Criteria for Use
Fentanyl Transdermal Systems

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VHA Pharmacy Benefits Management Service and the Medical Advisory Panel

These criteria were based on the best clinical evidence currently available. The recommendations in this document are dynamic, and will be revised as new clinical information becomes available. This guidance is intended to assist practitioners in providing consistent, high-quality, cost-effective drug therapy. These criteria are not intended to interfere with clinical judgment; the clinician must ultimately decide the course of therapy based on individual patient situations.

TRANSITIONING VETERAN *(This medication is on the DoD VHA Transitional Continuity of Care Drug List. If the criterion is met, then the remainder of the criteria for use is not applicable)*

☐ Veteran is transitioning care from the Department of Defense to VHA. A VA prescriber, after assessing and consulting with the Veteran, has determined that continuing the medication is safe and clinically appropriate.

Exclusion Criteria

Patient should NOT receive transdermal fentanyl if any of the following criteria are met.

☐ Use of transdermal fentanyl is for any of the following: (1) mild pain; (2) breakthrough or intermittent pain (i.e., for as-needed / p.r.n. analgesia situations); (3) postoperative pain, including outpatient or day surgeries; and (4) pain due to acute clinical conditions / situations (e.g., acute trauma, new onset herpes zoster / shingles).

☐ Patient is not opioid-tolerant, defined as taking less than or equal to 60 mg of oral morphine daily, 20 mg of oral methadone daily, 30 mg of oral oxycodone daily, 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid, for less than one week.

☐ Hypersensitivity to fentanyl or local hypersensitivity reaction to any components of the patch that is not adequately controlled with topical medications (e.g., corticosteroids).

☐ Patient has a contraindication to opioids (e.g., significant respiratory depression, acute or severe bronchial asthma or hypercarbia, or known or suspected paralytic ileus).

Inclusion Criteria

Patient must meet all of criteria A–D to use transdermal fentanyl patches. These criteria apply to new starts only; patients stable on transdermal fentanyl should not be required to discontinue it or switch to another opioid unless there is a clinical reason for doing so.

☐ A. Patient requires around-the-clock analgesia for moderate to severe, *persistent* chronic pain

☐ B. Patient is followed by a VA or VA-contracted provider for management of transdermal fentanyl therapy.

☐ C. Transdermal Fentanyl initiation and adjustments are restricted to the Pain Clinic, Addiction Medicine, and Addiction Psychiatry Specialists with pain management expertise, Oncology for advanced cancer pain, and Hospice and Palliative Specialty Care, or in consultation with a practitioner who has the relevant knowledge and expertise. Examples of local pain management expertise include the CARA mandated Pain Team, local facility-designated pain subject matter expert, Pain Clinic providers, or Clinical Pharmacy Specialist with a pain management scope of practice

☐ D. Patient meets at least one of the following conditions:

— is unable to swallow, tolerate, or absorb oral preparations

— is unable to adhere to an oral opioid regimen because of cognitive or psychiatric impairment

— requires *chronic and relatively stable* pain management as part of end-of-life care, and twice daily or more frequent oral administration of opioids is likely to be problematic for the patient or caregiver has a documented current or past history of intolerable adverse effects to long-acting morphine and long-acting oxycodone. *Intolerable adverse effects are those that persist despite aggressive measures to alleviate them and that prevent upward titration of dosage to achieve a satisfactory level of analgesia (e.g., constipation unresponsive to aggressive use of laxatives; or nausea inadequately controlled by antiemetics or gradual dose titration).*

Additional Safety Precautions

Verify doses. For patients who are admitted to the hospital and using fentanyl patches at home, the dose should be verified during medication reconciliation.

Implement Risk Mitigation Strategies. Ensure risk mitigation strategies are in place when starting fentanyl patches per the VA/DOD Clinical Practice Guideline on the Management of Opioid Therapy (OT) for Chronic Pain (2017) https://www.healthquality.va.gov/, These strategies include an informed consent conversation covering the risks and benefits of opioid therapy as well as alternative therapies. Other strategies and their frequency should be commensurate with risk factors and include:

- Ongoing, random urine drug testing (including appropriate confirmatory testing)
- Checking state prescription drug monitoring programs
- Monitoring for overdose potential and suicidality
- Providing overdose education
- Prescribing of naloxone rescue and accompanying education

Use extra caution with orders for "125-mcg/h" patches. Healthcare providers should remain cautious about orders for a 125 mcg/hour strength because the decimal point has been overlooked at times with orders for 12.5 mcg/h patches. When ordering 12.5-mcg/h patches, get into the habit of writing "12" or twelve mcg/h to avoid decimal point confusion. For CPRS orders, consider a pop-up reminder asking, "Did you really mean one hundred twenty-five mcg/h?"

Assess concomitant use of opioids. To reduce the risk of an overdose, take into consideration any other opioids prescribed for the patient when evaluating the appropriateness of the patient's dose.

Do not cut, damage, or alter fentanyl patches prior to application.

1. Do not process orders that require cutting fentanyl patches prior to application. The prescriber must be notified of the hazard as soon as possible.
2. Advise patients receiving fentanyl patches not to cut, damage, or alter the transdermal system before use.
3. Use an alternate opioid therapy when a patient requires transdermal fentanyl in fractions of the patch sizes available.
4. Repeated requests for cutting fentanyl patches prior to application should be referred to the Pharmacy Manager for review by the facility Medication Use or Pharmacy and Therapeutics Committee.

Remove previous patches before applying the next dose. This is especially important in inpatient settings. Check the patient carefully, including in skin folds, and remove old fentanyl patches before applying a new patch. Providers may encourage patients to place patches in view on the front torso or upper arms so they can be seen when looking in the mirror.

Avoid external heat on patch application site. All patients and their caregivers should be advised to avoid exposing the fentanyl patch application site to direct external heat sources, such as heating pads or electric blankets, heat lamps, saunas, hot tubs, and heated water beds, etc., while wearing the system. Avoid taking hot baths and sunbathing. Patients who develop fever or increased core body temperature (e.g., from strenuous exertion) should be monitored for opioid toxicity. There is a potential for temperature-dependent increases in fentanyl released from the system resulting in possible overdose and death.

Remove fentanyl transdermal patches prior to MRI. Advise patients to remove the patch temporarily during MRI and replace with a new one after the procedure (ISMP Medication Safety Alert, April 8th, 2004; http://www.ismp.org/Newsletters/acutecare/articles/20040408.asp)

Reduce the dose of fentanyl or CNS depressants when used concomitantly. The concomitant use of fentanyl transdermal system with other central nervous system depressants, including but not limited to other opioids, sedatives, hypnotics, tranquilizers (e.g., benzodiazepines), general anesthetics, phenothiazines, skeletal muscle relaxants, and alcohol, may cause respiratory depression, hypotension, and profound sedation or potentially result in coma. The VA/DOD Clinical Practice Guideline on the Management of Opioid Therapy (OT) for Chronic Pain (2017) https://www.healthquality.va.gov/, recommends against the concurrent use of opioids and benzodiazepines. When such combined therapy is contemplated, consider tapering one or both when risks exceed benefits and obtaining specialty consultation.

Use caution with concomitant CYP3A4 inhibitors. Patients receiving transdermal fentanyl and potent CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, ketoconazole, nefazodone, ritonavir, troleandomycin) should be carefully monitored for an extended period of time and dosage adjustments should be made if warranted, particularly when CYP3A4 inhibitors are added to existing transdermal fentanyl therapy or when the dose of a CYP3A4 inhibitor is increased.

Use extra caution when converting to or from fentanyl patches. Overestimating the transdermal fentanyl dose when converting patients from another opioid medication to transdermal fentanyl patches can result in fatal overdose with the first dose. *The conversion table in the Package Insert is unidirectional (i.e., from other opioids TO transdermal fentanyl). Do not use the conversion table in the Package Insert to convert patients FROM transdermal fentanyl to other opioids because the dosing table is conservative and may result in opioid toxicity if used in this manner.*

Provide and document mandatory patient education. Educate patient and / or caregiver on how to use the transdermal fentanyl patch; provide and review the patient *Medication Guide,*[1] and document this mandatory education in the patient's medical record. Also provide and view the *Patient Instructions for Use.*[1] In inpatient and outpatient settings, the discussion should include, at the minimum, indications; high potency; dose; safety precautions (e.g., avoid heating pads or hot tubs, remove old patch before application of a new patch); application, removal, and disposal processes; and signs of fentanyl toxicity. Emphasize the need to store medication in a **locked secure place** at work and home, out of the reach of children (and pets); the potential for fatal respiratory depression from fentanyl that still remains in used patches; and the suggestion to avoid application of the patch in front of children since children sometimes imitate adults. Pharmacists could use this counseling opportunity to verify that the patient is opioid-tolerant and being treated for chronic pain.

Allow adequate time for recovery from any fentanyl toxicity. Because the mean elimination half-life of transdermal fentanyl is 17 hours, patients who are thought to have had a serious adverse event, including overdose, will require monitoring and treatment for at least 24 hours after removal of patch(es).

Inform pregnant and lactating women that fentanyl may be harmful to babies. There are no adequate and well-controlled studies in pregnant women (Pregnancy Category C). Use fentanyl during pregnancy only if the potential benefit justifies the potential risk to the fetus. Fentanyl is not recommended for analgesia during labor and delivery. Fentanyl is not recommended for use in nursing women because of potential risks to their infants. Consult Product Information for further information.

DOSING AND ADMINISTRATION

Additional dosing information can be found in the *Fentanyl Transdermal Patch Dosing and Safety Information Paper* available at the VHA Pain Management Web site: http://www1.va.gov/Pain_Management/.

Fentanyl TDS is available in the following strengths: 12.5mcg/h, 25mcg/h, 50mcg/h, 75mcg/h, 100mcg/hr

Initial Dose

- **Transdermal fentanyl should NOT be used in opioid-naïve persons. It should only be started in patients who are opioid-tolerant; therefore, the initial dose is actually an initial *conversion dose*. See table for initial conversion doses below.**
- Initial conversion doses should be individualized. Conversion dosage requirements can vary widely between individuals and therefore it is difficult to recommend a fixed method for conversion. The patient's medical condition, the potency, dose, and type of previous opioid, the patient's degree of opioid exposure and tolerance, the patient's past analgesic response and adverse experiences, and the accuracy and reliability of opioid conversion factors may all influence the choice of starting dose.
- *Overestimating the transdermal fentanyl dose when converting patients from another opioid can result in fatal overdose with the first dose.*
- *Use caution in elderly, cachectic or debilitated patients as they may have altered pharmacokinetics due to poor fat stores, muscle wasting, or altered clearance*
- Since there is a delay in analgesic effects after the initial patch application, providers should consider providing the patient with short-acting analgesics to take on an as-needed basis until the patient achieves sufficient analgesic effects from the fentanyl patch (1 to 2 days)

Conversion of an oral opioid medication TO transdermal fentanyl

- *Table 1 conversions are unidirectional. Use Table 1 to convert patients from other opioids TO transdermal fentanyl only. Do not use this table to convert patients from transdermal fentanyl to other opioids; doing so may result in fentanyl overdose and toxicity.*

Table 1 INITIAL CONVERSION DOSE OF TRANSDERMAL FENTANYL PATCH BASED UPON DAILY DOSE OF CURRENT OPIOID

Current Oral Opioid	Daily Dose (mg/d)			
Codeine p.o.	150–447	448–747	748–1047	1048–1347
Hydrocodone p.o.	60	——	——	——
Hydromorphone p.o.	8–17	17.1–28	28.1–39	39.1–51
Levorphanol p.o.	8–17	17.1–28	28.1–39	39.1–51
Methadone p.o.	20–44	45–74	75–104	105–134
Morphine p.o.	60–134	135–224	225–314	315–404
Oxycodone p.o.	30–67	67.5–112	112.5–157	157.5–202
Oxymorphone p.o.	20–44	45–74	75–104	105–134

[1] Duragesic *Medication Guide* and *Patient Instructions for Use:* http://www.duragesic.com/duragesic/potential_patient_information.html. Mylan's generic fentanyl TD *Patient Application Instructions:* *http://www.mylanpharms.com/pdfs/Fentanyl_application.pdf*.

	↓↓↓	↓↓↓	↓↓↓	↓↓↓
Recommended Dose of Transdermal Fentanyl Patch	**25 mcg/h**	**50 mcg/h**	**75 mcg/h**	**100 mcg/h**

Source: Duragesic Product Information, 2/08; Opana (oxymorphone ER) Product Information, 2/08

According to this conversion table, every 90 mg/d(range, 60–134 mg/d) of oral morphine or equivalent converts to approximately 25 mcg/h of transdermal fentanyl (but not necessarily vice versa). Dosage conversions are only approximate. Refer to Package Insert or other appropriate references for alternative dose conversion methods. Refer to product information on transdermal fentanyl for converting from non-oral opioids to transdermal fentanyl.

Conversion FROM transdermal fentanyl to another opioid

- There is a lack of evidence-based guidance on switching patients from transdermal fentanyl to other opioids.
- The Product Information for oxycodone CR (OxyContin®, 2007) suggests starting oxycodone CR 18 hours after removal of the transdermal fentanyl patch, using a conservative oxycodone dose of approximately 10 mg q12h of oxycodone CR for each 25 mcg/h transdermal fentanyl patch.
- After discontinuing the fentanyl patch, carefully titrate the new opioid according to the patient's clinical response, using conservative initial doses and dosage conversion ratios, and taking into consideration that serum fentanyl concentrations derived from the patch decrease by 50% every 17 hours (range, 13–22 hours). As suggested for oxycodone CR, one approach is to start the new opioid about 18 hours after the fentanyl patch has been removed.
- Providers inexperienced in converting patients from transdermal fentanyl to another opioid should consult a clinician who has experience in dosing transdermal fentanyl

Dose Titration

- The initial conversion doses shown in Table 1 above are conservative and large interpatient variability in the conversion dose exists. Further dose adjustment may be needed.
- Short-acting analgesics should also be considered for predictable, incident breakthrough pain.
- Individualize dosing frequency and assess dosage modifications on a regular basis. **The dose of transdermal fentanyl may be increased on the basis of average daily use of supplemental opioid analgesic but dosage increases should generally not be increased sooner than 3 days after the initial dose or more frequently than every 6 days (i.e., after 2 patch applications) thereafter.** Some patients require patches to be applied every 2 days (48 hours) instead of every 3 days (72 hours) to achieve adequate analgesia. An increase in the transdermal fentanyl dose should be evaluated before changing dosing intervals in order to maintain patients on a 72-hour regimen. Patients who consistently request supplementation with short acting opioids to cover third day, end-of-dosing interval worsening of pain may benefit from q48 hour dosing.
- Appropriate dosage increments should be based on the daily use of supplemental opioids with the equivalency of morphine 45 mg/d orally to a 12 mcg/h increase in the transdermal fentanyl dose. Transdermal fentanyl-12 delivers 12.5 mcg/h of fentanyl.

Guidance on High-dose Transdermal Fentanyl

- Patients requiring transdermal fentanyl doses greater than 50 mcg/h should be evaluated by a specialist in pain management, anesthesiology, palliative care, or hematology/oncology

Suggestions on Perioperative Use

- Pain experts suggest continuing transdermal fentanyl throughout the perioperative period (e.g., for inpatient and outpatient post-operative pain). Abrupt discontinuation of the patch in the peri-operaive period may lead to opioid withdrawal or uncontrolled post-operative pain.

Provider-Related Guidance

Opioid Initiation/continuation. The VA/DOD Clinical Practice Guideline on the Management of Opioid Therapy (OT) for Chronic Pain (2017) https://www.healthquality.va.gov/, recommends against initiating long-term opioid therapy for chronic pain. For patients already on long-term opioid therapy, the guidelines recommend ongoing risk mitigation strategies, assessment for opioid use disorder, and consideration for tapering when risks exceed benefits.

Opioid Tapering Guidance. If a decision is made to taper the patient off opioids, ensure screening and treatment is offered for conditions that can complicate pain management before initiating an opioid taper. These include mental health

disorders (PTSD, anxiety, depression), opioid use disorder (OUD) and other substance use disorders (SUD), medical complications (e.g. lung disease, hepatic disease, renal disease), and sleep disorders including sleep apnea. Most commonly, tapering will involve dose reductions of 5% to 20% every 4 weeks. More specific guidance on opioid tapers is provided in the PBM Academic Detailing Service publication *Opioid Taper Decision Tool*.

Identifying and Managing Opioid Use Disorder. Aberrant behaviors may become more apparent and reveal an opioid use disorder when opioids are tapered or discontinued or as tolerance develops. DSM-5 Diagnostic Criteria for OUD include the following: craving or strong desire or urge to use opioids, tolerance, withdrawal, using a larger amount of opioids or over a longer period than originally intended, spending a lot of time to obtain, use, or recover from opioids, and continued use despite physical or psychological problems related to opioids. If an OUD is suspected, patients should receive addiction focused medical management in PACT or referral to an Interdisciplinary Pain Management Team with Addiction Medicine expertise and access to Medication-Assisted Treatment, or to Primary Care Mental Health or specialty care for evaluation and treatment of OUD/SUD. If they decline, offer treatment that can meet their needs in the setting they feel most comfortable with. Specific guidance on OUD is provided in the PBM Academic Detailing Service publication A VA Clinician's Guide to Identification and Management of Opioid Use Disorder (2016) and the VA/DOD Clinical Practice Guideline for the Management of Substance Use Disorder.

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