

## PRIOR AUTHORIZATION POLICY

**POLICY:** Lofexidine Prior Authorization Policy

- Lucemyra® (lofexidine tablets – US WorldMeds, generic)

**REVIEW DATE:** 07/31/2024; selected revision 10/02/2024

---

### OVERVIEW

Lofexidine, a central alpha-2 adrenergic agonist, is indicated for **mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation** in adults.<sup>1</sup>

Lofexidine 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.<sup>1</sup> Lofexidine treatment may continue for up to 14 days with dosing guided by symptoms. Discontinue lofexidine with a gradual dose reduction over a 2- to 4-day period to mitigate lofexidine 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.<sup>2</sup> 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).<sup>3</sup> 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 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.<sup>4</sup> In one strategy, alpha-2 adrenergic agonists (i.e., clonidine, lofexidine) are used along with other non-narcotic medications to reduce withdrawal symptoms such as nausea, vomiting, diarrhea, cramps, and sweating. 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 lofexidine and clonidine appear to be similarly effective in the treatment of opioid withdrawal with hypotension occurring less frequently with lofexidine. 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.

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of lofexidine. All approvals are provided for the duration noted below.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of lofexidine is recommended in those who meet the following criteria:

### FDA-Approved Indication

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

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of lofexidine is not recommended in the following situations:

- 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).<sup>5</sup> In this 11-week, placebo-controlled study, the combined intervention did not show efficacy as a treatment for cannabis use disorder.
- 2.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Lucemyra® tablets [prescribing information]. Louisville, KY: US WorldMeds; May 2018.
2. 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 29, 2024.
3. 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.
4. 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 29, 2024.
5. 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.

