BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

LUCEMYRA™ (lofexidine hydrochloride) 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:** Lucemyra (lofexidine) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a specialist in Addiction Medicine.

  2. Individual is 18 years of age or older.

  3. Individual has a confirmed diagnosis of **ONE** of **opioid abuse disorder, to be used for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation.**

  4. Individual is physically dependent on short acting opioid (e.g., heroin, hydrocodone, oxycodone)

5. Used in conjunction with a comprehensive management program for treatment of opioid use disorder.

6. Documented failure, contraindication per FDA label, or intolerance to **ALL** the following agents:
    a. Methadone
    b. Buprenorphine
    c. Clonidine

7. Will not be used in patients with:
    a. Severe coronary insufficiency
    b. Recent myocardial infarction
    c. Cerebrovascular disease
    d. Chronic renal failure
    e. Patients with marked bradycardia
    f. Congenital long QT syndrome

Approval duration:
14 days per treatment, maximum number of tablets of 224
No refills, each request for re-treatment to be evaluated as an initial request

- 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:

Lucemyra (lofexidine) is a central alpha-2 adrenergic agonist that binds to alpha-2A and alpha-2C receptors to reduce the release of norepinephrine and decrease sympathetic tone.

Efficacy of Lucemyra was evaluated by use of Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop) score. Scores were compared to patients given placebo. SOWS-Gossop is a patient-reported outcome (PRO) instrument that evaluates opioid withdrawal symptoms of: feeling sick, stomach cramps, muscle spasms/twitching, feeling of cold, heart pounding, muscular tension, aches and pains, yawning, runny eyes and insomnia/problems sleeping. For each opioid withdrawal symptom, patients rate their symptom severity using four response options (none, mild, moderate, and severe). The SOWS-Gossop total score ranges from 0-30 where a higher score indicates a greater withdrawal symptom severity.

Symptoms assessed using the SOWS-Gossop are recorded as absent or mild for almost all patients given Lucemyra and more patients given Lucemyra complete opioid withdrawal treatment.

There are two main strategies for the management of opioid withdrawal. The first involves providing a gradual tapering dose of an opioid agonists, using either methadone or buprenorphine. The other is the use of alpha- 2 adrenergic agonist with other non-narcotic medications to help reduce withdrawal symptoms.

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Opioid withdrawal results from over-activity of the noradrenergic system. Use of alpha-2 adrenergic agonists (clonidine, lofexidine) have a long history of use for the treatment of opioid withdrawal. Either of these agents are effective in alleviating some of the symptoms of opioid withdrawal.

Clonidine can be used at doses of 0.1–0.3 mg every 6–8 hours, with a maximum dose of 1.2 mg daily. It is often combined with other non-narcotic medications targeting other opioid withdrawal related symptoms such as use of benzodiazepines for anxiety, loperamide or bismuth-salycilate for diarrhea, acetaminophen or nonsteroidal anti-inflammatory medications (NSAIDs) for pain, various medications for insomnia, and ondansetron for nausea.

The 2015 American Society of Addiction Medicine (ASAM) National Practice Guideline for Use of Medications in the Treatment of Addiction Involving Opioid Use recommends, based on consensus opinion, the inclusion of clonidine as a practice to support opioid withdrawal. While clonidine is not US FDA-approved for the treatment of opioid withdrawal, it has been extensively used off-label for this purpose.

The 2018 Medications for opioid use disorder for healthcare professionals, policy makers, patients & families. HHS Publication No. (SMA) 18-5063PT3. U.S. Department of Health and Human Services Substance Abuse and Mental Health Services Administration Center for Substance Abuse treatment also recommends clonidine when opioid agonist medications are unavailable or not possible, to relieve withdrawal symptoms.

Definitions:

Clinical Opioid Withdrawal Scale (COWS):

Patient's name:_____	**Date and time:** ___/___/___:_____
Reason for this assessment:_____	
Resting pulse rate:_____beats/minute Measured after patient is sitting or lying for one minute	**GI upset:** Over last half-hour
0 pulse rate 80 or below 1 pulse rate 81 to 100 2 pulse rate 101 to 120 4 pulse rate greater than 120	0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: Over past half-hour not accounted for by room temperature or patient activity	**Tremor:** Observation of outstretched hands
0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness: Observation during assessment	**Yawning:** Observation during assessment
0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still l for more than a few seconds	0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment

	4 yawning several times/minute
Pupil size	**Anxiety or irritability**
0 pupils pinned or normal size for room light 1 pupil possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or joint aches: If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored	**Gooseflesh skin**
0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing: Not accounted for by cold symptoms or allergies	**Total score:**_____ The total score is the sum of all 11 items
0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Initials of person completing assessment:_____

Score: 5 to 12 = mild; 13 to 24 = moderate; 25 to 36 = moderately severe; more than 36 = severe withdrawal.
Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs 2003; 35:253.

Resources:

Lucemyra (lofexidine) product information, revised by USWM, LLC. 09-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 26, 2022.

Sevarino KA. Medically supervised opioid withdrawal during treatment for addiction. In: UpToDate, Saxon AJ, Friedman M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on April 12, 2022. Accessed July 26, 2022.

Stolbach A, Hoffman RS. Opioid withdrawal in the emergency setting. In: UpToDate, Traub SJ, Ganetsky M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on October 25, 2021. Accessed July 26, 2022.