Clinical Policy: Methadone Hydrochloride

Reference Number: CP.PMN.161
Effective Date: 12.01.18
Last Review Date: 11.24
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Methadone hydrochloride is an opioid agonist.

FDA Approved Indication(s)

Methadone is indicated:

- For the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.
  Limitation(s) of use:
  - 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 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.
  - Methadone tablets are not indicated as an as-needed (prn) analgesic.
- For the detoxification treatment of opioid addiction (heroin or other morphine-like drugs).
- For the maintenance treatment of opioid addiction (heroin or other morphine-like drugs), in conjunction with appropriate social and medical services.
  Limitation(s) of use:
  - Methadone products used for the treatment of opioid addiction in detoxification or maintenance programs are subject to the conditions for distribution and use required under 42 CFR 8.12.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

This policy is applicable to methadone 5 mg and 10 mg tablets for pain management. It is the policy of health plans affiliated with Centene Corporation® that methadone is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pain Management (must meet all)**:**

1. Prescribed for pain management for use around-the-clock (not prn);
2. Age ≥ 18 years;
3. Previous use of a short-acting narcotic analgesic with inadequate response (*See Appendix B)*;

4. Member meets one of the following (a, b, or c):
   a. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (see *Appendix E*);
   b. Prescribed by or in consultation with a pain management specialist, an oncologist, or for use in palliative or hospice care;
   c. Failure of fentanyl patch and morphine sulfate ER (MS Contin®), unless clinically significant adverse effects are experienced or both are contraindicated;
5. Provider confirms that member will discontinue all other around-the-clock opioids upon initiation of methadone;
6. Request does not exceed the health plan approved daily quantity limit.

Approval duration: Duration of request or 3 months (whichever is less)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Pain Management (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Prescribed for use around-the-clock (not prn);
4. Request does not exceed the health plan approved daily quantity limit.

Approval duration: Duration of request or 3 months (whichever is less)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
APAP: acetaminophen
FDA: Food and Drug Administration
prn: as-needed

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Short-acting opioid analgesics: codeine sulfate, hydromorphone, meperidine, morphine sulfate, oxycodone, tramadol, codeine/ acetaminophen (APAP), butalbital/APAP/caffeine/codeine, butalbital/aspirin/caffeine/codeine, hydrocodone/APAP, hydrocodone/ibuprofen, oxycodone/APAP, oxycodone/ibuprofen, tramadol/APAP	Varies	Not applicable

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): significant respiratory depression; acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment; known or suspected gastrointestinal obstruction, including paralytic ileus; hypersensitivity to methadone.

- Boxed warning(s):
  - Addiction, abuse, and misuse;
  - Requirement of a Risk Evaluation and Mitigation Strategy;
  - Life-threatening respiratory depression;
  - Accidental ingestion;
  - QT prolongation and serious arrhythmia;
  - Neonatal opioid withdrawal syndrome;
  - Cytochrome P450 interactions;
  - Risks from concomitant use with benzodiazepines or other CNS depressants;
  - Conditions for distribution and use of methadone products for the treatment of opioid addiction.

Appendix D: General Information
Code of Federal Regulations, Title 42, Part 8: Medications for the treatment of opioid use disorder

- Methadone products when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners, or institutions by formal agreement with the program sponsor) 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). See below for important regulatory exceptions to the general requirement for certification to provide opioid agonist treatment
- Regulatory exceptions to the general requirement for certification to provide opioid agonist treatment:
  - During inpatient care, when the patient was admitted for any condition other than concurrent opioid addiction [pursuant to 21 CFR 1306.07(c)], to facilitate the treatment of the primary admitting diagnosis.
  - During an emergency period of no longer than 3 days while definitive care for the addiction is being sought in an appropriately licensed facility [pursuant to 21 CFR 1306.07(b)].

Appendix E: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy

State	Step Therapy Prohibited?	Notes
MS	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pain management	For opioid naïve patients: 2.5 mg PO every 8 to 12 hours To convert to methadone tablets from another opioid: use available conversion factors to obtain estimated dose Titrate slowly with dose increases no more frequent than every 3 to 5 days	Not applicable

VI. Product Availability

Tablets: 5 mg, 10 mg

VII. References

1. Methadone Prescribing Information. Largo, FL: Hikma VistaPharm LLC.; May 2024. Available at: https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=4a44bde6-c348-4316-b0e0-c24b407cb823&type=pdf. Accessed August 13, 2024.
2. Dowell D, Haegerich TM, Chou R. CDC Guideline for prescribing opioids for chronic pain—United States, 2016. JAMA. 2016;315(15):1624-1645.
3. Chou R, Cruciani RA, Fiellin DA, et al.; American Pain Society; Heart Rhythm Society. Methadone safety: a clinical practice guideline from the American Pain Society and College on Problems of Drug Dependence, in collaboration with the Heart Rhythm Society. J Pain 2014;15:321–37.
4. The American Academy of Pain Medicine. The evidence against methadone as a "preferred" analgesic: A position statement from the American Academy of Pain Medicine. Available at: https://painmed.org/the-evidence-against-methadone-as-a-preferred-analgesic/. Accessed August 1, 2024.
5. Manchikanti L, Kaye AM, Knezevic NN, et al. Responsible, safe, and effective prescription of opioids for chronic non-cancer pain: American society of interventional pain physicians (ASIPP) guidelines. Pain Physician. 2017 Feb;20(2S):S3-S92.

6. Dowell D, Ragan KR, Jones CM, Baldwin GT, and Chou R. CDC clinical practice guideline for prescribing opioids for pain – United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1-95.
7. Code of Federal Regulations. Part 8 – Medications for the treatment of opioid use disorder. Last updated August 3, 2024. Available at: https://www.ecfr.gov/current/title-42/chapter-I/subchapter-A/part-8. Accessed August 1, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.21.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	06.25.21	11.21
4Q 2022 annual review: no significant changes; removed references to Dolophine as discontinued product; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.28.22	11.22
4Q 2023 annual review: added criterion that provider confirms that member will discontinue all other around-the-clock opioids upon initiation of methadone per PI; references reviewed and updated.	07.05.23	11.23
Added by-passing of redirection if state regulations do not allow step therapy in certain oncology settings along with Appendix E; added information regarding 42 CFR 8.12 to Appendix D.	06.05.24	
4Q 2024 annual review: no significant changes; references reviewed and updated.	08.01.24	11.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.