Prior Authorization
Lucemyra® (lofexidine tablets)

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Product Identifier(s)

Effective 1/1/23 to 2/27/23: 108268

Effective 2/28/23: 63002

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

Cigna covers lofexidine (Lucemyra®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior Authorization is recommended for prescription benefit coverage of Lucemyra. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Lucemyra as well as the monitoring required for adverse events, initial approval requires Lucemyra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

FDA Indication(s)

1. **Opioid Withdrawal Symptoms.** Approve for 2 weeks (14 days) if the individual meets the following criteria (A and B):
   - **A)** Lucemyra is being used to facilitate abrupt opioid discontinuation; AND
   - **B)** Individual has a history of clonidine use (e.g., patches, tablets) and experienced unacceptable toxicity and/or inadequate efficacy.

Conditions Not Covered

Lofexidine (Lucemyra) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Cannabis Use Disorder (Cannabis Dependence)**. One published study has evaluated the safety and efficacy of dronabinol and lofexidine in treating cannabis dependence (n = 156).[7] In this 11-week, placebo-controlled study, the combined intervention did not show efficacy as a treatment for cannabis use disorder.

Background

Overview
Lucemyra, a central alpha-2 adrenergic agonist, is indicated for **mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation** in adults.[1]

Lucemyra is typically dosed four times daily during the period of peak withdrawal symptoms (generally the first 5 to 7 days following last use of opioid) with dosing guided by symptoms and adverse events.[1] Lucemyra treatment may continue for up to 14 days with dosing guided by symptoms. Discontinue Lucemyra with a gradual dose reduction over a 2- to 4-day period to mitigate Lucemyra withdrawal symptoms.

Disease Overview
Opioid use disorder is a primary, chronic and relapsing central nervous system (CNS) disease of brain reward, motivation, memory, and related circuitry characterized by an individual pathologically pursuing reward and/or relief by substance use and other behaviors.[4] Since the 1990s, opioid use and abuse have risen markedly in the US.[5] Symptoms of opioid withdrawal usually begin two to three half-lives after the last opioid dose (6 to 12 hours for short half-life opioids such as heroin and morphine and 36 to 48 hours for long half-life opioids such as methadone).[6] Following cessation of a short half-life opioid, symptoms reach peak intensity within 2 to 4 days, with most of the physical withdrawal signs no longer apparent after 7 to 14 days. The duration of withdrawal also varies with the half-life of the opioid used and the duration of use. While opioid withdrawal is rarely life-threatening, the combination of uncomfortable symptoms and intense craving makes completion of withdrawal difficult for most people.

Guidelines
The American Psychiatric Association (APA) practice guideline for the treatment of patients with substance use disorders (2006) notes several strategies as effective treatments for opioid dependence including the abrupt discontinuation of the opioid with the use of clonidine to suppress withdrawal symptoms and clonidine-naltrexone detoxification, where withdrawal symptoms are precipitated by naltrexone and then suppressed by clonidine.[2] Clonidine reduces withdrawal symptoms such as nausea, vomiting, diarrhea, cramps, and sweating.[2,3] The guidelines note that the completion rate for clonidine-treated outpatients is relatively low and roughly comparable to that of methadone withdrawal.

The American Society of Addiction Medicine (ASAM) practice guideline for the treatment of opioid use disorder (2020) discusses two primary strategies for the management of opioid withdrawal.[3] In one strategy, alpha-2 adrenergic agonists (i.e., clonidine, Lucemyra) are used along with other non-narcotic medications to reduce withdrawal symptoms. The use of non-opioid medications may be the only option available in some healthcare settings and may also assist the transition of patients to opioid antagonist medications (i.e., naltrexone) helping to prevent subsequent relapse. Comparative data are limited but Lucemyra and clonidine appear to be similarly effective in the treatment of opioid withdrawal with hypotension occurring less frequently with Lucemyra. While clonidine is not FDA-approved for the treatment of opioid withdrawal, it has been extensively used off-label for this purpose. Clonidine can be combined with other non-narcotic medications targeting specific opioid withdrawal symptoms. ASAM states that alpha-2 adrenergic agonists are safe and effective for management of opioid withdrawal. However, the guideline notes that methadone and buprenorphine are more effective in reducing the symptoms of opioid withdrawal, in retaining patients in withdrawal management, and in supporting the completion of withdrawal management.

References

1. Lucemyra® tablets [prescribing information]. Louisville, KY: US WorldMeds; May 2018.
2. Kleber HD, Weiss RD, Anton Jr., RF, et al. American Psychiatric Association practice guideline for the treatment of patients with substance use disorders, second edition. *Am J Psychiatry*. 2007;164(Suppl 4):5-123. Available at: https://psychiatryonline.org/guidelines. Accessed on July 20, 2022.
3. Cunningham C, Edlund MJ, Fishman M, et al. The American Society of Addiction Medicine National Practice Guideline for the treatment of opioid use disorder. 2020 Focused Update. Available at: https://www.asam.org/Quality-Science/quality/2020-national-practice-guideline. Accessed on July 20, 2022.
4. American Society of Addiction Medicine. Opioid addiction 2016 facts & figures. Available at: http://www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf. Accessed on July 20, 2022.
5. Dixon DW, Peirson RP. Opioid abuse. Page last updated: November 17, 2021. Available at: http://emedicine.medscape.com/article/287790-overview#showall. Accessed on July 20, 2022.
6. Gowing L, Farrell M, Ali R, et al. Alpha2-adrenergic agonists for the management of opioid withdrawal (Review). *Cochrane Database Syst Rev*. 2016;5:CD002024.
7. Levin FR, Marjani JJ, Pavlicova M, et al. Dronabinol and lofexidine for cannabis use disorder: A randomized, double-blind, placebo-controlled trial. *Drug Alcohol Depend*. 2016;159:53-60.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	No criteria changes.	07/20/2022