

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

Reference Number: CP.PMN.127

Effective Date: 06.01.15

Last Review Date: 05.18

Line of Business: Medicaid, Commercial, HIM\*

[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<sup>®</sup>, Fentora<sup>®</sup>), fentanyl sublingual (Abstral<sup>®</sup>), fentanyl nasal spray (Lazanda<sup>™</sup>), fentanyl sublingual spray (Subsys<sup>™</sup>).

---

*\*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 ( $\geq 16$  years old for Actiq and  $\geq 18$  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 Centene Corporation<sup>®</sup> 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;
4. Age  $\geq$  16 years (for Actiq requests) OR age  $\geq$  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;
7. 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;
8. For Actiq requests on the HIM plan: dose does not exceed 4 lozenges per day.

**Approval duration:**

**HIM** – Actiq for 6 months (*Refer to HIM.PA.103 for Abstral, Fentora, Lazanda, Subsys*)

**Medicaid/Commercial** - 6 months

**B. Other diagnoses/indications**

1. 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.CPA.09 for commercial and HIM.PHAR.21 for health insurance marketplace.

**II. Continued Therapy**

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by reduction in breakthrough pain, no significant toxicity;

**Approval duration:**

**HIM** - Actiq for 12 months (*Refer to HIM.PA.103 for Abstral, Fentora, Lazanda, Subsys*)

**Commercial/Medicaid** - 12 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 12 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.CPA.09 for commercial and HIM.PHAR.21 for health insurance marketplace.

**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.CPA.09 for commercial and HIM.PHAR.21 for health insurance marketplace.

**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.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
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.tirfremssaccess.com/TirfUISplashWeb/index.html](http://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. 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	Varies  Use of more than 3 lozenges/buccal films/tablets per day

Drug Name	Dosing Regimen	Maximum Dose
	at least 4 hours before taking another dose. Maximum: 4 tablets simultaneously	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 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.	Varies  Use of more than 3 lozenges/buccal films/tablets per day indicates the need to increase the dose of fentanyl transdermal patches
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](http://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](http://www.fentora.com). Accessed February 21, 2018.
3. Abstral [Prescribing Information] Hunt Valley, MD: Pharmaceutics International, Inc.; December 2016. Available at [www.abstral.com](http://www.abstral.com). Accessed February 21, 2018.
4. Lazanda [Prescribing Information] Newark, CA: Depomed, Inc.; March 2017. Available at [www.lazanda.com](http://www.lazanda.com). Accessed February 21, 2018.
5. Subsys [Prescribing Information] Chandler, AZ: Insys Therapeutics, Inc.; December 2016. Available at [www.subsys.com](http://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
HIM: changed guidelines to new format	05.01.16	05.16
HIM: Clinical changes made to criteria: Updated criterion related to “Documented severe chronic pain requiring around-the-clock analgesia” to “Currently receiving an extended-release opioid analgesic”; Added requirement related to trial and failure of 2 formulary short acting narcotic analgesics unless contraindicated or clinically significant side effects are experienced. Non-clinical changes made to criteria: Converted to new template; Added quantity limit; References updated.	01.01.17	02.18
Commercial: Converted to new template. Minor changes to verbiage and grammar. References updated. Lazanda: added 300 mcg strength.	06.13.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: no significant changes from previously approved corporate policy; policies combined for HIM Commercial lines of business; Medicaid added; Commercial: added requirement for 2 immediate-release formulary opioid agents; changed approval durations to 6 months/12 months from Length of Benefit. HIM: replaced the requirement for a long-acting opioid analgesic with a requirement for concurrent use of fentanyl transdermal patches and added the requirement of a treatment plan; Changed initial approval duration to 6 months from 12 months; references reviewed and updated.	02.21.18	05.18

**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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene<sup>®</sup> and Centene Corporation<sup>®</sup> are registered trademarks exclusively owned by Centene Corporation.