Clinical Policy Title:	lofexidine
Policy Number:	RxA.410
Drug(s) Applied:	Lucemyra®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of Business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lofexidine (Lucemyra®)	Opioid withdrawal	Usual starting dosage: three 0.18 mg tablets orally four times daily 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

Dosage Forms

- Tablet: 0.18 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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

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

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

II. Continued Therapy Approval

A. Opioid Withdrawal (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance, 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

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

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

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

APA: American Psychiatric Association

ASAM: American Society of Addiction Medicine
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral IR tablet: clonidine (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). ○ 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: • 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)

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Opioid Withdrawal - DSM-5
  DSM-5 diagnostic criteria for opioid withdrawal are as follows:
  i. 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.
  ii. Three (or more) of the following developing within minutes to several days after Criterion i:
     - Dysphoric mood
     - Nausea or vomiting
     - Muscle aches
     - Lacrimation or rhinorrhea
     - Pupillary dilation, piloerection, or sweating
     - Diarrhea
     - Yawning
     - Fever
     - Insomnia
  iii. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
  iv. 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.
- Risk of Hypotension, Bradycardia, and Syncope: May cause a decrease in blood pressure, a decrease in pulse, and syncope. Monitor vital signs before dosing and advise patients on how to minimize the risk of these cardiovascular effects and manage symptoms, should they occur. Monitor symptoms related to bradycardia and orthostasis. When using in outpatients, ensure that patients are capable of self monitoring for signs and symptoms. Avoid use in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease, or chronic renal failure, as well as in patients with marked bradycardia.

References

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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. Accessed June 02, 2021.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	02/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was updated to all lines of business. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Initial and Continued Approval Duration was updated to included Commercial and Medicaid approval duration. 6. References were updated.	07/29/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Continued Therapy criteria II.A.1 was rephrased to " Member is currently receiving the medication that has been authorized by..." 3. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 4. Appendix B: was updated to remove drug name Catapres®. 5. Statement about drug listing format in	06/02/20221	09/14/2021

Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 6. Appendix D was updated to add" Risk of Hypotension…. marked bradycardia."Appendix D was updated to add "Risk of Hypotension, Bradycardia, and Syncope…" 7. References were reviewed and updated.		