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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	September 12, 2014
Subject:	Duragesic patch	**Page:**	1 of 11

Last Review Date: March 12, 2021

Duragesic patch

Description

Duragesic patch (fentanyl patch)

Background
The Duragesic transdermal system (patch) is used for the management of persistent, moderate to severe chronic pain in opioid-tolerant patients when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. Duragesic transdermal system is a topical patch which provides a time-released deliver of fentanyl, a full opioid agonist and schedule II controlled substance. It has an abuse potential similar to other opioid analgesics, whether used legally or illicitly (1).

As with other opioid therapies and fentanyl products, Duragesic patches have a high potential for abuse, addiction, and diversion. Duragesic patches are NOT intended for use as an as-needed analgesic (1).

Regulatory Status
FDA-approved indication: Duragesic is a transdermal formulation of fentanyl indicated for the management of persistent, moderate to severe chronic pain in opioid-tolerant patients 2 years of age and older when a continuous, around-the-clock opioid analgesic is required for an extended period of time, and the patient cannot be managed by other means such as non-steroidal analgesics, opioid combination products, or immediate-release opioids (1).

Patients considered opioid-tolerant are those who are taking at least 60 mg of morphine daily, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid for a week or longer (1).

Duragesic patches have a boxed warning regarding the abuse potential, fatal respiratory depression even in opioid tolerant patients, accidental exposure, cytochrome P450 3A4 interaction, and exposure to heat (at the application site and surrounding area) (1).

Duragesic patches should be used for individualized treatment as part of a pain management plan, and the initial dose should be selected based on the patient's medical history. Dosage titration should be based on patient's tolerance and to a level that provides adequate analgesia. It may take up to 6 days for fentanyl levels to reach equilibrium on a new dose. Therefore, evaluate patients for further titration after no less than two 3-day applications before any further increase in dosage is made. When no longer needed, tapering should occur as part of the pain management plan (1).

Avoid the use of Duragesic in patients with severe hepatic impairment or severe renal impairment. In patients with mild to moderate impairment, start with one half of the usual dosage of Duragesic and closely monitor for signs of sedation and respiratory depression (1).

Duragesic patches should not be used in the case of patients with respiratory depression or pulmonary impairment, paralytic ileus, or hypersensitivity to fentanyl. Caution should be used with hepatic or renally impaired patients and in patients with pancreatic/biliary disease. Use in children under the age of 18 should also be carefully monitored (1).

CDC guidelines find that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (2). The FDA also states that benzodiazepines "are also commonly abused and misused, often together with opioid pain relievers and other medicines" (7).

CDC guidelines finds that given uncertain benefits and substantial risks that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue longer than 3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care (2).

The CDC Guideline for Prescribing Opioids for Chronic Pain states that when starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting opioids. Clinicians should evaluate benefits and harms with

patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (2).

The American Pain Society Opioid Treatment Guidelines state that a reasonable definition for high dose opioid therapy is >200 mg daily of oral morphine (or equivalent). The Institute for Clinical Systems Improvement Chronic Pain Guideline states that among patients receiving opioids for non-malignant pain, the daily dose is strongly associated with opioid-related mortality. An average dose of 200 mg or more morphine (or equivalent) was associated with a nearly nine-fold increase in the risk of overdose relative to low doses (<20 mg of morphine or equivalent) (3-5).

The extended-release opioid drug post quantity limits are set to encompass the usual/starting dosage range recommendations in labeling, or up to one additional dose per day above the initial quantity limit without exceeding 200 MME per day (unless minimum FDA-labeled strength/dose/frequency exceeds 200 MME/day) to promote optimization of pain management, safe and effective use, and to reduce misuse, abuse, and overdose (3-5).

FDA warns that opioids can interact with antidepressants and migraine medicines to cause a serious central nervous system reaction called serotonin syndrome, in which high levels of the chemical serotonin build up in the brain and cause toxicity (see Appendix 1 for list of drugs) (3).

The FDA has determined that a REMS is necessary for all opioid analgesics intended for outpatient use to ensure that the benefits of these drugs continue to outweigh the risks. The Opioid Analgesic REMS is a strategy to reduce the risk of abuse, misuse, addiction, overdose, and deaths due to prescription opioid analgesics (6).

The safety and effectiveness of Duragesic patches in pediatric patients less than 2 years of age have not been established (1).

Related policies
Abstral, Actiq, Butrans, Extended Release Opioid Drugs, Fentanyl Powder, Fentora, Immediate Release Opioid Drugs, IR Opioid Combo Drugs, Methadone, Opioid Injectables, Opioid Powders, Suboxone Drug Class, Subsys

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Duragesic patches may be considered **medically necessary** in patients that are 2 years of age and older with pain severe enough to require daily, around-the-clock long term opioid treatment and if the conditions indicated below are met.

Duragesic patches may be considered **investigational** in patients less than 2 years of age and for all other indications.

Prior-Approval Requirements

Prior authorization is not required if prescribed by an oncologist and/or the member has paid pharmacy claims for an oncology medication(s) in the past 6 months

Age 2 years of age or older

Diagnosis

Patient must have the following:

1. Pain, severe enough to require daily, around-the–clock long term opioid treatment

AND ALL of the following:

a. Doses up to 112.5 mcg **only**: If adequate pain control **cannot** be achieved using a 72-hour regimen, an increase in the dose has been evaluated before changing dosing intervals in order to maintain patients on a 72-hour regimen
b. Prescriber has considered the risks of opioid/substance abuse or addiction in the patient
c. **NO** dual therapy with other long acting opioid analgesic(s)
d. Alternative treatment options have been ineffective, not tolerated or inadequate for controlling the pain
    i. These include non-opioid analgesic and immediate release opioids
e. Prescriber agrees to assess the benefits of pain control (i.e. Care Plan signs of abuse, severity of pain) after 3 months of therapy
f. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome

g. Prescriber agrees to participate in the Opioid Analgesic REMS program and to monitor for abuse, misuse, addiction, and overdose and discontinue if necessary
(*https://opioidanalgesicrems.com*)
h. Patient must have **ONE** of the following:
    i. Previous immediate-release opioid therapy for at least 10 days in the last 90 days
    ii. Previous extended-release opioid therapy in the past 180 days
i. **NO** other opioid at prior authorization limits
j. **NO** dual therapy with opioid addiction treatment or methadone
k. **NO** dual therapy with an anti-anxiety benzodiazepine(s)
    i. Alprazolam (Xanax)
    ii. Clonazepam (Klonopin)
    iii. Diazepam (Valium)
    iv. Lorazepam (Ativan)
    v. Oxazepam (Serax)
    vi. Chlordiazepoxide (Librium)
    vii. Clorazepate dipotassium (Tranxene)
l. **NO** cumulative morphine milligram equivalent (MME) over 300 MME

Prior – Approval *Renewal* Requirements

Age 2 years of age or older

Diagnosis

Patient must have the following:

1. Pain, severe enough to require daily, around-the–clock long term opioid treatment

AND ALL of the following:
a. **NO** dual therapy with other long acting opioid analgesic(s)
b. Prescriber agrees to assess the benefits of pain control (i.e. Care Plan signs of abuse, severity of pain) after 3 months of therapy
c. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome

d. Prescriber agrees to participate in the Opioid Analgesic REMS program and to monitor for abuse, misuse, addiction, and overdose and discontinue if necessary (*https://opioidanalgesicrems.com*)
e. **NO** other opioid at prior authorization limits
f. **NO** dual therapy with opioid addiction treatment or methadone
g. **NO** dual therapy with an anti-anxiety benzodiazepine(s)
   i. Alprazolam (Xanax)
   ii. Clonazepam (Klonopin)
   iii. Diazepam (Valium)
   iv. Lorazepam (Ativan)
   v. Oxazepam (Serax)
   vi. Chlordiazepoxide (Librium)
   vii. Clorazepate dipotassium (Tranxene)
h. **NO** cumulative morphine milligram equivalent (MME) over 300 MME

Policy Guidelines

Pre - PA Allowance

Quantity 30 patches every 90 days

***Patients will not be eligible for a Pre-PA Allowance for Extended Release (ER) if patients have **NOT** been on a previous immediate-release opioid therapy for at least 10 days in the last 90 days unless switching from another extended release opioid. Members using dual therapy with opioid addiction treatment or methadone in the last 30 days will not be eligible for Pre-PA Allowance.

****Patients are only eligible for a combination of opioids not exceeding 300 MME

Prior - Approval Limits

Dosage **Change every 72 hours**

Strength	Quantity Limit	Morphine Milligram Equivalent Daily Dosing
12.5 mcg	30 patches per 90 days **OR**	30 MME/day
25 mcg	30 patches per 90 days **OR**	60 MME/day
37.5 mcg	30 patches per 90 days **OR**	90 MME/day
50 mcg	30 patches per 90 days **OR**	120 MME/day

62.5 mcg	30 patches per 90 days **OR**	150 MME/day
75 mcg	30 patches per 90 days **OR**	180 MME/day
87.5 mcg	30 patches per 90 days **OR**	210 MME/day
100 mcg	30 patches per 90 days	240 MME/day

Maximum 3 day (72 hr) limit of any combination: 125 mcg (300 MME)

Change every 48 hours

Strength	Quantity Limit	Morphine Milligram Equivalent Daily Dosing
12.5 mcg	45 patches per 90 days **OR**	30 MME/day
25 mcg	45 patches per 90 days **OR**	60 MME/day
37.5 mcg	45 patches per 90 days **OR**	90 MME/day
50 mcg	45 patches per 90 days **OR**	120 MME/day
62.5 mcg	45 patches per 90 days **OR**	150 MME/day
75 mcg	45 patches per 90 days **OR**	180 MME/day
87.5 mcg	45 patches per 90 days **OR**	210 MME/day
100 mcg	45 patches per 90 days	240 MME/day

Maximum 2 day (48 hr) limit of any combination: 125 mcg (300 MME)

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Duragesic patches are a fentanyl dermal slow-release system. They are used to treat persistent, moderate to severe pain in patients who are opioid tolerant. They have an abuse potential similar to other opioid analgesics. Fentanyl patches are not meant for use in patients without persistent chronic pain. Duragesic patches have a boxed warning regarding the abuse potential, fatal respiratory depression even in opioid tolerant patients, accidental exposure, cytochrome P450 3A4 interaction, and exposure to heat (at the application site and surrounding area). The safety and effectiveness of fentanyl patches in pediatric patients less than 2 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of fentanyl patches while maintaining optimal therapeutic outcomes.

References

1. Duragesic patches [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; October 2019.
2. Dowell D, Haegerich T, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain. CDC Guidelines 2016.
3. FDA Safety Release. FDA Drug Safety Communication: FDA warns about several safety issues with opioid pain medicines; requires label changes. March 22, 2016.
4. Chou R, Fanciullo G, Fine P, et al. Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain The Journal of Pain 2009;10:113-130.
5. Hooten W, Timming R, Belgrade M, et al. Institute for Clinical Systems Improvement. Assessment and Manage-ment of Chronic Pain. Updated November 2013.
6. Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). Drug Safety and Availability: U.S. Food & Drug Administration. September 19, 2018.
7. FDA News Release. FDA Drug Safety Communication: FDA requiring labeling changes for benzodiazepines. September 23, 2020.

Policy History

Date	Action
September 2014	New addition to PA
February 2015	Addition of 3 new strengths (37.5, 62.5, 87.5mcg)
March 2015	Change to PA MDL to allow for use every 48 hrs. (45 per 90 days) If adequate pain control cannot be achieved using a 72-hour regimen
March 2016	Annual editorial review Policy code changed from 5.02.31 to 5.70.31
September 2016	Annual review Addition of prescriber agrees to assess the benefits of pain control (i.e. Care Plan signs of abuse, severity of pain) after 3 months of therapy; prescriber agrees to assess patient for serotonin syndrome; no dual therapy with opioid addiction treatment; no dual therapy with an anti-anxiety benzodiazepine(s): alprazolam (Xanax), clonazepam (Klonopin), diazepam (Valium), lorazepam (Ativan), oxazepam (Serax), chlordiazepoxide (Librium), clorazepate dipotassium (Tranxene)

March 2017	Annual review Addition of age limit to renewal criteria
June 2017	Addition of no dual therapy with methadone
September 2017	Annual review
February 2018	Addition of “prior authorization is not required if the member has paid pharmacy claims for an oncology medication(s) in the past 6 months”
March 2018	Annual editorial review and reference update
October 2018	Addition of Opioid Analgesic REMS requirement
November 2018	Annual review and reference update Addition of Opioid Analgesic REMS link per SME
January 2019	Addition of initiation and Pre-PA requirement of patient must have previous IR opioid therapy for at least 10 days in the last 90 days or previous ER opioid therapy
March 2019	Annual review Addition of requirement of no other opioid at prior authorization limits
December 2019	Annual review. Addition of requirement of no cumulative MME over 300 Changed maximum dosage limit to 125 mcg
March 2020	Annual editorial review and reference update. Updated Opioid Analgesic REMS link
March 2021	Annual editorial review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.

Appendix 1 - List of Serotonergic Medications

Selective Serotonin Reuptake Inhibitors (SSRIs)

paroxetine	Paxil, Paxil CR, Pexeva, Brisdelle
fluvoxamine	Luvox, Luvox CR
fluoxetine	Prozac, Prozac Weekly, Sarafem, Selfemra, Symbyax
sertraline	Zoloft
citalopram	Celexa
escitalopram	Lexapro

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

venlafaxine	Effexor XR
desvenlafaxine	Pristiq, Khedezla
duloxetine	Cymbalta
milnacipran	Savella

Tricyclic Antidepressants (TCAs)

amitriptyline	No brand name currently marketed
desipramine	Norpramin
clomipramine	Anafranil
imipramine	Tofranil, Tofranil PM
nortriptyline	Pamelor, Aventyl
protriptyline	Vivactil
doxepin	Zonalon, Silenor
trimipramine	Surmontil

Monoamine Oxidase Inhibitors (MAOIs)

isocarboxazid	Marplan
phenelzine	Nardil
selegiline	Emsam, Eldepryl, Zelapar
tranylcypromine	Parnate

Other Psychiatric Medicines

amoxapine	No brand name currently marketed
maprotiline	No brand name currently marketed
nefazodone	No brand name currently marketed
trazodone	Oleptro
buspirone	No brand name currently marketed
vilazodone	Viibryd
mirtazapine	Remeron, Remeron Soltab
lithium	Lithobid

Migraine Medicines

almotriptan	Axert
frovatriptan	Frova
naratriptan	Amerge
rizatriptan	Maxalt, Maxalt-MLT
sumatriptan	Imitrex, Imitrex Statdose, Alsuma, Sumavel Dosepro, Zecuity, Treximet
zolmitriptan	Zomig, Zomig-ZMT

Antiemetics

ondansetron	Zofran, Zofran ODT, Zuplenz
granisetron	Kytril, Sancuso
dolasetron	Anzemet
palonosetron	Aloxi

Other Serotonergic Medicines

dextromethorphan	Bromfed-DM, Delsym, Mucinex DM, Nuedexta
linezolid	Zyvox
cyclobenzaprine	Amrix
methylene blue	
St. John’s wort	
tryptophan	