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5.70.43

Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	August 14, 2015
Subject:	Butrans	**Page:**	1 of 11

Last Review Date: March 12, 2021

Butrans (buprenorphine patch)

Description

Butrans (buprenorphine patch)

Background
Butrans patch is indicated for the management of chronic pain severe enough to require daily, around-the-clock, long-acting opioid treatment for which alternative treatment options are inadequate. Butrans is a topical patch which provides time-released delivery of buprenorphine, a partial opioid agonist and schedule III controlled substance. Butrans can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when Butrans is used for treatment in situations where misuse, abuse, or diversion is a concern. Butrans is not intended for use on an as-needed pain relief basis (1).

Regulatory Status
FDA-approved indication: Butrans is a partial opioid agonist product indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate (1).

Limitations of Use:
Due to the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Butrans for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise

inadequate to provide sufficient management of pain. Butrans is not indicated as an as-needed (prn) analgesic (1).

Buprenorphine has boxed warnings for the following (1):

- Serious, life-threatening, or fatal respiratory depression may occur with use of Butrans. Monitor for respiratory depression, especially during initiation of or following a dose increase. Misuse or abuse of Butrans by chewing, swallowing, snorting or injecting buprenorphine extracted from the transdermal system will result in the uncontrolled delivery of buprenorphine and pose a significant risk of overdose and death.

- All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

- Prolonged use of opioid agonists during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening.

- Accidental exposure to even one dose of Butrans, especially by children, can result in a fatal overdose of buprenorphine.

Butrans is contraindicated in patients who have significant respiratory depression, paralytic ileus, acute or severe bronchial asthma and hypersensitivity to any of its components or the active ingredient, buprenorphine (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” (5).

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).

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 (4).

Butrans has not been studied and is not approved for use in the management of addictive disorders. Safety and effectiveness in patients under the age 18 have not been established (1).

Related policies
Abstral, Actiq, Duragesic, 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.

Butrans may be considered **medically necessary** in patients 18 years of age and older requiring management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time and if the conditions indicated below are met.

Butrans is considered **investigational** in patients below 18 year 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 18 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) or buprenorphine products
b. Prescriber is knowledgeable in the use of potent opioids for the management of chronic pain
c. Alternative treatment options have been ineffective, not tolerated or inadequate for controlling the pain
    i. These include: non-opioid analgesics and immediate release analgesics
d. Prescriber agrees to assess the benefits of pain control (i.e. Care Plan, signs of abuse, severity of pain) after 3 months of therapy
e. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome
f. 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*)
g. 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
h. **NO** other opioid at prior authorization limits
i. **NO** dual therapy with opioid addiction treatment or methadone
j. **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)
k. **NO** cumulative morphine milligram equivalent (MME) over 300 MME

Prior – Approval *Renewal* Requirements

Age 18 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 the following:

a. **NO** dual therapy with other long acting opioid analgesic(s) or buprenorphine products
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

Age 18 years of age or older

Quantity

Butrans patch -

Strength	Morphine Milligram Equivalent Daily Dosing	Quantity Limit per 84 days
5 mcg/hr	9 MME/day	12 patches per 84 days
7.5 mcg/hr	13.5 MME/day	
10 mcg/hr	18 MME/day	
15 mcg/hr	27 MME/day	
20 mcg/hr	36 MME/day	

Maximum daily limit of any combination: 20mcg/hr per day

*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

***Utilizing the highest strengths available to achieve the dosage is recommended to minimize dosing errors and improve compliance

Prior – Approval Limits

Quantity

Butrans patch

Strength	Quantity Limit per 84 days	Morphine Milligram Equivalent Daily Dosing
5 mcg/hr	24 patches per 84 days **OR**	18 MME/day
7.5 mcg/hr	24 patches per 84 days **OR**	27 MME/day
10 mcg/hr	24 patches per 84 days **OR**	36 MME/day

15 mcg/hr	12 patches per 84 days **OR**	27 MME/day
20 mcg/hr	12 patches per 84 days	36 MME/day

Maximum daily limit of any combination: 20mcg/hr per day

Duration 6 months

Prior – Approval *Renewal* Limits

Quantity

Butrans patch

Strength	Quantity Limit per 84 days	Morphine Milligram Equivalent Daily Dosing
5 mcg/hr	24 patches per 84 days **OR**	18 MME/day
7.5 mcg/hr	24 patches per 84 days **OR**	27 MME/day
10 mcg/hr	24 patches per 84 days **OR**	36 MME/day
15 mcg/hr	12 patches per 84 days **OR**	27 MME/day
20 mcg/hr	12 patches per 84 days	36 MME/day

Maximum daily limit of any combination: 20mcg/hr per day

Duration 12 months

Rationale

Summary
Butrans patch is indicated for the management of chronic pain severe enough to require daily, around-the-clock, long-acting opioid treatment for which alternative treatment options are inadequate. Butrans is a topical patch which provides time-released delivery of buprenorphine, a partial opioid agonist and schedule II controlled substance. As with other opioid therapies Butrans patch has a high potential for abuse, addiction, and diversion. Butrans is not intended for use on an as-needed pain relief basis (1).

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

References

1. Butrans [package insert]. Stamford, CT: Purdue Pharma L.P.; 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. Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). Drug Safety and Availability: U.S. Food & Drug Administration. September 19, 2018.
5. FDA News Release. FDA Drug Safety Communication: FDA requiring labeling changes for benzodiazepines. September 23, 2020.

Policy History

Date	Action
July 2015	New addition to PA
September 2015	Annual review
March 2016	Annual editorial review Policy number changed from 5.02.43 to 5.70.43
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 editorial review
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
December 2019	Annual review. Addition of requirement of no cumulative MME over 300
March 2020	Annual editorial review and reference update. Updated Opioid Analgesic REMS link
March 2021	Annual 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	