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Last P&T Approval/Version: 01/28/2026
Next Review Due By: 01/2027
Policy Number: C16350-A

Lucemyra (lofexidine)

PRODUCTS AFFECTED

Lucemyra (lofexidine), lofexidine

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Opioid withdrawal

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. OPIOID WITHDRAWAL POTENTIAL:

1. Documented diagnosis of opioid dependence or opioid use disorder
   AND
2. Member is currently or will be undergoing abrupt opioid discontinuation within the next seven days
   AND
3. (a) Member has had continuous use of opioids or prescriber attests that the member has a high probability of experiencing withdrawal symptoms
   OR
   (b) Documentation member is scheduled to be administered an opioid antagonist (e.g., naltrexone) after a period of opioid use
   AND
4. (a) Documented historical trial, failure or FDA labeled contraindication to clonidine (See Background, References 9, 10)
   OR
   (b) Lucemyra was initiated at an in-patient setting and being continued up to 14 days total on discharge
   AND
5. Prescriber attests member has been referred and/or counseled for post-withdrawal support for opioid dependence or opioid use disorder
   AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Lucemyra (lofexidine) include: avoid use in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease, or chronic renal failure, as well as patients with marked bradycardia, and avoid in patients with congenital long QT syndrome]

CONTINUATION OF THERAPY:
N/A; Each request for re-treatment to be evaluated as a new review.

DURATION OF APPROVAL:
Initial Authorization: 14 days of therapy, Maximum of 224 tablets. If Lucemyra was initiated in the inpatient setting, the total course of therapy should not exceed 14 days.
Continuation of Therapy: N/A

PRESCRIBER REQUIREMENTS:
Prescribed by a physician specializing in addiction medicine, pain management, or physician working with the addicted population.

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Maximum 16 tablets per day

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Agent for Opioid Withdrawal

FDA-APPROVED USES:
Indicated for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Clinical Opiate Withdrawal Scale (COWS)
For each item, circle the number that best describes the patient' s signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

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* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset:** *over last 1/2 hour* 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 1/2 hour not accounted for by room temperature or patient activity.* 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	**Tremor** *observation of outstretched hands* 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* 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 for more than a few seconds	**Yawning** *Observation during assessment* 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 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 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* 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	**Gooseflesh skin** 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* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Lucemyra is a central alpha-2 adrenergic agonist indicated for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults.

Two randomized, multicenter, double-blind, placebo-controlled trials supported the efficacy of Lucemyra. Study 1 was a 2-part study. The first part of the study was a randomized, double-blind, placebo-controlled design consisting of 7 days of inpatient treatment with either Lucemyra 2.16 mg total daily dose (0.54 mg 4 times daily) (n=229), Lucemyra 2.88 mg total daily dose (0.72 mg 4 times daily) (n=222), or matching placebo (n=151). The second part of the study (Days 8-14) was an open-label design where all patients who successfully completed Days 1-7 were eligible to receive treatment with variable-dose Lucemyra (as determined by the investigator, but not to exceed 2.88 mg total daily dose) for up to an additional 7 days (Days 8-14) in either an inpatient or outpatient setting. No patient received Lucemyra for more than 14 days. The primary outcome of this study was the mean Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop) on Days 1-7. The secondary outcome was the proportion of patients that completed 7 days of treatment. The mean SOWS-Gossop scores for Days 1 – 7 were 8.8,6.5, and 6.1 for placebo, Lucemyra 2.16 mg and Lucemyra 2.88 mg, respectively. Both doses of Lucemyra resulted in significantly lower mean SOWS- Gossop scores compared to placebo with a difference of -2.3 (95% CI, -3.4 to -1.2) between Lucemyra 2.16 mg and placebo and a difference of -2.7 (95% CI, -3.9 to -1.6) between Lucemyra 2.88 mg and placebo.

Symptoms assessed on the SOWS-Gossop were recorded as absent or mild for almost all patients remaining to the end of the assessment period. Of the randomized and treated patients, 28% of placebo patients, 41% of Lucemyra 2.16 mg, and 40% of Lucemyra 2.88 mg patients completed 7 days of treatment. The difference in proportion in both Lucemyra groups was significant compared to placebo.

Patients in the placebo group were more likely to drop out of the study prematurely due to lack of efficacy than patients treated with Lucemyra.

In Study 2, patients were treated with Lucemyra 2.88 mg total daily dose (0.72 mg 4 times daily) (n=134) or matching placebo (n=130) for 5 days (Days 1-5). All patients then received placebo on Days 6 and 7 and discharged on Day 8. The two endpoints to support efficacy were the mean SOWS-Gossop score on Days 1 – 5 of treatment and the proportion of patients that completed 5 days of treatment. The mean SOWS-Gossop scores for Days 1 – 5 were 8.9 and 7.0 for placebo and LUCEMYRA 2.88 mg, respectively. Lucemyra treatment resulted in significantly lower mean SOWS-Gossop scores compared to placebo with a difference of -1.9 (95% CI, -3.2 to -0.6). Of the randomized and treated patients, 33% of placebo patients and 49% of Lucemyra patients completed 5 days of treatment. The difference in proportion between the two groups was significant. Patients in the placebo group were more likely to drop out of the study prematurely due to lack of efficacy than patients treated with Lucemyra.

The safety of Lucemyra was supported by 3 randomized, double-blind, placebo-controlled clinical trials, an open-label study, and clinical pharmacology studies with concomitant administration of either methadone, buprenorphine, or naltrexone.

Orthostatic hypotension, bradycardia, hypotension, dizziness, somnolence, sedation, and dry mouth were notably more common in subjects treated with Lucemyra than subjects treated with placebo.

Syncope occurred in 0.9%, 1.4% and 0% of patients using Lucemyra 2.16 mg/day and 2.88 mg/day and placebo, respectively. Elevations in blood pressure above normal values (≥ 140 mmHg systolic) and above a subject's pre-treatment baseline are associated with discontinuing Lucemyra and peakon the second day after discontinuation. In one study, 39.7% (23/58) of patients completing a 5-day

course of Lucemyra 2.88 mg daily had ≥ 140 mmHg systolic and ≥ 20 mmHg increase from baseline compared to 16.2% (6/37) of patients using placebo two days after discontinuation. In that same study, 8.6% (5/58) of patients completing a 5-day course of Lucemyra 2.88 mg daily had ≥ 170 mmHg systolic and ≥ 20 mmHg increase from baseline compared to 0% (0/37) of patients using placebo two days after discontinuation. Blood pressure elevations of a similar magnitude and incidence were observed in a small number of patients (N=10) that had a one-day, 50% dose reduction prior to discontinuation.
Lofexidine is marketed in other countries for relief of opioid withdrawal symptoms and the following events have been identified during post-marketing use. The most frequently reported adverse event has been hypotension. There has been one report of QT prolongation, bradycardia, torsades de pointes, and cardiac arrest with successful resuscitation in a patient that received lofexidine and three reports of clinically significant QT prolongation in subjects concurrently receiving methadone with lofexidine.

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.
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 a benzodiazepine for anxiety, loperamide or bismuth-salicylate for diarrhea, acetaminophen or nonsteroidal anti-inflammatory medications (NSAIDs) for pain, various medications for insomnia, and ondansetron for nausea.

The 2020 American Society of Addiction Medicine (ASAM) National Practice Guideline for the Treatment of Opioid Use Disorder recommends alpha-2 adrenergic agonists to support opioid withdrawal. They state that while comparative data are limited, lofexidine and clonidine appear to be similarly effective in the treatment of opioid withdrawal. Hypotension occurs less frequently with lofexidine.
While clonidine is not US FDA-approved for the treatment of opioid withdrawal, it has been extensively used off-label for this purpose.

The 2021 Medications for opioid use disorder for healthcare and addiction professionals, policy makers, patients & families. HHS Publication No. PEP21-02-01-002. 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.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Lucemyra (lofexidine) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Lucemyra (lofexidine) include: avoid use in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease, or chronic renal failure, as well as patients with marked bradycardia, and avoid in patients with congenital long QT syndrome.

OTHER SPECIAL CONSIDERATIONS:

Patients who complete opioid discontinuation are at increased risk of fatal overdose should they resume opioid use. Patients should not discontinue therapy without consulting their healthcare provider. Dose should be reduced gradually when discontinuing therapy.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

Lofexidine HCl TABS 0.18MG
Lucemyra TABS 0.18MG

REFERENCES

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6. Substance Abuse and Mental Health Services Administration (SAMHSA) – 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 Kampman K, Jarvis M, Comer S, et al.: American Society of Addiction Medicine (ASAM) National Practice Guideline for Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med 2015; 9(5):358-367
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9. The Asam National Practice Guideline for the treatment of opioid use disorder: 2020 focused update. (2020). Journal of Addiction Medicine, 14(2S), 1-91. doi:10.1097/adm.0000000000000633

SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q1 2026
REVISION- Notable revisions: Available Dosage Forms References	Q1 2025
REVISION- Notable revisions: Required Medical Information Drug Class	Q1 2024
REVISION- Notable revisions: Required Medical Information Duration of Approval Appendix Background Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file