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for Workers' Compensation

June 2018

Drug of the Month

Lucemyra® (lofexidine hydrochloride)

On May 16, 2018, the Food and Drug Administration (FDA) granted "Fast Track" approval to the drug company US WorldMeds LLC for Lucemyra (lofexidine hydrochloride), the first non-opioid agent with a label indication for "mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults."[1]

The FDA reviewed Lucemyra under "Priority Review," which is granted to submissions for medications that would provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. FDA Commissioner Scott Gottlieb, MD, remarked, "FDA will continue to encourage the innovation and development of therapies to help those suffering from opioid addiction transition to lives of sobriety, as well as address the unfortunate stigma that's sometimes associated with use of medication-assisted treatments."[2]

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.

Lucemyra is an alpha 2-adrenergic receptor agonist that works by suppressing a neurochemical surge that produces withdrawal symptoms.[3] It is not a treatment for opioid use disorder (OUD), 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.[3]

Dosing is initiated at three tablets, taken by mouth four times per day, adjusted for symptom response and continued for a maximum of 14 days. Lucemyra should be discontinued by gradual reduction over two to four days. Cardiac (ECG) monitoring is recommended when co-administered with methadone or naltrexone, which are commonly prescribed for OUD discontinuation treatment. The most common side effects of Lucemyra are low blood pressure, slow heart rate, lightheadedness, dizziness, sleepiness, and dry mouth.[1]

Also of note, the FDA is requiring 15 post-marketing studies on the new drug. Additional studies are required to support longer term use beyond 14 days (e.g., gradual opioid tapers in pain patients discontinuing opioids) and use in children less than 17 years of age.

Requests for Lucemyra should be reviewed for relatedness to the workplace injury (i.e., is the drug being requested as part of a comprehensive opioid discontinuation plan? Are opioid medications being tapered or discontinued?), and approval for use should be limited to the 14-day timeline evaluated for safety and efficacy by the FDA. US World Meds, LLC. reports that commercial release of Lucemyra is planned for August 2018.[3]

References:
1. Lucemyra® [Prescribing Information]. Louisville, KY: US WorldMeds, LLC; 2018
2. FDA approves the first non opioid treatment for management of opioid withdrawal symptoms in adults. Available at: https: //www.fda.gov/newsevents/newsroom/PressAnnouncements/ucm607884.htm Accessed: May 16, 2018.
3. FDA Approves US WorldMeds Lucemyra (lofexidine) After Priority Review for the management of opioid withdrawal symptoms. Available at: https://www.prnewswire.com/news/us-worldmeds-llc Accessed: May 16, 2018.

Regulatory Update

Alaska

Alaska has adopted amendments to Rule 12 AAC 52.855, et seq. regarding changes to the Board of Pharmacy's Prescription Drug Monitoring Program (PDMP). Licensed pharmacists must register with the PDMP's controlled substance prescription database before dispensing a Schedule II, III, or IV controlled substance. There are also new requirements for how a pharmacist must register with the PDMP and how the PDMP must be accessed. The rule becomes effective June 7, 2018.

Illinois

Pursuant to the IWCC's Rules, as found in Section 50 of the Illinois Administrative Code, parties will receive case activity notices electronically beginning on July 2, 2018. The IWCC will no longer send case notices via U.S. mail as of this date. All parties (law firms on behalf of clients and *pro se* litigants) will be required to maintain a designated electronic mail ("e-mail") address for receiving case notices.

Maryland

Effective July 1, 2018, Maryland has adopted House Bill 517 regarding a prescriber's responsibility to monitor the controlled substance database. The following changes are addressed:

- Establishes that prescribers must request at least the prior four months of prescription monitoring data for a patient before initiating a course of treatment for the patient that includes prescribing or dispensing opioids.
- Provides specific exclusions for not checking the database.

New Jersey

New Jersey Rule N.J.A.C. 12:235-1.9 regarding e-billing, in response to Assembly Bill 3401, requires certain providers to submit bills electronically. This rule becomes effective May 21, 2018. Significant changes, include, but are not limited to, the following:

- All health care providers that submit 25 or more medical bills per month must submit complete electronic medical bills for payment on standardized electronic forms.
- Requires carriers to accept electronic bills for the payment of medical services and to provide payment for a complete electronic medical bill within 60 days.
- Allows the establishment of payment deadlines through PPO or Independent Practice Association contracts or other agreements with health care providers in a non-prescribed format or timeline, independent of the guidelines.

New York

New York State (NYS) is implementing 046-1012 to amend the Pharmacy Formulary list that consists of preferred (authorized) and non-preferred (not authorized) drugs. NYS has finalized their formulary rules, which are expected to go into effect on July 1, 2018. Amendments to the formulary include definitions for prescription drug terminology, dispensing rules, and prior authorization rules for non-preferred medications. Additional information, recorded sessions, and guideline updates are available at: www.wcb.ny.gov/drug-formulary-regulation.

Oklahoma

OK Senate Bill 1446 to providing limitations on quantities of certain opioid prescriptions was signed by Governor Mary Fallin on May 3, 2018. The rule provides various definition rules, documentation requirements, and subsequent prescription rules. Under the rule, practitioners must not prescribe an initial prescription for an opioid to treat acute pain exceeding a seven-day supply. Practitioners may issue subsequent seven-day supply prescriptions; however, documentation must be provided confirming the medication is necessary and appropriate. The applied rules will go into effect on November 1, 2018.

South Carolina

Senate Bill 918 establishes limitations for initial opioid prescriptions, and was signed by the governor on May 15, 2018. The rule limits initial opioid prescriptions for acute or post-operative pain management to a seven-day supply with various exceptions. Exceptions include: treatment for chronic pain, cancer pain, hospice care, palliative care, major trauma, major surgery, sickle cell disease, and treatment of neonatal abstinence syndrome or medication-assisted treatment for substance use disorder. The bill also provides various definitions and subsequent fill rules (renewal, refill, or new opioid prescription) for treatment of the same pain, and went into effect May 15, 2018.

Coventry's Regulatory and Legislative Affairs (RLA) group will continue to monitor further discussion on these topics. If you have questions regarding these changes, please contact your First Script Account Manager.

Ask The Pharmacist

To suggest a topic, send an email to: AskThePharmacist@cvty.us.com

What are the general recommendations for taking a person off of opioids?

This question certainly does not have a simple, straight-forward answer, but fortunately, there are several resources and guidance available related to the subject of opioid discontinuation. Some of the general recommendations will be outlined here.

There may be various reasons to discontinue opioid use which can include:

- The end of planned treatment course or improvements in underlying pain condition being treated
- Intolerable adverse effects
- Lack of improvements in function
- Transition to long-term non-opioid pain management techniques
- Instances where the patient is exhibiting signs of substance use disorder or aberrant behavior (e.g., opioid diversion, overdose event, misuse or risky use of opioid),
- Whenever the risks associated with continued use outweigh the benefits of opioid therapy (e.g., concurrent use of other medications or co-occurring health conditions that increase risk of overdose)

Whatever the reason for discontinuation, physical dependence must be considered, and a taper or weaning schedule is advised for these types of drugs due to the nature of opioids' interaction with the central nervous system. Abrupt discontinuation may lead to signs and symptoms of opioid withdrawal syndrome which are likened to the effects of a really bad flu and can include diarrhea, fever, yawning, insomnia, muscle cramps and aches, watery eyes, runny nose, dilated pupils, sweating, and goose bumps.

In order to avoid withdrawal and ensure the best chance of success, an individualized tapering treatment plan should be developed with regular follow up, oversight, and coordination and referral with specialists and treatment experts as needed. If it is determined that weaning or discontinuation of the opioid is advised, there are several considerations and recommendations for assisting this process. The treating provider should be engaged in the process of opioid weaning, and this should be agreed upon and done under supervision from the injured worker's health care professional. The duration of therapy, type, and dose of opioid as well as the patient's comorbid conditions, including substance use disorder and the need for additional treatment, may affect the rate, intensity, and duration of the taper, as well as whether the patient is best-suited for in-patient or out-patient detoxification. For example, psych conditions, risk of suicide, or a high risk of aberrant behavior could indicate that tapering in a primary care setting may be more appropriate. All of these considerations should be discussed with the provider.

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Opioid Weaning

Individualize considerations

- Rate, intensity, duration of taper
- Type of opioid
- Comorbid conditions
- In-patient vs. out-patient detoxification
- Substance use disorder treatment
- Medication assisted therapy (MAT)

Example general schedule

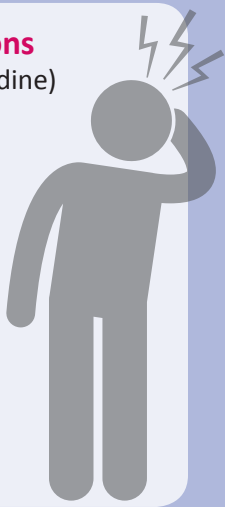
- 10%↓ per week (CDC)
- 5-20%↓ / 4 weeks (USVA)

Withdrawal symptom medications

- **Alpha-2 agonists (**Lucemyra*, clonidine)
- **Muscle relaxants** (methocarbamol, baclofen)
- **Stomach relaxants** (dicyclomine)
- **Anti-inflammatory pain relievers** (ibuprofen, naproxen)
- **Sleep aids** (trazodone, amitriptyline, hydroxyzine)
- **Anti-anxiety agents** (hydroxyzine, phenobarbital**)

**FDA-approved for opioid withdrawal symptoms*

***May be habit forming (limit use to short-term)*



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Some examples of general weaning schedules, as recommended in the literature, are to decrease the opioid at a rate of 10% every one to four weeks[1,2] or to decrease the opioid at 5-20% of the original opioid dose every four weeks[3] in order to allow time for neurobiological, psychological, and behavioral adaptations. Whatever rate or method chosen for weaning, the patient should be continually evaluated at regular intervals and adjustments to the intensity of the taper should be made as needed. Evaluations for opioid use disorder and any need for mental health treatment or biopsychosocial support should also be explored.

Several medications have been studied and found to assist in managing the typical symptoms of opioid withdrawal. In fact, Lucemyra (lofexidine), an alpha-2 agonist, recently became the first FDA-approved medication indicated for opioid withdrawal symptoms. Other examples of medications that may be used off-label to assist in management of withdrawal symptoms include another alpha-2 agonist, clonidine, which is typically used in heart-related conditions. This drug has been found to be helpful in attenuating the autonomic symptoms of withdrawal such as hypertension, nausea, cramps, sweating, and/or tachycardia. Antihistamines or trazodone have been used to help with insomnia and restlessness. NSAIDs (nonsteroidal anti-inflammatory drugs) can be used for muscle aches, dicyclomine for abdominal cramps, and Pepto-Bismol® for diarrhea. Medication-assisted treatment (MAT) with methadone or buprenorphine products may also be used to facilitate withdrawal from other opioids.

It is important to keep in mind that many of these assistive medications are not typically seen in workers' comp and will be flagged for prior authorization. It would be wise for claims managers to anticipate such medications and to coordinate with the treating provider and PBM to evaluate appropriateness should any of these medications be requested for an injured worker to help them detox or wean off of opioids. For further insight into opioid discontinuation or for questions related to a specific injured worker's care, please consider contacting our team of clinical pharmacists at askthepharmacist@cvty.com.

References:

1. U.S. Centers for Disease Control and Prevention. Pocket Guide: Tapering Opioids for Chronic Pain. Available at: https://www.cdc.gov/drugoverdose/pdf/clinical_pocket_guide_tapering-a.pdf Accessed: May 31,2018.
2. Work Loss Data Institute. Official Disability Guidelines – Pain (Chronic). Available at: http://www.odg-twc.com (subscription required). Accessed: May 31, 2018.
3. Department of Veterans Affairs/Department of Defense. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain. Available at: https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPGProviderSummary022817.pdf. Accessed: May 31, 2018.