: Insys Therapeutics, Inc.; February 2020. Available at www.subsys.com. Accessed March 2, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.21.21	05.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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