Drug Monograph

Drug/Drug Class:	**Lucemyra™ (lofexidine hydrochloride) tablet/ Sympatholytics**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary [1]

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Lucemyra™ is available in a film coated tablet that contains 0.18 mg lofexidine, which is equivalent to 0.2 mg of lofexidine hydrochloride. Manufactured for: US WorldMeds, LLC, Louisville, KY 40241
Summary of Findings:	The efficacy and safety of Lucemyra™ in opioid-dependent patients was supported by 3 randomized, double-blind, placebo-controlled clinical trials with concomitant administration of either methadone, buprenorphine, or naltrexone. The 935 patients, who were enrolled in these trials, were dependent on short-acting opioids and undergoing abrupt opioid withdrawal. The patients were monitored before each dose. The mean difference between Lucemyra 2.16 mg and placebo was -2.3 with a 95%CI of (-3.4, -1.2), while the mean difference between Lucemyra 2.88 mg and placebo was -2.7 with 95% CI of (-3.9, -1.6), which indicated that both were statistically significant. The opioid withdrawal symptoms were assessed on the Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop) and were absent or mild for almost all patients who completed the 14-day treatment period.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☒ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☐ Appropriate Indications ☒ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [2]

Opioid misuse in the US is a problem, with more than 115 people dying every day after overdosing on opioids. The Centers for Disease Control and Prevention estimates total economic burden of prescription opioid misuse in the US at $78.5 billion per year.

Opioid withdrawal symptoms may occur both in patients who have been using prescribed opioids appropriately and in patients with Opioid Use Disorder (OUD). Withdrawal symptoms, while not life-threatening, may be very uncomfortable and can occur when opioids are stopped abruptly or reduced in patients with physical dependence. These symptoms include anxiety, agitation, sleep problems, muscle aches, runny nose, sweating, nausea, vomiting, diarrhea, and drug craving. Avoidance of withdrawal symptoms is thought to contribute significantly to continued drug-seeking behavior in OUD patients.

Dosage Form(s) [1]

Lucemyra™ is available in a film coated tablet that contains 0.18 mg lofexidine, which is equivalent to 0.2 mg of lofexidine hydrochloride.

Manufacturer [1]

Manufactured for: US WorldMeds, LLC, Louisville, KY 40241

Indication(s) [1]

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

Clinical Efficacy [1,3] (mechanism of action/pharmacology, comparative efficacy)

Lucemyra™ is a central alpha-2 adrenergic agonist that that binds to receptors on adrenergic neurons. This reduces the release of norepinephrine and decreases sympathetic tone.

Pharmacokinetics:

	Lucemyra™
Protein Binding	55% bound to plasma proteins
Metabolism	CYP2D6, CYP1A2 and CYP2C19
Excretion	Feces; 0.92% Urine; 93.5%
Half-life	11- to 13 hours (first dose); 17 to 22 hours (steady state)

Clinical Trials Experience

STUDY DESIGN	2 randomized, double-blind, placebo controlled clinical trials (n=866).
INCLUSION CRITERIA	Patients aged 18 years and older meeting Diagnostic and Statistical Manual-IV criteria for opioid dependence who were physically dependent on opioids and undergoing abrupt opioid discontinuation.
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients were randomized to receive Lucemyra 2.16 mg total daily dose, 2.88 mg total daily dose, or matching placebo.
RESULTS	The studies evaluated benefit using the Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop), which is a patient-reported outcome instrument that assesses opioid withdrawal symptoms. These symptoms include feeling sick, stomach cramps, muscle spasms/twitching, feeling of coldness, heart pounding, muscular tension, aches and pains, yawning, running eyes, and insomnia/problems sleeping. For each opioid withdrawal symptom, patients were asked to rate their symptom severity using four response options (non, mild, moderate, and severe), with the SOWS-GOSSOP total score ranging from 0 to 30, where a higher score indicated a greater withdrawal symptom severity. SOWS-Gossop scores were lower for patients treated with Lucemyra compared to placebo, and more patients completed the treatment period of the studies in the Lucemyra group compared to placebo.
SAFETY	The most common side effects are low blood pressure, slow heart rate, lightheadedness, dizziness, sleepiness, and dry mouth.

Contraindications [(1)]

- None

Warnings and Precautions [(1)]

- Risk of hypotension, bradycardia, and syncope. Patients should be instructed to self-monitor symptoms of hypotension, orthostasis, and bradycardia.
- Risk of QT Prolongation. Monitoring of ECG is recommended in patients with congenital long QT syndrome, heart failure, bradyarrhythmias, hepatic or renal impairment.

- Increased risk of CNS depression with concomitant use of CNS depressant drugs like benzodiazepines, barbiturates, and alcohol.
- Increased risk of opioid overdose after opioid discontinuation due to reduced tolerance to opioids and patients are at an increased risk of fatal overdose on resumed opioid use.
- Risk of discontinuation symptoms. Stopping Lucemyra abruptly can cause rise in blood pressure.

Adverse Effects [1]

Most common, ≥ 10%	Lucemyra 2.16 mg (N=229)	Lucemyra 2.88 mg (N=222)	Placebo (N=151)
Insomnia	51%	55%	48%
Orthostatic Hypotension	29%	42%	5%
Bradycardia	24%	32%	5%
Hypotension	30%	30%	1%
Dizziness	19%	23%	3%
Somnolence	11%	13%	5%
Sedation	13%	12%	5%
Dry Mouth	10%	11%	0%

Drug Interactions [1]

- Methadone
- Oral Naltrexone
- CYP2D6 Inhibitors (Paroxetine)
- CNS Depressant Drugs

Dosage and Administration [1]

The FDA recommended dose is three 0.18 mg tablets taken orally 4 times daily during withdrawal period with or without food for up to 14 days. Discontinue Lucemyra™ with a gradual dose reduction over a 2-4 day period. Dose adjustments are recommended based on the degree of hepatic or renal impairment.

Cost [3]

GENERIC NAME	BRAND NAME	MANUFACTURER	DOSE	COST/ DAY
Lofexidine	Lucemyra	US WorldMeds	0.54 mg (3 tablets) 4 times daily	$248.28*
Clonidine	N/A	Alembic	0.2 mg (2 tablets) 3 times daily	$0.12**

* Wholesale Acquisition Cost

** Maximum Allowable Cost

Conclusion

Lucemyra™ (lofexidine hydrochloride) is the first oral FDA-approved non-opioid treatment for the management of opioid withdrawal symptoms in adults that provides an opportunity for providers to select the best treatment suited to a patient. It is not a treatment for opioid use disorder; however, it may prove useful as an adjunct to comprehensive, long-term treatment plans for managing opioid discontinuation. While Lucemyra™ might reduce the severity of withdrawal symptoms; it may not completely prevent them. The safety and efficacy of Lucemyra™ was supported by two randomized, double-blind, placebo controlled clinical trials, which evaluated the benefit of using the Short Opiate Withdrawal Scale of Gossop (SOWS-Gossop) to assess opioid withdrawal symptoms. These trials showed that SOWS-Gossop scores were lower for patients treated with Lucemyra™ group compared to placebo.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List (PDL).

References

1) Lucemyra. Retrieved 7/16/2018 from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=bdcfe803-b556-47db-a54f-ae0f0e5be016#section-1
2) NIH. Opioid Overdose Crisis. Retrieved 7/16/2018 from: https://www.drugabuse.gov/drugs-abuse/opioids/opioid-overdose-crisis
3) Lexicomp. Retrieved 7/16/2018 from: https://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/4854487

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Date: July 16, 2018