LOFEXIDINE (Lucemyra) Fact Sheet

Bottom Line:

Lofexidine is an alpha-2 agonist (similar to clonidine and guanfacine) that is used to reduce the intensity of opioid withdrawal symptoms. It effectively blunts some of the most distressing symptoms such as anxiety and tachycardia. It is generally not effective for pain symptoms such as generalized achiness and headache, so it should be used with an analgesic like ibuprofen or acetaminophen. Data indicate that lofexidine is similarly effective to clonidine for management of opioid withdrawal but with a marginally better side effect profile (Kuszmaul AK et al, *J Am Pharm Assoc* 2020;60(1):145–152). However, given its much higher price tag, we recommend you stick to clonidine.

FDA Indications:

Opioid withdrawal.

Dosage Forms:

Tablets: 0.18 mg.

Dosage Guidance:

- Start three 0.18 mg tablets QID at five- to six-hour intervals during peak withdrawal symptoms (typically the first five to seven days after last use of opioid). Withdrawal symptoms should be used clinically to guide gradual dose reduction.
- Maximum daily dose is 2.88 mg (16 tablets), and no single dose should exceed 0.72 mg (four tablets).
- Discontinue gradually by reducing in increments of one tablet per dose every one to two days. Taper typically should take two to four days, and should be no more than 14 days.

Monitoring: Monitor blood pressure and pulse. Monitor ECG in patients with congestive heart failure, bradyarrhythmia, or risk for QT prolongation.

Cost: $$$$$

Side Effects:

- Most common: Orthostatic hypotension, bradycardia, dizziness, somnolence, sedation, dry mouth.
- Serious but rare: Syncope, QT interval prolongation.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Alpha-2 receptor agonist.
- Metabolized primarily by CYP2D6; t ½: 11–12 hours.
- Caution when used with CYP2D6 inhibitors (such as paroxetine) or in poor 2D6 metabolizers as there may be an increased risk for hypotension. Caution with other agents that may increase QT interval (eg, methadone). Caution when used with CNS depressants (additive CNS depression).

Clinical Pearls:

- Analog of clonidine, another alpha-2 agonist, available since 1992 in the UK.
- Has been approved for use in Europe since the 1990s, but was not approved by the FDA until 2018. Approval was based on two randomized, double-blind, placebo-controlled clinical trials of 866 adults with opioid dependence; lofexidine lessened severity of withdrawal symptoms more than placebo.
- Decide on how rapidly to taper the dose by using a symptom-triggered assessment such as the Clinical Opiate Withdrawal Scale (see the "COWS" fact sheet for more details).
- Lower the dose if symptomatic hypotension or bradycardia occurs, and in patients with impaired hepatic or renal function.
- Some patients may experience markedly increased blood pressure if the lofexidine dose is lowered or discontinued too quickly. For these patients with rebound hypertension, consider slowing down the taper or temporarily treating with another antihypertensive agent.
- Has been studied for alcohol withdrawal but was not found to be effective.

Fun Fact:

Case reports support its use for hot flashes associated with menopause.