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Section:	Prescription Drugs	**Effective Date:**	January 1, 2026
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	May 22, 2015
Subject:	Methadone	**Page:**	1 of 14

Last Review Date: December 12, 2025

Methadone

Description

Dolophine (methadone oral tablets), Methadone Hydrochloride Intensol (methadone oral concentrate), Methadose* Oral Concentrate (methadone oral concentrate), Methadose* Dispersible Tablets (tablets for oral suspension)

*Prior authorization for the brand formulation applies only to formulary exceptions due to being a non-covered medication

Background
Methadone hydrochloride is a long-acting opioid agonist at mu-opioid receptors that is used to manage pain that requires long-term, daily opioid treatment when other pain treatments do not manage pain sufficiently or are not tolerated. It is also used for detoxification and maintenance treatment of opioid addiction, such as heroin or other morphine-like drugs, as part of a comprehensive plan that includes appropriate medical and social services. Methadone used to treat opioid addiction must only be dispensed by Opioid Treatment Programs approved by state authority and certified by the Substance Abuse and Mental Health Services Administration (SAMHSA) and registered by the Drug Enforcement Administration (DEA). Methadone must be used in accordance with the treatment requirements stipulated in the Federal Opioid Treatment Standards (1-5).

Maximum daily limit of methadone without a PA is 90 MME/day. Maximum daily limit of methadone with a PA is 200 MME/day.

Regulatory Status

FDA-approved indications: Methadone oral tablets (Methadose, Dolophine), methadone oral solution, methadone oral concentrate (Methadone Intensol Oral Concentrate) and methadone tablets for oral suspension are indicated for the following (1-3):

1. Management of pain severe enough to require daily, around-the clock, long-term opioid treatment and for which alternative treatment options are inadequate.
   Limitations of Use
   a. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioids, reserve methadone hydrochloride tablets, oral solution and oral concentrate 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.
   b. Methadone hydrochloride tablets, oral solution, and oral concentrate are not indicated as an as needed (prn) analgesic.
2. Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
3. Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Methadose Dispersible tablets and Methadose Oral Concentrate are indicated for the following (4-5):

1. Detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
2. Maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.

Methadone tablets, oral solution, and oral concentrate include a boxed warning for the following (1-5):

1. Respiratory depression is the chief hazard of opioid agonists, including morphine sulfate, which if not immediately recognized and treated, may lead to respiratory arrest and death. To reduce the risk of respiratory depression, proper dosing, titration, and monitoring are essential.
2. All patients treated with opioids require careful monitoring for signs of abuse, misuse, and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use. The risk for opioid abuse increases in patients with a personal or family history of substance abuse or mental illness. Patients should be assessed for the risk of developing abuse prior to the start of treatment and should be routinely monitored during therapy.

3. Prolonged use of opioid agonists during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening.
4. Treatment with methadone may cause serious arrhythmia (torsades de pointes) and QT interval prolongation. Closely monitor patients for changes in cardiac rhythm during initiation and titration of methadone hydrochloride tablets, oral solution, and oral concentrate.
5. When used to treat opioid addiction through detoxification or maintenance programs, methadone may only be dispensed by certified opioid treatment programs certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority. Certified treatment programs shall dispense and use methadone in oral form only and according to the treatment requirements stipulated in the Federal Opioid Treatment Standards (42 CFR 8.12).

Methadone 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, methadone (1-5).

As with other opioids, physical dependence, respiratory depression, and overdose may also occur; hence monitoring and frequent patient evaluation should be used as part of an overall treatment plan (1-5).

The FDA requires healthcare providers to go through the Risk Evaluation and Mitigation Strategy (REMS) program before prescribing methadone tablets, oral solution, or oral concentrate that are indicated for use as analgesics (6).

As of January 1, 2008, manufacturers of methadone hydrochloride tablets 40mg (dispersible) have voluntarily agreed to restrict distribution of this formulation to only those facilities authorized for detoxification and maintenance treatment of opioid addiction, and hospitals (7).

Methadone is a long-acting opioid whose duration of analgesic action (typically 4 to 8 hours) approximates that of morphine and has an elimination half-life that is substantially longer (typically 8 to 59 hours). Methadone's pharmacokinetic properties, coupled with high inter-patient variability in its absorption, metabolism, and relative analgesic potency necessitate a cautious and highly individualized approach to prescribing. The complexities associated with methadone dosing can contribute to cases of iatrogenic overdose, particularly during treatment initiation and dose titration. Studies indicate that methadone-related fatalities were primarily related to respiratory depression during initial treatment along with poly-substance use (8-11).

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 (9). The FDA also states that benzodiazepines "are also commonly abused and misused, often together with opioid pain relievers and other medicines" (13).

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 (9).

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) (10).

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. Prescribers should counsel patients and caregivers about the use of naloxone for opioid overdose and consider prescribing naloxone if clinically indicated (12).

The safety and effectiveness of methadone hydrochloride in pediatric patients below the age of 18 have not been established (1-5).

Related policies
Abstral, Actiq, Buprenorphine and Methadone Powders, Fentanyl Powder, Fentora, Opioid Drugs, 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.

Methadone may be considered **medically necessary** if the conditions indicated below are met.

Methadone may be considered **investigational** 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

Diagnoses

Patient must have **ONE** of the following:

1. Pain associated with cancer
2. Pain associated with sickle cell disease
3. Treatment associated with hospice, palliative, or end-of-life care

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Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Pain

   AND ALL of the following:

   a. Alternative treatment options have been ineffective, not tolerated, or inadequate for controlling the pain (i.e., non-opioid analgesics and other immediate release opioids)
   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 evaluate the patient's response to therapy before changing dose
   d. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome
   e. 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*)
   f. **NO** dual therapy with other opioids
   g. **NO** dual therapy with opioid addiction treatment
   h. **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)

i. **NO** morphine milligram equivalent (MME) over 200 MME/day
(e.g., https://www.mdcalc.com/morphine-milligram-equivalents-mme-calculator, https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf, https://www.cdc.gov/opioids/providers/prescribing/app.html)

2. Opioid addiction
AND ONE of the following:
a. Opioid addiction requiring detoxification treatment
b. Opioid addiction requiring maintenance treatment in conjunction with appropriate social and medical services

AND ALL of the following:
a. Patient will be monitored during therapy for signs and symptoms of abuse/misuse as well as compliance and the potential diversion to others
b. Patient is **NOT** taking **exclusively** for pain control
c. **NO** dual therapy with other opioids
d. **NO** dual therapy with another medication for opioid addiction
e. **NO** morphine milligram equivalent (MME) over 200 MME/day
(e.g., https://www.mdcalc.com/morphine-milligram-equivalents-mme-calculator, https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf, https://www.cdc.gov/opioids/providers/prescribing/app.html)

Prior – Approval *Renewal* 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

Diagnoses

Patient must have **ONE** of the following:
1. Pain associated with cancer
2. Pain associated with sickle cell disease
3. Treatment associated with hospice, palliative, or end-of-life care

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Pain
   AND ALL of the following:
   a. Prescriber agrees to continue to assess the benefits of pain control (i.e., care plan, signs of abuse, severity of pain) after 3 months of therapy
   b. Prescriber agrees to evaluate patient's response to therapy before changing dose
   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** dual therapy with other opioids
   f. **NO** dual therapy with opioid addiction treatment
   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** morphine milligram equivalent (MME) over 200 MME/day
      (e.g., https://www.mdcalc.com/morphine-milligram-equivalents-mme-calculator, https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf, https://www.cdc.gov/opioids/providers/prescribing/app.html)

2. Opioid addiction
   AND ALL of the following:
   a. Opioid addiction requiring maintenance treatment in conjunction with appropriate social and medical services
   b. Patient is **NOT** taking exclusively for pain control
   c. **NO** dual therapy with other opioids
   d. **NO** dual therapy with another medication for opioid addiction
   e. **NO** morphine milligram equivalent (MME) over 200 MME/day
      (e.g., https://www.mdcalc.com/morphine-milligram-equivalents-mme-calculator, https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf,

https://www.cdc.gov/opioids/providers/prescribing/app.html)

Policy Guidelines

Pre - PA Allowance

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

Quantity

- **Maximum daily limit of methadone without a PA is 90 MME/day.**

Tablets, Solutions, or Concentrates ≤ 90 MME/day

Drug Strength	Quantity	MME
Dolophine 5mg	3 units per day (Max: 270 tablets per 90 days) **OR**	70.5 MME/day
Dolophine 10mg	1 unit per day (Max: 90 tablets per 90 days) **OR**	47 MME/day
Methadone 5mg/5mL (oral solution)	15 units per day (Max: 1350 mL per 90 days) **OR**	70.5 MME/day
Methadone 10mg/5mL (oral solution)	7 units per day (Max: 630 mL per 90 days) **OR**	65.8 MME/day
Methadone Intensol 10mg/mL (oral concentrate)	1 unit per day (Max: 90 mL per 90 days)	47 MME/day

Maximum daily limit of any combination: 90MME

Prior – Approval Limits

Quantity

- The diagnoses pain associated with cancer, pain associated with sickle cell disease, or treatment associated with hospice, palliative, or end-of-life care **ONLY** are not subject to the maximum MME daily limit
- **Maximum daily limit of methadone with a PA is *200 MME/day.**

<u>Pain</u>

Tablets, Solutions, or Concentrates ≤ 200 MME/day

Opioid	Morphine Milligram Equivalent (MME) Conversion Factor*
Methadone	4.7

Maximum daily limit of any combination: 200 MME

Addiction

Tablets, Solutions, or Concentrates ≤ 200 MME/day

Drug Strength	Morphine Milligram Equivalent (MME) Conversion Factor*
Methadone	4.7
Methadose 40mg (tablet for suspension, oral) Methadone 40mg (tablet for suspension, oral) Diskets 40mg (40mg rapid dissolve, oral)	**Should only be dispensed by a methadone clinic**

Maximum daily limit of any combination: 200 MME

*Multiply the dose for each opioid by the conversion factor to determine the dose in MMEs
**MME limit does not apply to medication supplied by SAMHSA certified methadone clinics

Duration 6 months

12 months for pain associated with cancer, pain associated with sickle cell disease, or treatment associated with hospice, palliative, or end-of-life care

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Methadone hydrochloride is used in the treatment pain severe enough to require long-term, around-the-clock, daily opioid treatment for which alternative options are inadequate, detoxification treatment of opioid addiction, and maintenance treatment of opioid addiction in conjunction with appropriate social and medical services. Patients should be assessed for their risk of developing substance abuse prior to being prescribed methadone. When used for the detoxification and maintenance treatment of opioid addiction, methadone should only be prescribed by qualified physicians in conjunction with appropriate medical and social services and should only be dispensed by certified treatment programs in accordance with the treatment requirements stipulated in the Federal Opioid Treatment Standards (1-7). The MME limits in this policy do not apply to medication supplied by SAMHSA certified methadone clinics. The safety and effectiveness of methadone hydrochloride in pediatric patients below the age of 18 have not been established (1-5).

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

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Policy History

Date	Action
May 2015	Addition to PA

March 2016	Annual editorial review and reference update Policy number changed from 5.02.41 to 5.70.41
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 Addition of age requirement to the renewal section
May 2017	Addition of patient will NOT be receiving other opioids if patients currently on opioid therapy must be tapered off within 30 days and the confirmation on renewal of no opioid therapy. Also, the addition of 1 month taper for patients on opioid therapy Addition of patient is not taking exclusively for pain control to opioid addiction section Change in Standard Allowance
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
March 2019	Annual review
December 2019	Annual review. Revised quantity limits for methadone to fall within the MME allowance. Added statement that methadone 40 mg should only be dispensed by a methadone clinic
March 2020	Annual editorial review and reference update. Updated Opioid Analgesic REMS link
March 2021	Annual review
December 2021	Annual review. Per FEP, removed PA quantity limits and decreased PA limits to 200 MME per day. Added requirement “Prescriber agrees to evaluate patient’s response to therapy before changing dose.”
February 2022	Updated Pre-PA allowance with oncology step edit statement. Per FEP: added “Prescribers should counsel patients and caregivers about the use of naloxone for opioid overdose” under regulatory status, and added MME calculating links
March 2022	Annual review

March 2023	Per SME, addition to regulatory status that prescriber should consider prescribing naloxone if clinically indicated. Added statement to quantity table that the 200 MME limit does not apply to medication provided through a SAMHSA certified methadone clinic. Changed policy number to 5.70.041
May 2023	Adjusted MME for methadone per CDC update
September 2023	Annual review
December 2023	Annual review. Streamlined requirements. Added indications of cancer pain, sickle cell disease pain, and hospice/palliative/end-of-life care with an approval duration of 12 months. Removed SAMHSA requirement for opioid addiction treatment
March 2024	Annual review
December 2024	Annual review
June 2025	Annual review
December 2025	Annual review. Per FEP, Methadose concentrated 10 mg/ml and methadone 40mg tablets noted to require FE

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.

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	