Clinical Policy: Lofexidine (Lucemyra)

Reference Number: CP.PMN.152
Effective Date: 07.31.18
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Lofexidine (Lucemyra®) is a central alpha-2 adrenergic agonist.

FDA Approved Indication(s)

Lucemyra is indicated for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that lofexidine and Lucemyra are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

*For members in **Nevada**, medical management techniques, including quantity management, beyond step therapy is not allowed.

A. Opioid Withdrawal (must meet all)**:**

1. Diagnosis of opioid dependence or opioid use disorder;
2. Prescribed by or in consultation with a physician specializing in one of the following areas: emergency medicine/inpatient care, pain management, or addiction psychiatry;
3. Age ≥ 18 years;
4. Member is undergoing or is scheduled to undergo abrupt opioid discontinuation within the next seven days, and meets one of the following (a or b):
   a. Current use of ≥ 1 opioid for ≥ 3 weeks;
   b. Received or planned administration of an opioid antagonist (e.g., naltrexone) after a period of opioid use;
5. Medical justification supports inability to use an opioid taper (e.g., buprenorphine, methadone);
6. Member meets one of the following (a or b):*
   ** For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395.*
   a. Failure of clonidine, unless contraindicated or clinically significant adverse effects are experienced;
   b. Lofexidine (Lucemyra) was initiated in an inpatient setting (e.g., emergency department);
7. For brand Lucemyra requests, member must use generic lofexidine, unless contraindicated or clinically significant adverse effects are experienced;

8. Lofexidine (Lucemyra) has not been prescribed for a prior opioid withdrawal event within the last 30 days, or medical justification supports retreatment;
9. Total number of tablets per duration per course of treatment does not exceed 224 tablets per 14 days;
10. Dose does not exceed 2.88 mg (16 tablets) per day.

Approval duration: 7 days (112 tablets)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

*For members in **Nevada**, medical management techniques, including quantity management, beyond step therapy is not allowed.

A. Opioid Withdrawal (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Lofexidine (Lucemyra) for a covered indication and has received this medication for less than 14 days;
2. Member is responding positively to therapy;
3. For brand Lucemyra requests, member must use generic lofexidine, unless contraindicated, clinically significant adverse effects are experienced;
4. Total number of tablets per duration per course of treatment does not exceed 224 tablets per 14 days;
5. If request is for a dose increase, new dose does not exceed 2.88 mg (16 tablets) per day.

Approval duration: 7 days (112 tablets)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
APA: American Psychiatric Association
ASAM: American Society of Addiction Medicine
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral IR tablet: clonidine (Catapres® 0.1, 0.2 and 0.3 mg immediate release [IR] tablet) *Transdermal patch:* clonidine (Catapres®-TTS-1, TTS-2 or TTS-3 representing 0.1, 0.2 and 0.3 mg/24 hr)	***Opioid withdrawal symptoms (off-label)***	
	American Psychiatric Association (APA) 2006 guidelines: • 0.1 mg TID is usually sufficient to suppress signs of opioid withdrawal although inpatients can generally receive higher doses to block withdrawal symptoms because of the availability hypotension and sedation monitoring (formulation not specified). • Outpatients should not be given more than a 3-day supply of clonidine for unsupervised use because treatment requires careful dose titration and clonidine overdoses can be life-threatening.	Outpatient use: 0.3 mg/day; 3-day supply (APA 2006) General treatment course duration: 4-6 days (APA 2006)
	American Society of Addiction Medicine (ASAM) 2015 guidelines:	1.2 mg/day (ASAM 2015)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• 0.1–0.3 mg every 6–8 hours (IR tablet or transdermal patch [see package insert for detailed transdermal patch dosing information including maximum dose per day]).	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: Opioid Withdrawal - DSM-5
DSM-5 diagnostic criteria for opioid withdrawal are as follows:

A. Presence of either of the following:
   - Cessation of (or reduction in) opioid use that has been heavy and prolonged (i.e., several weeks or longer).
   - Administration of an opioid antagonist after a period of opioid use.

B. Three (or more) of the following developing within minutes to several days after Criterion A:
   - Dysphoric mood
   - Nausea or vomiting
   - Muscle aches
   - Lacrimation or rhinorrhea
   - Pupillary dilation, piloerection, or sweating
   - Diarrhea
   - Yawning
   - Fever
   - Insomnia

C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Opioid withdrawal	• Usual starting dosage: three 0.18 mg tablets PO QID during peak withdrawal symptoms (generally the first 5 to 7 days following last use of opioid) - dosing guided by symptoms and side effects; 5 to 6 hours between each dose; with or without food. • Discontinue with a gradual dose reduction over a 2- to 4-day period to mitigate Lucemyra withdrawal	Per dose: 0.72 mg (4 tablets) Per day: 2.88 mg (16 tablets)

Indication	Dosing Regimen	Maximum Dose
	symptoms (e.g., reducing by 1 tablet per dose every 1 to 2 days). • Dose should be reduced, held, or discontinued for individuals who demonstrate a greater sensitivity to Lucemyra side effects.	Maximum number of days: 14 Maximum number of tablets: 224

VI. Product Availability

Tablet: 0.18 mg

VII. References

1. Lucemyra Prescribing Information. Louisville, KY: US WorldMeds; September 2024. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b748f308-ba71-4fd9-84ec-ec7e0f210885. Accessed April 23, 2025.
2. Gorodetzky CW, Walsh SL, Martin PR, et al. A phase III, randomized, multi-center, double blind, placebo controlled study of safety and efficacy of lofexidine for relief of symptoms in individuals undergoing inpatient opioid withdrawal. Drug and Alcohol Dependence 176 (2017) 79–88.
3. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med. 2015 Sep-Oct;9(5):358-67.
4. Prunty LM, Prunty JJ. Acute Opioid withdrawal: Identification and treatment strategies. US Pharm. 2016;41(11):HS2-HS6.
5. Gowing L, Farrell M, Ali R, White JM. Alpha2-adrenergic agonists for the management of opioid withdrawal. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD002024.
6. Treatment of patients with substance use disorders, second edition. American Psychiatric Association. Am J Psychiatry. 2006 Aug; 163 (8 Suppl): 5-82.
7. VA/DoD Clinical practice guideline for the management of substance use disorders. Department of Veterans Affairs. Department of Defense. Version 4.0 (2021).
8. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington 2013.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: no significant changes; moved requirement for total number of tablets per duration per course of treatment from the approval duration section to the criteria contents; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	05.12.21	08.21
3Q 2022 annual review: no significant changes; changes in verbiage in Section I to clarify intent; removal of hypertension dosing regimen in Appendix B; references reviewed and updated.	04.13.22	08.22
Template changes applied to other diagnoses/indications.	10.04.22	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.20.23	08.23
Added disclaimer that medical management techniques, including quantity management, beyond step therapy is not allowed for members in NV per SB 439.	05.30.24	
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.31.24	08.24
Added redirection to generic lofexidine per SDC request.	01.23.25	
3Q 2025 annual review: added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	04.23.25	08.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.