

CLINICAL POLICY

Transmucosal immediate-release fentanyl



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

Reference Number: IL.PMN.127

Effective Date: 1.1.20

Last Review Date: 4.14.23

Line of Business: Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

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

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, and Subsys) 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, Lazanda, or 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 Centene Corporation[®] that 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. Member is on fentanyl transdermal patches;
4. Age \geq 16 years (for Actiq requests) OR age \geq 18 years (for 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. 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;

Approval duration:

Medicaid - 6 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cancer Pain (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);
2. Member is responding positively to therapy as evidenced by reduction in breakthrough pain, no significant toxicity.

Approval duration:

Medicaid – 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid

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 policies – CP.PMN.53 for Medicaid

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: 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 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.tirfremssaccess.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, and Subsys is always 100 mcg with the only exception being patients already using Actiq. Patients switching from Actiq to Fentora, 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

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 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
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 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

Drug Name	Dosing Regimen	Maximum Dose
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 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
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 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

V. 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 nasal spray (Lazanda)	Metered dose nasal spray: 100 mcg, 300 mcg, 400 mcg per spray Each 5 mL 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

VI. References

1. Actiq Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2021. Available at www.actiq.com. Accessed January 11, 2023.
2. Fentora Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; November 2022. Available at www.fentora.com. Accessed January 11, 2023.

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3. Lazanda Prescribing Information. North Brook, IL: West Therapeutic Development, LLC; March 2021. Available at www.lazanda.com. Accessed January 11, 2023.
4. Subsys Prescribing Information. Chandler, AZ: Insys Therapeutics, Inc.; April 2021. Available at www.subsys.com. January 11, 2023.
5. Aronoff GM, Brennan MJ, Pritchard DD, et al. Evidence-based oral transmucosal fentanyl citrate (OTFC) dosing guidelines. *Pain Medicine*. 2005;6(4):305-14.
6. Micromedex[®] Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 28, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created, adapted from CP.PMN.127 Fentanl IR (Abstral, Actiq, Fentora, Lazanda, Subsys) policy.	11.21.19	1.7.20
2Q2021 annual review: Updated <i>Appendix B: Contraindications/Boxed Warnings</i> ; Updated <i>Appendix C: General Information</i> ; Updated table Dosage and Administration; Reviewed and updated references		
2Q2022 annual review: no significant changes; references reviewed and updated	8.2.22	
2Q 2023 annual review: no significant changes; removed references to Abstral due to discontinuation of product; references reviewed and updated.	4.14.23	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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