Medication Policy Manual

# Topic:
- Fentanyl-containing medications:
  - Actiq®, fentanyl citrate oral transmucosal lozenges
  - Abstral® fentanyl sublingual tablets
  - Fentora®, fentanyl buccal tablet
  - Fentanyl citrate oral transmucosal lozenges (generic)
  - Lazanda™, fentanyl nasal spray
  - Onsolis™ fentanyl buccal soluble film
  - Subsys™ fentanyl sublingual spray

Policy No: dru073

# Date of Origin:
July 12, 2002

Committee Approval Date: September 16, 2013

Next Review Date: September 2014

Effective Date: October 1, 2013

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

**Benefit determinations should be based in all cases on the applicable contract language.** To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

The fentanyl transmucosal products Actiq (lozenge), Abstral (sublingual tablet), Fentora (buccal tablet), Lazanda (nasal spray), Onsolis (buccal film), and Subsys (sublingual spray) contain the same potent opioid medication used to manage breakthrough cancer pain. Treatment of acute non-cancer pain (such as migraine headaches) is not indicated due to the potential for breathing problems which can lead to death in patients who are not already taking other opioid pain medicines and whose bodies are not used to these medicines (not opioid tolerant).
Policy/Criteria

I. Most contracts require prior authorization approval of the transmucosal fentanyl products Actiq (lozenge), Abstral (sublingual tablet), Fentora (buccal tablet), Lazanda (nasal spray), Onsolis (buccal film), and Subsys (sublingual spray) prior to coverage. The transmucosal fentanyl products may be considered medically necessary when criteria A, B and C below are met.

A. Use is for breakthrough cancer pain.

AND

B. Other formulary short-acting strong narcotic analgesic alternatives (other than fentanyl) have been ineffective, not tolerated, or contraindicated. Examples include, but are not limited to, concentrated morphine oral solution, oxycodone, and hydromorphone.

AND

C. Patient is opioid tolerant and taking at least the equivalent of 60 mg of oral morphine daily (see Appendix 1).

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers all of the transmucosal fentanyl products to be self-administered medications.

B. When prior authorization is approved, fentanyl citrate oral transmucosal lozenges, fentanyl sublingual tablets, fentanyl buccal tablets, fentanyl buccal film, fentanyl nasal spray, and fentanyl sublingual spray whether alone or in combination, may be authorized in quantities of 90 total doses per month. Quantities exceeding 90 per month are considered not medically necessary.

C. Authorization shall be reviewed at least every 6 months to confirm that current medical necessity criteria are met and that the medication is effective.

III. Transmucosal fentanyl products are considered investigational when used for any condition other than breakthrough cancer pain including, but not limited to the treatment of pain associated with migraine headaches.

Position Statement

- Transmucosal fentanyl products are potent opioid medications used for the management of breakthrough cancer pain in patients who are receiving and are tolerant to opioid therapy for their underlying chronic pain. [1, 13, 16]
Due to the significant safety concerns associated with these products and lack of high quality evidence indicating superior pain relief to generic immediate-release opioids, the transmucosal fentanyl products are considered investigational for indications other than breakthrough cancer pain in opioid tolerant patients.

Breakthrough pain is defined as intermittent exacerbations of pain that can occur spontaneously or in relation to specific activity. [2]

Most patients experience fewer than three episodes of breakthrough pain daily [3]; therefore, most patients do not need more than 90 doses per month. More frequent use of rescue medication may indicate the need for re-evaluation of the overall pain regimen.

Transmucosal fentanyl products are contraindicated in the management of acute or postoperative pain because of the potential for life threatening respiratory depression. [1, 13, 16]

The prescribing information for transmucosal fentanyl products include a boxed warning that the products are to be used only in patients with cancer pain who are tolerant to opioids. [1, 13, 16]

The prescribing information for the transmucosal fentanyl products also includes a boxed warning due to differing bioavailability between dosage forms. The transmucosal fentanyl products cannot be substituted on a mcg per mcg basis. [13, 16]

**Clinical Efficacy**

Morphine is considered the gold standard for the treatment of cancer pain.

There is insufficient evidence to establish that transmucosal fentanyl is superior to oral morphine in treating breakthrough pain.

* There is one trial comparing the efficacy of oral transmucosal fentanyl citrate with morphine in the treatment of breakthrough cancer pain. [4] There is low confidence in the results of the trial because of significant flaws including different definitions of pain relief between treatment groups.

* There is one trial comparing the efficacy of nasal fentanyl with immediate-release morphine in the treatment of breakthrough cancer pain. We have uncertain confidence in the study results due to large numbers of drop-outs and because it is not clear that doses of the nasal fentanyl and MSIR were comparable. [20]

There is insufficient evidence to establish that fentanyl buccal tablet is superior to oxycodone immediate-release in treating breakthrough pain. There is low confidence in the study results of the one comparative trial due to selection bias, large numbers of drop-outs and a lack of intent to treat analysis (ITT). [21]

There is moderate certainty that transmucosal fentanyl products (Actiq, Abstral, Fentora, Lazanda, Onsolis and Subsys) relieve breakthrough cancer pain relative to placebo based on several low confidence trials that consistently reported improvement in pain relief.
There are no trials comparing fentanyl buccal tablet (Abstral), film (Onsolis) or sublingual spray (Subsys) to other short-acting, strong narcotic analgesics in the treatment in breakthrough pain.

There is low certainty that the transmucosal fentanyl products (Abstral, Fentora, Lazanda, Onsolis and Subsys) are superior to available generic alternatives.

There is insufficient evidence to establish that any short-acting opioid is superior to another, or that branded short-acting opioids are superior to available generic alternatives.

**Safety**

The long-term safety of transmucosal fentanyl products in chronic non-cancer pain conditions has not been established.

Transmucosal fentanyl products must be used in patients who are opioid tolerant (generally defined as ≥ 60 mg of morphine equivalents per day). While respiratory depression may occur at any dose, there is a greater potential risk in patients who are not opioid tolerant. [1, 13, 16]

Transmucosal fentanyl products are contraindicated in the management of acute or postoperative pain. Acute pain may include headache, migraine, and pain due to injury. [1, 13, 16]

Transmucosal fentanyl products should be limited to four or fewer doses per day once a successful dose is found. [1, 13, 16]

Transmucosal fentanyl products cannot be substituted for one another on a mcg per mcg basis as each dosage form delivers different amounts of fentanyl to the blood. [1, 13, 16-19]

### Appendix 1: Oral morphine equivalents, chronic dosing [6]

<table>
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<tr>
<th>Opioid</th>
<th>Equianalgesic Dose</th>
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<tbody>
<tr>
<td>morphine</td>
<td>60 mg per 24 hours</td>
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<tr>
<td>fentanyl</td>
<td>25 mcg per hour (transdermal)</td>
</tr>
<tr>
<td>hydrocodone</td>
<td>60 mg per 24 hours</td>
</tr>
<tr>
<td>hydromorphone</td>
<td>15 mg per 24 hours</td>
</tr>
<tr>
<td>levorphanol</td>
<td>2 mg per 24 hours</td>
</tr>
<tr>
<td>meperidene</td>
<td>600 mg per 24 hours</td>
</tr>
<tr>
<td>methadone</td>
<td>4 to 8 mg per 24 hours</td>
</tr>
<tr>
<td>oxycodone</td>
<td>30 to 40 mg per 24 hours</td>
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<tr>
<td>codeine</td>
<td>360 to 400 mg per 24 hours</td>
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Cross References

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Codes

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References


19. SUBSYS™ (fentanyl sublingual spray) prescribing information. Insys Therapeutics, Inc. Phoenix, AZ. March 2012.


21. Ashburn, MA, Slevin, KA, Messina, J, Xie, F. The efficacy and safety of fentanyl buccal tablet compared with immediate-release oxycodone for the management of breakthrough pain in opioid-tolerant patients with chronic pain. Anesth Analg. 2011 Mar;112(3):693-702. PMID: 21304148