Effective Date: 9/2016
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Policy Number: C9698-A

Methadone

PRODUCTS AFFECTED

Dolophine, methadose, methadone

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Severe pain

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy wasapproved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case- by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. CHRONIC, SEVERE NON-CANCER PAIN:
   1. Member has a diagnosis of severe pain AND the same source of pain is chronic (> 6 months) in nature
      AND
   2. Documentation member is opioid-tolerant and requires around-the clock-long-term opioid treatment

AND

3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to methadone includes: patients with respiratory depression(in the absence of resuscitative equipment or in unmonitored settings), and in patients with acute bronchial asthma or hypercarbia, any patient who has or is suspected of having a paralytic ileus.
   AND
4. Prescriber attests that they have reviewed the members history for risk of QT prolongation, respiratory depression, and drug-drug interactions per FDA label
   AND
5. Prescriber attestation that non-pharmacologic therapy (e.g. physical therapy, exercise, Cognitive Behavioral Therapy, weight loss) and non-opioid therapy (e.g. topical diclofenac, nonsteroidal anti-inflammatory drugs (NSAIDs), tricyclic antidepressants (TCAs), and serotonin and norepinephrine reuptake inhibitors (SNRIs), or anticonvulsants) were maximized prior to prescribing opioids or as concurrent therapy
   AND
6. (a) FOR STATES WITH PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs): Prescriber attestation that they utilized (and will continue to utilize) the applicable State PDMP prior to issuanceof a prescription or continuation of therapy request
   OR
   (b) FOR STATES WITHOUT PDMPs: Prescriber attestation that they will review member's records ona periodic basis or as necessary to ensure no abuse or diversion
   AND
7. Prescriber agrees to administer random clinical drug testing a minimum of twice per year (*or morefrequently as appropriate for member)
   AND
8. Prescriber attestation that the member can safely take the requested dose of the requested drugbased on their current opioid use history.
   AND
9. Prescriber attestation that member has a signed Patient-Provider agreement for controlled substance therapy
   AND
10. Prescriber attests that member has a treatment plan or other measures to provide a baseline statusfor stabilization/improvement in the patient. A treatment plan may include: Pain intensity (scales or ratings), Functional status (physical and psychosocial), Patient's goal of therapy (level of pain acceptable and/or functional status), and current non- pharmacological treatment
    AND
11. Documentation that the member had an adequate trial (MINIMUM OF 2 WEEKS) and therapeuticfailure or documented intolerance to ONE formulary ORAL immediate-acting products
    AND
12. FOR DOSING REQUESTS GREATER THAN MED LIMIT (PERSTATE/LOB): Documentation that prescriber hasdiscussed the high dose with the patient, provides a therapeutic clinical rational for a dose higher than the maximum allowed MED, an appropriate titration schedule to the current dose and plan formaintenance dosing once goals are reached.

B. ACTIVE TREATMENT OF CANCER RELATED PAIN:
   1. Documentation of cancer diagnosis and need for pain therapy
      AND
   2. Documentation that the member had an adequate trial and therapeutic failure or documented intolerance to ONE preferred formulary ORAL immediate acting products

C. ACUTE PAIN:

1. ALL PRESCRIPTIONS FOR ACUTE PAIN WILL BE EXEMPT FROM THE CHRONIC PAIN CRITERIA BUT WILL BE LIMITED TO A 7 DAY SUPPLY FOR MEMBERS >18 YEARS
   AND
2. WILL BE LIMITED TO A MORPHINE EQUIVALENCE PER STATE/LINE OF BUSINESS REGULATION
   AND
3. Documentation that the member hada historic trial and therapeutic failure or documented intolerance to up to three PREFERRED FORMULARY ORAL immediate acting products at maximally tolerated doses.

D. METHADONE USE FOR OPIOID USE DISORDER: by law [Certification of Opioid Treatment Programs, 42 Code of Federal Regulations (CFR) 8], only a SAMHSA-certified treatment program (OTP) can dispense methadone for the treatment of OUD. Members taking methadone to treat OUD must receive the medication under the supervision of a practitioner. If needed please send a referral to case management for the substance use disorder support.

CONTINUATION OF THERAPY:

A. CHRONIC, SEVERE NON-CANCER PAIN:
   1. Documentation of updated treatment plan within the last 6 months
      AND
   2. (a) FOR STATES WITH PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs): Prescriber attestation that they utilized (and will continue to utilize) the applicable State PDMP prior to issuance of a prescription or continuation of therapyrequest
      OR
      (b) FOR STATES WITHOUT PDMPs: Prescriber attestation that they will review member's records on a periodic basis or as necessary to ensure no abuse or diversion
      AND
   3. Prescriber agrees to administer random clinical drug testing a minimum of twice peryear (*or more frequently as appropriate for member)
      AND
   4. Documentation of positive clinical response as demonstrated by improvement or stabilization in pain symptoms and/or pain control.
      AND
   5. FOR DOSING REQUESTS GREATER THAN MED LIMIT (PERSTATE/LOB):
      i. Dose requested is titrated down from initial authorization. If not, the prescriber has explained medical necessity for continued dosing above maximum state/line of business MME: (i) A treatment plan that includes a proposed regimen for reducing the dose of opioid or a reason is given why a dose decrease is not recommended for the member. (ii) Documentation of member's response to the requested medication (ex. decreased pain, improved level of functioning or quality of life.)
      AND
      ii. Provider has submitted an attestation that the following risk assessment was performed the WITHIN THE LAST 2 WEEKS: Checked the state's Prescription Monitoring Program/ Prescription Drug Monitoring Program (PMP/PDMP) for opioid over dosages or dangerous combinations, Reviewed a urine drug screen(UDS) or serum medication level, Offered a prescription for naloxone to patientsor patient's household if member has risk factors of prior overdose, substance use disorder, doses in excess of 90 Morphine Equivalent Dosing (MED)/ day or concomitant benzodiazepines use, For evidence of Substance use Disorder, prescriber will offer or arrange for evidence based treatment where needed AND
      iii. Documentation of sustained improvement in Pain or Function (e.g., PEG scalewith a 30% response from baseline); if no response, a tapering plan has beeninitiated to discontinue treatment

B. ACTIVE TREATMENT OF CANCER RELATEDPAIN:
   1. Documentation of positive clinical response as demonstrated by improvement or stabilization in pain symptoms and/or pain control.

DURATION OF APPROVAL:
Initial authorization: 6-months, Continuation of Therapy: 12 -months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with an oncologist, palliative care specialist or a pain specialist-
NOTE- NOTAPPLICABLE FOR ACUTE PAIN REQUESTS [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
methadone 5mg and 10mg #360 tabs/30 days
NOTE*Medications with a Morphine Equivalent Dosing (MED) > 200 for those patients without a diagnosis of cancer, end-of-life or palliative care, will require a medical director Review

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Opioid Agonists

FDA-APPROVED USES:
- 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,
- Detoxification treatment of opioid addiction (heroin or other morphine-like drugs) and Maintenance treatment of opioid addiction (heroin or othermorphine-like drugs), in conjunction with appropriate social and medical services and delivered from a certified OTP (opioid treatment program). Methadone can not be prescribed for this indication in a non-OTP setting.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Do not abruptly discontinue in a physically dependent member

Conditions for Distribution and Use of Methadone Products for The Treatment Of Opioid Addiction Code of Federal Regulations, Title 42, Sec 8

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 stateauthority. 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. Failure to abide by the requirements in these regulations may result in criminal prosecution, seizure of the drug supply, revocation of the programapproval, and injunction precluding operation of the program.

Regulatory Exceptions to The General Requirement for Certification To Provide Opioid Agonist Treatment: During inpatient care, when the member was admitted for any condition other than concurrent opioid addiction (pursuant to 21CFR 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 21CFR 1306.07(b)). Note: Outpatient maintenance and outpatient detoxification treatment may be providedonly by Opioid Treatment Programs (OTPs) certified by the Federal Substance Abuse and Mental Health Services Administration (SAMHSA) and registered by the Drug Enforcement Administration (DEA). This does not preclude the maintenance treatment of a member with concurrent opioid addiction who is hospitalized for conditions other than opioid addiction and who requires temporarymaintenance during the critical period of his/her stay, or of a member whose enrollment has been verified in a program which has been certified for maintenance treatment with methadone

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of METHADONE are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to methadone include: Hypersensitivity (e.g., anaphylaxis) to methadone or any component of the formulation; significant respiratory depression (in the absence of resuscitative equipment or in unmonitored settings); acute or severe bronchial asthma (in the absence of resuscitative equipment or in an unmonitored setting); hypercarbia; GI obstruction, including paralytic ileus (known or suspected), Documentation of allergenic cross-reactivity for opioids is limited. However, becauseof similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.

Warnings and Precautions:

- CNS depression: May cause CNS depression, which may impair physical or mental abilities; patientsmust be cautioned about performing tasks that require mental alertness (eg, operating machinery, driving).
- Constipation: May cause constipation, which may be problematic in patients with unstable angina and patients post-myocardial infarction (MI). Consider preventive measures (e.g., stool softener, increased fiber) toreduce the potential for constipation.
- Hypotension: May cause severe hypotension (including orthostatic hypotension and syncope); use withcaution in patients with hypovolemia, cardiovascular disease (including acute MI), or drugs which may exaggerate hypotensive effects (including phenothiazines or general anesthetics). Monitor for symptoms of hypotension following initiation or dose titration. Avoid use in patients with circulatory shock.
- QT prolongation: [US Boxed Warning]: QT interval prolongation and serious arrhythmias (torsades

de pointes) have occurred during treatment. Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction. Closely monitor patients with risk factors for development of QT interval (eg, cardiac hypertrophy, concomitant diuretic use, hypokalemia, hypomagnesemia), a history of cardiacconduction abnormalities, and those taking medications affecting cardiac conduction for changes in cardiac rhythm during initiation and titration of methadone. QT interval prolongation and torsades de pointes may be more commonly associated with, but not limited to, higher dose treatment >200 mg/day. QT prolongation has been reported in patients with no prior cardiac history who have received high doses of methadone. Only initiatetherapy in patients for whom anticipated benefit outweighs the risk of QT prolongation and development of dysrhythmias. Other agents should be used in patients with a baseline QTc interval ≥500 msec (Chou 2014). If methadone is continued in a patient who develops a QT interval ≥500 msec, consider decreasing the dose, discontinuing other medications that prolong the QT interval, or eliminating other risk factors (ASAM 2020).

- Respiratory depression: [US Boxed Warning]: Respiratory depression, including fatal cases, has been reported during initiation and conversion of patients to methadone, and even when the drug has been used as recommended and not misused or abused. Proper dosing and titration are essential, and methadone should onlybe prescribed by healthcare professionals who are knowledgeable in the use of methadone for detoxification and maintenance treatment of opioid addiction. Monitor for respiratory depression, especially during initiation of methadone or following a dose increase. The peak respiratory depressant effect of methadone occurs later, andpersists longer than the peak analgesic effect, especially during the initial dosing period. Carbon dioxide retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids. Patients and caregivers should be educated on how to recognize respiratory depression and the importance of getting emergency assistance immediately (eg, calling 911) in the event of known or suspected overdose.
- Serotonin syndrome: May occur with concomitant use of serotonergic agents (eg, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, triptans, tricyclic antidepressants), lithium, St. John's wort, agents that impair metabolism of serotonin (eg, monoamine oxidase inhibitors), or agents that impair metabolism of tramadol (e.g., CYP2D6 and 3A4 inhibitors). Monitor patients for serotonin syndrome such as mental status changes (eg, agitation, hallucinations, coma); autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia); neuromuscular changes (eg, hyperreflexia, incoordination); and/or GI symptoms(eg, nausea, vomiting, diarrhea).

OTHER SPECIAL CONSIDERATIONS:

Transition period/fills can be allowed for members already established on methadone therapy and/or on concurrent use of methadone AND benzodiazepine and/or muscle-relaxant as appropriate with goal of stopping concurrent therapy. Pharmacist will need to override the MED edit as appropriate for approval daily dose

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Dolophine TABS 10MG
Dolophine TABS 5MG
Methadone HCl SOLN 10MG/5ML
Methadone HCl SOLN 5MG/5ML
Methadone HCl TABS 10MG
Methadone HCl TABS 5MG
Methadone HCl TBSO 40MG
Methadone HCl Intensol CONC 10MG/ML
Methadose CONC 10MG/ML
Methadose CONC 5MG/0.5ML
Methadose TBSO 40MG
Methadose Sugar-Free CONC 10MG/ML

REFERENCES

1. Dolophine (methadone) [prescribing information]. Eatontown, NJ: West-Ward Pharmaceuticals; June2021.
2. Methadone Hydrochloride Intensol [prescribing information]. Eatontown, NJ: Hikma PharmaceuticalsUSA Inc; April 2021.
3. Methadone Hydrochloride oral solution [prescribing information]. Eatontown, NJ: West-Ward Pharmaceuticals Corp; July 2020
4. Methadone Hydrochloride tablets [prescribing information]. Largo, FL: VistaPharm Inc; September 2021.
5. Methadose oral concentrate and Methadose sugar-free oral concentrate (methadone hydrochloride)[prescribing information]. Webster Groves, MO: Mallinckrodt Inc; June 2021.
6. Methadose (methadone) tablet for oral suspension [prescribing information]. WebsterGroves, MO: SpecGx LLC; September 2021.
7. Centers for Disease Control and Prevention. 2018 Annual Surveillance Report of Drug- Related Risks and Outcomes — United States. Surveillance Special Report 2. Centers forDisease Control and Prevention, U.S. Department of Health and Human Services. Published August 31, 2018.
8. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. JAMA. 2016;315(15):1624–1645. doi:10.1001/jama.2016.1464
9. Chou, R., Cruciani, R., Fiellin, D., Compton, P., Farrar, J., & Haigney, M. et al. (2014). 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.The Journal Of Pain, 15(4), 321- 337. doi: 10.1016/j.jpain.2014.01.494
10. Chou, R., Fanciullo, G., Fine, P., Adler, J., Ballantyne, J., & Davies, P. et al. (2009). Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. TheJournal OfPain, 10(2), 113-130.e22. doi: 10.1016/j.jpain.2008.10.008