Fenzytynyl (TIRF)
Prior Autorization Through
Generic and Quantity Limit
Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, FocusRx and KeyRx formularies.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage</th>
</tr>
</thead>
</table>
| Abstral® (fentanyl sublingual tablet) | Management of breakthrough pain in cancer patients 18 years of age and older who are already receiving, and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain | • Initial dose is always 100 mcg, with the only exception being patients already using Actiq.  
• If adequate analgesia is not obtained 30 minutes after a single dose, the patient may take only one additional dose of the same strength for that episode, as directed by their prescriber.  
• No more than 2 doses may be used to treat any episode of breakthrough pain.  
• Wait at least 2 hours before treating another episode of breakthrough pain.  
• If further dose escalation is appropriate, the package labeling provides additional details and a titration process table.  
• Once titrated to an effective dose, the patient should use only one tablet of the appropriate strength per dose.  
• Limit consumption to treat four or fewer breakthrough pain episodes per day once a successful dose is found.  
• If more than 4 breakthrough pain episodes are experienced per day, re-evaluate the dose of the |
long-acting opioid used for persistent underlying cancer pain.
- Efficacy and safety of a dose higher than 800 mcg has not been evaluated in clinical studies.
- Abstral is not equivalent on a mcg per mcg basis with other fentanyl products.

**Actiq**
(fentanyl transmucosal lozenge)®
200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, 1600 mcg

Management of breakthrough pain in cancer patients 16 years of age and older who are already receiving, and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain

- Initial dose is always 200 mcg and should be consumed over 15 minutes.
- An initial titration supply of only 6 units should be prescribed to limit the number of units in the home during titration.
- If adequate analgesia is not obtained 15 minutes after completion of the Actiq unit (30 minutes after the start of the unit), the patient may take only one additional dose of the same strength for that episode, as directed by their prescriber.
- No more than 2 doses may be used to treat any episode of breakthrough pain.
- Wait at least 4 hours before treating another episode of breakthrough pain.
- Only when a single administration of the current dose fails to adequately treat the breakthrough pain episode for several consecutive episodes, should the Actiq dose be increased.
- Once titrated to an effective dose, the patient should generally use only one Actiq unit of the appropriate strength per breakthrough pain episode.
- Limit consumption to four or fewer units per day once a successful dose is found.
- If more than 4 breakthrough pain episodes are experienced per day, re-evaluate the dose of the long-acting opioid used for persistent underlying cancer pain.
| **Fentora®**<br>(fentanyl buccal tablet) | Management of breakthrough pain in cancer patients 18 years of age and older who are already receiving, and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain | • Initial dose is always 100 mcg, with the only exception being patients already using Actiq.  
• If adequate analgesia is not obtained 30 minutes after a single dose, the patient may take only one additional dose of the same strength for that episode, as directed by their prescriber.  
• No more than 2 doses may be used to treat any episode of breakthrough pain.  
• Wait at least 4 hours before treating another episode of breakthrough pain.  
• Only when a single administration of the current dose fails to adequately treat the breakthrough pain episode for several consecutive episodes, should the Fentora dose be increased.  
• Once titrated to an effective dose, patients should generally use only one Fentora unit of the appropriate strength per breakthrough pain episode.  
• If more than 4 breakthrough pain episodes are experienced per day, re-evaluate the dose of the long-acting opioid used for persistent underlying cancer pain.  
• Fentora is not equivalent on a mcg per mcg basis with other fentanyl products. |
| 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg | | |

| **Lazanda®**<br>(fentanyl nasal spray) | Management of breakthrough pain in cancer patients 18 years of age and older who are already receiving, and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain | • Initial dose is always one 100 mcg spray (1 spray in 1 nostril).  
• If adequate analgesia is not obtained after 30 minutes, patients may use a rescue medication as directed by their prescriber (but would NOT administer another dose/spray of Lazanda at that time).  
• Wait at least 2 hours before treating another episode of breakthrough pain. |
| 100 mcg, 300 mcg, 400 mcg | | |
Management of breakthrough pain in cancer patients 18 years of age and older who are already receiving, and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain

| Subsys® (fentanyl sublingual spray) | 100 mcg, 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, 1600 mcg | • Initial dose is always 100 mcg, with the only exception being patients already using Actiq.
  • If adequate analgesia is not obtained 30 minutes after a single dose, the patient may take only one additional dose of the same strength for that episode, as directed by their prescriber.
  • No more than 2 doses should be used for any episode of breakthrough pain.
  • Wait at least 4 hours before treating another episode of breakthrough pain.
  • Only when a single administration of the current dose fails to adequately treat the breakthrough pain episode for several consecutive episodes, should the Subsys dose be increased.
  • Once titrated to an effective dose, patients should generally use only one Subsys dose of the appropriate strength per breakthrough pain episode.
  • Limit consumption to four or fewer doses per day once a successful dose is found.
  • Subsys is not equivalent on a mcg per mcg basis with other fentanyl products.

| • Limit consumption to four or fewer doses per day once a successful dose is found.
  • If more than 4 breakthrough pain episodes are experienced per day, re-evaluate the dose of the long-acting opioid used for persistent underlying cancer pain.
  • Efficacy and safety of a dose higher than 800 mcg has not been evaluated in clinical studies.
  • Lazanda is not equivalent on a mcg per mcg basis with other fentanyl products.

a – Generic equivalent available
CLINICAL RATIONALE
Transmucosal immediate release fentanyl (TIRF) products are indicated only in patients who are already receiving opioid therapy and who are tolerant to opioid therapy. Life-threatening respiratory depression and death could occur at any dose in opioid non-tolerant patients. 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 per hour of transdermal fentanyl, 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. Patients must remain on around-the-clock opioids while taking TIRF products.1-5

Safety
TIRF products carry a boxed warning for the following: 1-5
- Life-threatening respiratory depression
- Accidental ingestion, especially by children
- Concomitant use with CYP3A4 inhibitors
- Concomitant use with benzodiazepines and/or other CNS depressants
- Risk of medication errors (e.g. conversion or substitution with other fentanyl products)
- Addiction, abuse, and misuse
- Neonatal opioid withdrawal syndrome (i.e., prolonged use during pregnancy)

TIRF products have the following contraindications: 1-5
- Opioid non-tolerant patients
- Significant respiratory depression
- Management of acute or postoperative pain including headache, migraines, dental pain, or use in the emergency department
- Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction
- Known hypersensitivity to fentanyl or any other components of the agent

Abstral, Actiq, Fentora, Lazanda, and Subsys are available only through a restricted program called the TIRF REMS Access program. Outpatients, healthcare professionals who prescribe to outpatients, pharmacies, and distributors are required to enroll in the program. 1-5

For additional clinical information see Prime Therapeutics Formulary Chapter 10.2A: Opioid Analgesics.

REFERENCES
Transmucosal Immediate Release Fentanyl (TIRF) Prior Authorization (Through Generic) and Quantity Limit

TARGET AGENTS
- Abstral® (fentanyl sublingual tablet)
- Actiq® (fentanyl transmucosal lozenge)
- Fentora® (fentanyl buccal tablet)
- Lazanda® (fentanyl nasal spray)
- Subsys™ (fentanyl sublingual spray)
  a – generic fentanyl lozenge included as a target in program

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstral (fentanyl sublingual tablet)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 mcg tablet</td>
<td>65100025100710</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>200 mcg tablet</td>
<td>65100025100720</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>300 mcg tablet</td>
<td>65100025100725</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>400 mcg tablet</td>
<td>65100025100730</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>600 mcg tablet</td>
<td>65100025100740</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>800 mcg tablet</td>
<td>65100025100750</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>Actiq (fentanyl transmucosal lozenge)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 mcg lozenge</td>
<td>65100025108450</td>
<td>M, N, O, or Y</td>
<td>4 lozenges</td>
</tr>
<tr>
<td>400 mcg lozenge</td>
<td>65100025108455</td>
<td>M, N, O, or Y</td>
<td>4 lozenges</td>
</tr>
<tr>
<td>600 mcg lozenge</td>
<td>65100025108460</td>
<td>M, N, O, or Y</td>
<td>4 lozenges</td>
</tr>
<tr>
<td>800 mcg lozenge</td>
<td>65100025108465</td>
<td>M, N, O, or Y</td>
<td>4 lozenges</td>
</tr>
<tr>
<td>1200 mcg lozenge</td>
<td>65100025108475</td>
<td>M, N, O, or Y</td>
<td>4 lozenges</td>
</tr>
<tr>
<td>1600 mcg lozenge</td>
<td>65100025108485</td>
<td>M, N, O, or Y</td>
<td>4 lozenges</td>
</tr>
<tr>
<td>Fentora (fentanyl buccal tablet)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 mcg tablet</td>
<td>65100025100310</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>200 mcg tablet</td>
<td>65100025100320</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
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<tr>
<td>400 mcg tablet</td>
<td>65100025100330</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>600 mcg tablet</td>
<td>65100025100340</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>800 mcg tablet</td>
<td>65100025100350</td>
<td>M, N, O, or Y</td>
<td>4 tablets</td>
</tr>
<tr>
<td>Lazanda (fentanyl nasal spray)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 mcg/spray</td>
<td>65100025102050</td>
<td>M, N, O, or Y</td>
<td>1 bottle</td>
</tr>
<tr>
<td>300 mcg/spray</td>
<td>65100025102057</td>
<td>M, N, O, or Y</td>
<td>1 bottle</td>
</tr>
<tr>
<td>400 mcg/spray</td>
<td>65100025102060</td>
<td>M, N, O, or Y</td>
<td>1 bottle</td>
</tr>
<tr>
<td>Subsys (fentanyl sublingual spray)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 mcg spray</td>
<td>65100025000910</td>
<td>M, N, O, or Y</td>
<td>4 sprays</td>
</tr>
<tr>
<td>200 mcg spray</td>
<td>65100025000920</td>
<td>M, N, O, or Y</td>
<td>4 sprays</td>
</tr>
<tr>
<td>400 mcg spray</td>
<td>65100025000930</td>
<td>M, N, O, or Y</td>
<td>4 sprays</td>
</tr>
<tr>
<td>600 mcg spray</td>
<td>65100025000940</td>
<td>M, N, O, or Y</td>
<td>4 sprays</td>
</tr>
<tr>
<td>800 mcg spray</td>
<td>65100025000950</td>
<td>M, N, O, or Y</td>
<td>4 sprays</td>
</tr>
<tr>
<td>1200 mcg spray</td>
<td>65100025000960</td>
<td>M, N, O, or Y</td>
<td>8 sprays (4 dose packages of 2 x 600 mcg sprays)</td>
</tr>
<tr>
<td>1600 mcg spray</td>
<td>65100025000970</td>
<td>M, N, O, or Y</td>
<td>8 sprays (4 dose packages of 2 x 800 mcg sprays)</td>
</tr>
</tbody>
</table>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Target Agent will be approved when ALL of the following are met:
1. The patient has a diagnosis of chronic cancer pain due to active malignancy
   AND
2. The patient is currently opioid tolerant (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 per hour of transdermal fentanyl, 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)

AND

3. The patient is taking a long-acting opioid concurrently with the requested TIRF agent within the past 90 days

AND

4. ONE of the following:
   a. The patient is NOT currently being treated with any other TIRF agent in any other strength within the past 90 days
   OR
   b. The patient is currently being treated with another TIRF agent and/or strength within the past 90 days AND will discontinue prior to starting the requested TIRF agent

AND

5. ONE of the following:
   a. The request is for a generic TIRF agent
   OR
   b. The request is for a brand TIRF agent AND ONE of the following:
      i. The patient’s medication history includes use of at least one generic TIRF agent within the past 90 days
      OR
      ii. Information has been provided that indicates the patient is currently being treated with the requested agent within the past 90 days
      OR
      iii. The prescriber states the patient is currently being treated with the requested agent within the past 90 days AND is at risk if therapy is changed
      OR
      iv. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL generic TIRF agents

AND

6. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

7. ONE of the following:
   a. The requested quantity does NOT exceed the program quantity limit
   OR
   b. The requested quantity is greater than the program quantity limit AND ONE of the following:
      i. ALL of the following:
         1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose
         AND
         2. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
         AND
         3. Episodes of breakthrough pain cannot be controlled by modifying the dose of the maintenance long-acting opioid used for underlying persistent pain
         AND
         4. The prescriber has submitted information in support of therapy with a higher quantity (dose)
      OR
      ii. ALL of the following:
1. The requested quantity (dose) is greater than the maximum FDA labeled dose
   AND
2. Episodes of breakthrough pain cannot be controlled by modifying the dose of the maintenance long-acting opioid used for underlying persistent pain
   AND
3. The prescriber has submitted information in support of therapy with a higher quantity (dose)

**Length of Approval:** 1 month for increased dose requests during a dose titration period
Up to 6 months for all other requests
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE

The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL

The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm
   OR

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
   OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria