Clinical Policy: Lofexidine (Lucemyra)

Reference Number: ERX.NPA.88
Effective Date: 07.31.18
Last Review Date: 08.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Lucemyra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of opioid dependence (may be limited to physiologic dependence/tolerance) 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, addiction psychiatry;
3. Age ≥ 18 years;
4. Member is currently or will be undergoing abrupt opioid discontinuation within the next seven days, and meets one of the following (a or b):
   a. Has taken one or more opioids for at least the last three weeks;
   b. Has been or will be administered an opioid antagonist (e.g., naltrexone) after a period of opioid use;
5. Medical justification supports why an opioid taper (e.g., with buprenorphine, methadone, or other opioid) cannot be used;
6. One of the following (a or b):
   a. Failure of clonidine, unless contraindicated or clinically significant adverse effects are experienced;
   b. Lucemyra has already been initiated (e.g., in an inpatient/ER setting);
7. Lucemyra has not been prescribed for a prior opioid withdrawal event within the last 30 days, or medical justification supports retreatment;
8. Dose does not exceed 2.88 mg (16 tablets) per day.

Approval duration: 7 days (112 tablets) *Total number of tablets per duration per course of treatment should not exceed 224 tablets per 14 days.*

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Lucemyra for a covered indication and has received this medication for less than 14 days;
2. Member is responding positively to therapy;
3. 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) *Total number of tablets per duration per course of treatment should not exceed 224 tablets per 14 days.*

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 14 days (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 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)	***FDA-approved dosing for hypertension***	
	• Oral IR tablet: ○ Initial dose: Up to 0.1 mg tablet PO BID. ○ Titration: Increase in increments of 0.1 mg per day per week. ○ Maintenance dose: From 0.2 mg to 0.6 mg per day in divided doses. • Transdermal patch: ○ Up to 0.6 mg/day. ○ Patch is programmed to release a constant rate over 7 days with therapeutic levels reached 2 to 3 days after application. • Taper over 2 or 4 days when discontinuing.	Oral IR tablet: 0.6 mg/day; rarely 2.4 mg/day Transdermal patch: 0.6 mg/day
	Off-label dosing for opioid withdrawal symptoms*	
	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).	Outpatient use: 0.3 mg/day; 3-day supply (APA 2006) General treatment course duration:

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	○ 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.	4-6 days (APA 2006)
	American Society of Addiction Medicine (ASAM) 2015 guidelines: • 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]).	1.2 mg/day (ASAM 2015)

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 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.	Per dose: 0.72 mg (4 tablets) Per day: 2.88 mg (16 tablets) 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 2020. Available at: http://www.lucemyra.com/content/pdf/LUCEMYRA-pi.pdf. Accessed May 12, 2021.
2. Food and Drug Administration Lucemyra approval letter dated May 16, 2018 (NDA 209229). Available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/209229Orig1s000ltr.pdf. Accessed June 2018.
3. Food and Drug Administration: Center for Drug Evaluation and Research. Meeting of the Psychopharmacology Drugs Advisory Committee. March 27, 2018. Available at https://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/psychopharmacologicdrugsadvisorycommittee/ucm602417.pdf. Accessed June 2018.
4. 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.
5. 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.
6. Prunty LM, Prunty JJ. Acute Opioid withdrawal: Identification and treatment strategies. US Pharm. 2016;41(11):HS2-HS6.
7. 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. DOI: 10.1002/14651858.CD002024.pub5.
8. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. JAGS 2015. DOI: 10.1111/jgs.13702.
9. Treatment of patients with substance use disorders, second edition. American Psychiatric Association. Am J Psychiatry. 2006 Aug; 163 (8 Suppl): 5-82.
10. VA/DoD Clinical practice guideline for the management of substance use disorders. Department of Veterans Affairs. Department of Defense. Version 3.0 (2015).
11. 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
Policy created	07.31.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.20.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	05.11.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	05.12.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.