BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

METHADONE oral non-dispersible tablet

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy**: Methadone (5 mg and 10 mg non-dispersible tablet) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Individual is 18 years of age or older

  2. Individual has a confirmed diagnosis of **ONE** of the following:
     a. Cancer related pain

     b. Pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options such as **short acting immediate release opioid analgesics** and **non-opioid analgesic therapy** are ineffective, not tolerated, or inadequate to provide sufficient management of pain

3. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for at least **TWO medications** listed below:
    a. Morphine Extended Release (brand or generic)
    b. Nucynta ER tablet
    c. Oxycodone ER tablet (brand or generic)
    d. Fentanyl transdermal

4. Requested use **IS NOT** for Detoxification or Maintenance treatment of opioid addiction

5. There is documentation that coordination of care will be performed between different prescribers for **ALL** controlled substances

6. **For non-cancer pain**: For **morphine equivalent dosing (MED) greater than 180mg/day**: A dosing schedule to bring individual to a lower dosage of MED less than 180mg/day (titration schedule required)

7. **For non-cancer pain**: A **treatment plan** including:
    a. Pain intensity (scales or ratings)
    b. Functional status (physical and psychosocial)
    c. Patient's goal of therapy (level of pain acceptable and/or functional status)
    d. Current non-pharmacological treatment

8. **For non-cancer pain**: Physician-patient **pain management contract** must be provided

9. **For non-cancer pain**: Individual has been evaluated and must **not** have an active addiction to illicit substances or prescription drugs **OR** a history of risky, harmful, non-medical or inappropriate use of these and other substances that might be unhealthy, hazardous or a problem (i.e., multiple providers, multiple pharmacies, or multiple controlled substances)

10. **For non-cancer pain**: Documentation must be included for **random urine or blood tests** twice a year

11. **For non-cancer pain**: Documentation of **Prescription Drug Monitoring Program (PDMP) reviewed** by the prescriber every time a prescription for controlled substance is provided

12. **For non-cancer pain**: **ONE pharmacy (and another 24-hour closest pharmacy)** must be selected for all the controlled substances prescription services (limitation may vary by specific member's benefit plan*)

13. There is **NO** concomitant use with a benzodiazepine such as clonazepam, lorazepam, diazepam etc. **OR** there is a treatment plan to taper use and to coordinate care among all prescribers

14. There are **NO** FDA-label contraindications such as:
    a. Significant respiratory depression
    b. Acute or severe bronchial asthma
    c. Known or suspected gastrointestinal obstruction, including paralytic ileus

15. There are **NO** significant drug interactions such as:
    a. Simultaneous use of monoamine oxidase inhibitors (MAOI) or use within 14 days (e.g., phenelzine, tranylcypromine, linezolid)
    b. Simultaneous use of mixed agonist-antagonist and partial agonist opioids, such as pentazocine, nalbuphine, butorphanol, and buprenorphine

16. Requested agent is **NOT** being used in combination with any other long-acting opioid therapy

Initial approval duration:
- For pain not related to cancer will be approved at the requested dosage for 6 months
- For pain related to cancer will be approved at the requested dosage for 12 months
- For non-cancer pain, one pharmacy (and another 24-hour closest pharmacy) must be selected for all the controlled substances prescription services (limitation may vary by specific member's benefit plan*)

- **Criteria for continuation of coverage (renewal request):** Methadone (5 mg and 10 mg non-dispersible tablet) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual's pain is controlled

2. Requested use **IS NOT** for Detoxification or Maintenance treatment of opioid addiction

3. There is documentation that coordination of care is being performed between different prescribers for **ALL** controlled substances

4. Individual's condition has not progressed or worsened while on therapy and has not developed severe side effects such as:
    a. Apnea, dyspnea, epistaxis, hemoptysis, hyperventilation, hypoxia, upper respiratory infection etc.
    b. Confusion/speech disturbance
    c. Dehydration
    d. Atrial fibrillation/arrhythmia/chest pain
    e. Life threatening QT prolongation
    f. Ascites

5. **For non-cancer pain**: A **treatment plan** including:
    a. Pain intensity (scales or ratings)
    b. Functional status (physical and psychosocial)
    c. Patient's goal of therapy (level of pain acceptable and/or functional status)
    d. Current non-pharmacological treatment

6. **For non-cancer pain**: Physician-patient **pain management contract** must be provided

7. **For non-cancer pain**: Individual has been evaluated and must **not** have an active addiction to illicit substances or prescription drugs **OR** a history of risky, harmful, non-medical or inappropriate use of these and other substances that might be unhealthy, hazardous or a problem (i.e., multiple providers, multiple pharmacies, or multiple controlled substances)

8. **For non-cancer pain**: Documentation must be included for **random urine or blood tests** twice a year

9. **For non-cancer pain**: Documentation of **Prescription Drug Monitoring Program (PDMP) reviewed** by the prescriber every time a prescription for controlled substance is provided

10. **For non-cancer pain**: **ONE pharmacy (and another 24-hour closest pharmacy)** must be selected for all the controlled substances prescription services (limitation may vary by specific member's benefit plan*)

11. There is **NO** concomitant use with a benzodiazepine such as clonazepam, lorazepam, diazepam etc. **OR** there is a treatment plan to taper use and to coordinate care among all prescribers

12. Requested agent is **NOT** being used in combination with any other long-acting opioid therapy

13. There are no significant drug interactions such as:
    a. Simultaneous use of monoamine oxidase inhibitors (MAOI) or use within 14 days (e.g., phenelzine, tranylcypromine, linezolid)
    b. Simultaneous use of mixed agonist-antagonist and partial agonist opioids, such as pentazocine, nalbuphine, butorphanol, and buprenorphine

Renewal duration:
- For pain not related to cancer will be approved at the requested dosage for 12 months
- For pain related to cancer will be approved at the requested dosage for 12 months
- For non-cancer pain, one pharmacy (and another 24-hour closest pharmacy) must be selected for all the controlled substances prescription services (limitation may vary by specific member's benefit plan*)

*For Qualified Health Plans (**QHP**) for Individuals/Families and Small Groups:
"Narcotics Designated Network Program" is a program that requires certain members taking narcotic medications to obtain prescriptions for all covered narcotic medications from one designated eligible physician or other provider and to obtain all covered narcotic medications from one network pharmacy designated by BCBSAZ and/or the PBM.

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

- **Patients should be tapered off or dosage lowered if any of the following apply: See "Definitions" section for Tapering guidelines**
  - There is a history of risky, harmful, non-medical or inappropriate use of these and other substances that might be unhealthy, hazardous or a problem (i.e.; multiple providers, multiple pharmacies, or multiple controlled substances)
  - The patient makes no progress toward therapeutic goals

- **For all patients receiving more than 200 mg morphine or equivalent per 24 hours: See "Definitions" section for Tapering guidelines**
  - Taper patient to a lower dosage
  - Provide a Naloxone prescription to avoid side effects
  - Initiate/augment non-opioid treatments

- Provide GH/Case management support to help with the taper

Description:

Methadone (5 mg and 10 mg non-dispersible tablets) is indicated for use in the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Methadone should be reserved for use in patients for whom alternative treatment options (e.g., non-opioid analgesics, immediate release opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. In addition, methadone is **not** indicated for use as an as-needed analgesic.

Methadone is also FDA-approved for detoxification and maintenance treatment of opioid addiction. When used for the treatment of opioid addiction in detoxification or maintenance programs, it is dispensed **only** by opioid treatment programs (agencies, practitioners, or institutions by formal agreement with the program sponsor) that are certified by the Substance Abuse and Mental Health Services Administration (SAMHSA) and approved by the 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).

Most long-acting opioids are associated with boxed warnings regarding the potential for abuse and misuse, life-threatening respiratory depression, neonatal opioid withdrawal syndrome, interaction with alcohol, and accidental ingestion risks. Methadone products have additional boxed warnings regarding life-threatening QT prolongation.

Pain is a subjective episode described as an unpleasant, multi-dimensional, sensory, and emotional experience associated with actual or potential tissue damage or described in relation to such damage. The perception of pain is further influenced by physical, psychological, social, cultural, and hereditary factors. Persistent pain will often require treatment with regularly scheduled analgesics and supplemental analgesics for breakthrough periods.

Chronic pain can be defined as any pain that persists beyond the anticipated time of normal tissue healing, which is generally assumed to be three months. Chronic pain may be caused by numerous medical conditions and syndromes with widely divergent pathophysiology.

Opioid analgesic medications relieve a wide variety of pain syndromes and are generally accepted for the treatment of severe acute pain and chronic pain related to active cancer. In contrast, the use of chronic opioid therapy to treat other types of chronic pain not associated with malignancy remains controversial. There is a large amount of clinical experience with opioids for the treatment numerous pain syndromes, yet there are limited data on the safety and efficacy of long-term opioid therapy for chronic non-cancer pain.

There are many agents available with brand and generic options for the treatment of pain. Several agents are available as both immediate- (or short-) acting and long-acting formulations. There are clinically meaningful differences in potency, time to onset, elimination, and duration of action among the various compounds.

Long-acting opioids are more convenient than short-acting opioids for the treatment of chronic pain conditions, although there is no reliable evidence of their superiority. There is no reliable comparative evidence demonstrating that one long-acting opioid is more effective than another opioid analgesic, including immediate-acting or other long-acting formulations.

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Specific central nervous system (CNS) opiate receptors and endogenous compounds with morphine-like activity have been identified throughout the brain and spinal cord and are likely to play a role in the expression and perception of pain. Opioid receptors have also been identified within the peripheral nervous system (PNS). The primary site of therapeutic action of opioids is within the CNS. Opioid agonists are thought to reduce pain by acting primarily through interaction with opioid mu-receptors located in the brain, spinal cord, and smooth muscle. Opioid agonists produce respiratory depression by direct action on the brain stem respiratory center.

All opioids have the potential to cause respiratory depression, abuse and physical dependence. None have been proven to be safer than another. One method employed by manufacturers to mitigate abuse of opioids has been formulating products that are difficult to extract the main opioid ingredient from the original form. No opioid formulation or reformulation prevents use of large dosage units which is the most common method of abuse. There is concern that use of abuse deterrent formulations may shift use to other opioids, including heroin.

Providers should individualize treatment of pain in every case, using non-opioid analgesics, opioids on an as needed basis, combination products, and when appropriate chronic opioid therapy in a progressive comprehensive plan of pain management.

The World Health Organization's (WHO) guidelines for cancer pain management recommends a three-stepped approach with consideration for the type of pain and response to therapy. Initial therapy includes non-opioid analgesics such as non-steroidal anti-inflammatory drugs (NSAIDs). For mild to moderate pain, oral combinations of acetaminophen and NSAIDs with opioids are recommended. For moderate to severe pain, opioid analgesics are recommended. Titration of dose and frequency is individualized to the patient's response and development of adverse effects. For patients with inadequate pain relief and intolerable opioid-related toxicity/adverse effects, a switch to an alternative opioid may be an option for obtaining symptomatic relief.

The National Comprehensive Cancer Network (NCCN) 2015 Clinical Practice Guideline in Oncology: Adult Cancer Pain outlines numerous steps in managing opioid medications in cancer pain that can be adapted for non-cancer pain management. Examples of some of the recommendations include: use short-acting opioid medications for titration, for persistent pain initiate regular schedule of opioid with a rescue dose as needed, calculate opioid dose increase based on the total 24-hour dose (around the clock/scheduled and as needed doses), when possible, use the same short-acting and long-acting opioid formulation, and simplify regimen for improved adherence.

In theory, opioids have no maximum or ceiling dose; however recent guidelines suggest close evaluation of individuals using large doses of opioid medications to identify unique opioid related adverse effects. Morphine is a full opioid agonist and is relatively selective for the mu-opioid receptor, although it can bind to other opioid receptors at higher doses.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

CDC Recommendations for Opioid Prescribing for Chronic Pain:

A. Determining when to initiate or continue opioids for chronic pain

1. Opioids are not first-line or routine therapy for chronic pain
2. Establish and measure goals for pain and function

3. Discuss benefits and risks and availability of non-opioid therapies with patient

B. Opioid selection, dosage, duration, follow-up, and discontinuation

1. Use immediate-release opioids when starting
2. Start low and go slow - Use caution at any dose and avoid increasing to high dosages
3. When opioids are needed for acute pain, prescribe no more than needed
    - Do NOT prescribe ER/LA opioids for acute pain
4. Follow-up and re-evaluate risk of harm; reduce dose or taper and discontinue if opioids cause harm or are not helping

C. Assessing risk and addressing harms of opioid use

1. Evaluate risk factors for opioid-related harms
2. Check CSPMP for high dosages and prescriptions from other providers at the beginning of the treatment and at least quarterly while on the opioid treatment
3. Use urine drug testing to identify prescribed substances and undisclosed use
4. Avoid concurrent benzodiazepine and opioid prescribing
5. Arrange treatment for opioid use disorder if needed

Prescriber Education:

A. **Guidelines for Prescribing Opioids for Chronic Pain**
https://www.cdc.gov/drugoverdose/pdf/TurnTheTide_PocketGuide-a.pdf
http://www.agencymeddirectors.wa.gov/Files/FY16-288SummaryAMDGOpioidGuideline_FINAL.pdf
https://www.cdc.gov/drugoverdose/pdf/Guidelines_Factsheet-a.pdf

B. **Checklist for prescribing opioids for chronic pain**
https://www.cdc.gov/drugoverdose/pdf/PDO_Checklist-a.pdf

C. **Tapering Opioids for Chronic Pain**
https://www.cdc.gov/drugoverdose/pdf/Clinical_Pocket_Guide_Tapering-a.pdf

D. **Non-Opioid Treatments**
https://www.cdc.gov/drugoverdose/pdf/nonopioid_treatments-a.pdf

E. **Assessing Benefits and Harms of Opioid**
https://www.cdc.gov/drugoverdose/pdf/Assessing_Benefits_Harms_of_Opioid_Therapy-a.pdf

F. **Calculating Total Daily Dose of Opioids for Safer Dosage**
https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

G. **Checking Controlled Substances Prescription Monitoring Program (CSPMP)**
https://arizona.pmpaware.net/login
https://pharmacypmp.az.gov/

H. **Educational Webinar Series for Prescribers**
https://www.cdc.gov/drugoverdose/pdf/COCA-webinar-series-allslides-a.pdf
https://www.cdc.gov/drugoverdose/prescribing/trainings.html
http://www.coperems.org/

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I. **CDC Guideline for Prescribing Opioids for Chronic Pain**
https://www.cdc.gov/drugoverdose/prescribing/clinical-tools.html

J. **Washington State Opioid Taper Plan Calculator**
www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf

K. **Tapering Long-Term Opioid Therapy in Chronic Non-Cancer Pain**
www.mayoclinicproceedings.org/article/S0025-6196(15)00303-1/fulltext

L. **UpToDate**
https://www-uptodate-com

Sustained release (SR) and extended release (ER) and controlled release (CR) formulation:
A dose form where active drug is released slowly over a prolonged period of time thereby allowing for less frequent administration throughout the day
Also known as long-acting formulation

Immediate release formulation:
A dose form where active drug is released quickly over a short period of time and usually requires more frequent/multiple administration throughout the day
Also known as short-acting formulation

Opioid Risk Assessment Tool:

Score each that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Rx drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Rx drugs	5	5
Age between 16-45 years	1	1
History of preadolescent sexual abuse	3	0
Psychological disorders		
ADD, OCD, Bipolar, Schizophrenia	2	2
Depression	1	1
Total score		
Assessment of risk		
Low risk for abuse	≤ 3	
Moderate risk for abuse	4-7	
High risk for abuse	≥ 8	
Definitions of risk		
Low = unlikely to abuse Moderate = as likely will as will not abuse High = likely to abuse		

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Resources:

Methadone non-dispersible tablet product information, revised by Hikma Pharmaceuticals USA, Inc. 01-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R: CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. MMWR Recomm Rep. 2022;71(3):1. Epub 2022 Nov 4. Accessed April 17, 2023. Re-evaluated March 21, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.