

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

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 precertification 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:** Levorphanol tartrate is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
 1. Individual is 18 years of age or older
 2. A confirmed diagnosis of **ONE** of the following:
 - a. Cancer related pain
 - b. Confirmed diagnosis of pain severe enough to require an opioid analgesic for which other alternative treatments are inadequate
 3. Failure, contraindication per FDA label, or intolerance to **at least 2** medications listed below:
 - a. Acetaminophen (APAP) with codeine
 - b. Hydrocodone with APAP

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

- c. Hydromorphone immediate release
 - d. Morphine immediate release
 - e. Oxycodone immediate release
 - f. Oxycodone immediate release
 - g. Tramadol immediate release
4. Failure, contraindication per FDA label, or intolerance to at least **2 Non-Opioid therapies** as per diagnosis:
- a. **MIGRAINES:**
 - i. PREVENTATIVE TREATMENTS
 1. Anticonvulsant (topiramate)
 2. Beta-Blockers (propranolol, atenolol)
 3. TCAs (amitriptyline, imipramine)
 4. Calcium Channel Blockers (amlodipine, verapamil)
 5. Nonpharmacological treatments (Cognitive behavioral therapy, Relaxation, Biofeedback, Exercise therapy)
 - ii. ACUTE TREATMENTS
 1. Aspirin, acetaminophen, NSAIDS (naproxen, ibuprofen, meloxicam, diclofenac) may be combined with caffeine
 2. Anti-nausea medication (ondansetron, promethazine)
 3. Triptans - migraine-specific (rizatriptan, sumatriptan)
 - b. **NEUROPATHIC PAIN:**
 - i. TCAs (amitriptyline, imipramine)
 - ii. SNRIs (duloxetine, venlafaxine)
 - iii. Gabapentin/pregabalin (generic or brand Lyrica)
 - iv. Topical Aspercreme 4% cream or Patches
 - v. Nonpharmacological treatments (Exercise, Weight loss, patient education)
 - c. **OSTEOARTHRITIS:**
 - i. FIRST LINE
 1. Acetaminophen
 2. Oral NSAIDs (naproxen, ibuprofen, meloxicam, diclofenac)
 3. Topical NSAIDs (Diclofenac Gel)
 - ii. SECOND LINE
 1. Capsaicin
 - d. **FIBROMYALGIA:**
 - i. Duloxetine
 - ii. Pregabalin (generic or brand Lyrica)
 - iii. Gabapentin
 - iv. TCAs (amitriptyline, imipramine)
 - v. Nonpharmacological treatments (Low impact aerobic exercise such as brisk walking, swimming, water aerobics or bicycling. Cognitive behavioral therapy, biofeedback, interdisciplinary rehabilitation)
 - e. **OTHER CHRONIC PAIN INDICATION:**
 - i. Acetaminophen
 - ii. NSAIDs (e.g., naproxen, ibuprofen, meloxicam, diclofenac, etc.)

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

iii. Gabapentin

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:** Documentation must be included for **random urine or blood tests** twice a year
8. **For non-cancer pain:** Documentation of **PDMP reviewed** by the prescriber every time a prescription for controlled substance is provided
9. **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*)
10. **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 pharmacy or multiple controlled substances)
11. There is **NO** concomitant use with benzodiazepines such as clonazepam, lorazepam, diazepam etc. **OR** there is a plan to taper use and to coordinate care among all prescribers
12. There is documentation that coordination of care will be performed between different prescribers for **ALL** controlled substances
13. Absence of **ALL** FDA-label contraindications and warnings

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):** Levorphanol tartrate 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 with these products
 2. The 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.

ORIGINAL EFFECTIVE DATE: 09/21/2017 | ARCHIVE DATE: | LAST REVIEW DATE: 05/19/2022 | LAST CRITERIA REVISION DATE: 08/1/2022

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

- b. Confusion/speech disturbance
 - c. Dehydration
 - d. Atrial fibrillation/arrhythmia/chest pain
 - e. Ascites
3. **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
4. **For non-cancer pain:** Physician-patient **pain management contract** must be provided
5. **For non-cancer pain:** Documentation must be included for **random urine or blood tests** twice a year
6. **For non-cancer pain:** Documentation of **PDMP reviewed** by the prescriber every time a prescription for controlled substance is provided
7. **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*)
8. **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 pharmacy or multiple controlled substances)
9. There is **NO** concomitant use with benzodiazepines such as clonazepam, lorazepam, diazepam etc. **OR** there is a plan to taper use and to coordinate care among all prescribers
10. There is documentation that coordination of care is being performed between different prescribers for **ALL** controlled substances

Renewal duration:

For pain not related to cancer:

Levorphanol tartrate will be approved at the requested dosage for 6-months

For pain related to cancer:

Levorphanol tartrate 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.

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

- 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**
-

Description:

Levorphanol tartrate tablet is indicated for the management of moderate to severe pain where use of an opioid analgesic is appropriate. It is a potent synthetic opioid mu-receptor agonist similar in action to morphine. Like other opioid mu-receptor agonists, it is believed to act at receptors in both the brain and spinal cord to alter the transmission and perception of pain. The onset and peak analgesic effects following administration of levorphanol are similar to morphine when administered at equal analgesic doses. Levorphanol produces a degree of respiratory depression similar to that produced by morphine at equal analgesic doses, and like many opioid mu-receptor agonists, levorphanol produces euphoria or has a positive effect on mood in many individuals. Oxaydo (oxycodone hydrochloride) is an opioid agonist indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Oxycodone 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. The principal therapeutic action is analgesia.

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Oxaydo (oxycodone hydrochloride) for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or non-opioid combination products) have not been tolerated or are not expected to be tolerated, or have not provided adequate analgesia or are not expected to provide adequate analgesia.

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. There are many agents available with brand and generic options for the treatment of pain. Several of these 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. There is no reliable comparative evidence demonstrating that one opioid is more effective than another opioid analgesic.

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.

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

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. 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.

Definitions:

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
 - a. 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

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

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://pharmacympm.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/>

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](http://www.mayoclinicproceedings.org/article/S0025-6196(15)00303-1/fulltext)

L. UpToDate

<https://www.uptodate.com>

PHARMACY COVERAGE GUIDELINE

Levorphanol Tartrate oral

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		

Resources:

Levorphanol tartrate product information, revised by Lannett Company, Inc. 12/2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 21, 2022.

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.