Drug Class Literature Scan: Substance Use Disorders, Opioid, and Alcohol

Date of Review: December 2020

Date of Last Review: November 2019

Literature Search: 06/20/19 – 8/14/20

Current Status of PDL Class:
See Appendix 1.

Conclusions:

- Since the last class update on drugs used to manage substance use disorders (SUDs), 3 new systematic reviews\(^1\)\(^2\)\(^3\) were published and 2 guidelines were updated.\(^4\)\(^5\)
- A moderate-quality 2019 systematic review and meta-analyses aimed to ascertain whether varenicline improves drinking-related outcomes in subjects with alcohol use disorders (AUDs).\(^1\) In the meta-analyses, no significant differences in percentage of heavy drinking days (weighted mean difference [WMD] = -1.09; 95% confidence interval [CI], -4.86 to 2.69), number of drinks per drinking day (WMD = -0.71; 95% CI, -1.44 to 0.03), or percentage of days abstinent (WMD=3.89; 95% CI,-1.25 to 9.02) were noted varenicline 2 mg once daily.\(^1\) A statistically significant decrease in craving was observed (n=436; standard mean difference [SMD] = -0.63; 95% CI,-1.18 to -0.08).\(^1\) In this systematic review and meta-analyses, varenicline was shown to reduce alcohol craving but not improve drinking-related outcomes in subjects with AUDs.\(^1\)
- A systematic review funded by United States (U.S.) Department of Veterans Affairs (VA) in 2020 reviewed the benefits and risks for the treatment of cannabis use disorder (CUD).\(^2\) Overall, there is limited evidence due to the small number of studies investigating most drug classes, small sample sizes, high attrition rates, and other methodological flaws in nearly half the trials.\(^2\) Low- to moderate-strength evidence shows that buspirone, cannabinoids, and SSRIs are ineffective for decreasing cannabis use or improving abstinence.\(^2\) Insufficient evidence was available to draw conclusions about the effectiveness of managing CUD for other drug classes including mood stabilizers, antipsychotics, and anticonvulsants.\(^2\)
- In May 2020, the Agency for Healthcare Research and Quality (AHRQ) published a systematic review evaluating behavioral, pharmacologic and combined interventions for adolescents aged 12 to 20 years with problematic SUD.\(^3\) Motivational interviewing (MI) reduced heavy alcohol use days by 0.7 days/month (low strength of evidence [SoE], alcohol use days by 1.2 days/month (moderate SoE), and overall substance use problems with a SMD of 0.5 days (low SoE), compared with treatment as usual.\(^3\) Brief MI did not reduce cannabis use days (net mean difference of 0; moderate SoE).\(^3\) Across multiple intensive interventions, family focused therapy was most effective, reducing alcohol use days by 3.5 days/month compared with treatment as usual (low SoE).\(^3\) No intensive interventions reduced cannabis use days (low SoE).\(^3\) Pharmacologic treatment of OUD led to a more than 4 times greater likelihood of abstinence with extended courses (2 to 3 months) of buprenorphine compared to short courses (14 to 28 days; low SoE).\(^3\)
- In January 2020, the Substance Abuse and Mental Health Services Administration (SAMHSA) published an updated treatment protocol focused on medications for opioid use disorder (OUD).\(^4\) Pertinent recommendations include: updating the expanded list of “other qualifying practitioners” who are eligible to apply for a waiver to prescribe buprenorphine; clarifying that buprenorphine is available in an extended-release injection and subdermal formulations; and adding information about possible clinical interactions between formulations of buprenorphine, naltrexone, and other medications.\(^4\)

Author: Deanna Moretz, PharmD, BCPS
In June 2020, the U.S. Preventative Services Task Force (USPSTF) updated its 2008 recommendations for screening for unhealthy drug use in adults and adolescents.⁵ This recommendation statement applies to adults 18 years or older, including pregnant and postpartum persons, and adolescents aged 12 to 17 years in primary care settings.⁵ In adults, the USPSTF concludes with moderate certainty that screening by asking questions about unhealthy drug use has moderate net benefit when services for accurate diagnosis of unhealthy drug use or drug use disorders, effective treatment, and appropriate care can be offered or referred.⁵ In adolescents, because of the lack of evidence, the USPSTF concludes that the benefits and harms of screening for unhealthy drug use are uncertain and that the balance of benefits and harms cannot be determined.⁵ The USPSTF recommends screening by asking questions about unhealthy drug use in adults 18 years or older.⁵

Recommendations:
- Based on the review of recently published evidence, no changes to the preferred drug list (PDL) or prior authorization (PA) criteria are recommended.
- After review of costs in executive session, no PDL changes were made.

Summary of Prior Reviews and Current Policy
In January 2017, the Pharmacy & Therapeutics (P and T) Committee recommended removal of PA criteria for naltrexone extended-release injection and preferred buprenorphine/naloxone sublingual tablets and film (unless the daily dose of buprenorphine exceeds 24 mg) in order to minimize barriers to care and provide increased access to medications for the treatment of SUD. At the January 2019 P & T Committee meeting, a policy evaluation assessing the impact of removing PA requirements for preferred medication assisted-treatments (MAT) for management of OUD was presented. It was reported that utilization of buprenorphine/naloxone and medical claims for MAT continue to increase. After removal of the PA criteria in January 2017, approximately 83% of patients prescribed MAT had an initial paid claim compared to 40% of patients in the year prior to the PA removal.

In January 2019, a class update focused on drugs used to manage SUDs was presented to the P & T Committee. At that meeting, lofexidine (Lucemyra™) tablets and extended-release subcutaneous buprenorphine injection (Sublocade™) were designated as non-preferred on the PDL and PA criteria were implemented to ensure appropriate utilization.

At the November 2019 P and T meeting, buprenorphine sublingual tablets, disulfram tablets, and buprenorphine/naloxone film (Bunavail®) were designated as voluntary non-preferred, while buprenorphine injection (Sublocade®) was designated as preferred on the PDL after reviewing costs in executive session. The recommendation was made to designate new products in this class as voluntary non-preferred due to legislation designed to ensure open access to SUD treatments. Appendix 1 lists the current PDL status for medications used in treatment of SUD. Buprenorphine monotherapy and buprenorphine/naloxone products exceeding 24 mg per day and lofexidine require PA as outlined in the clinical PA criteria listed in Appendix 4. In the second quarter of 2020 (May through September 2020), most of the OHP FFS pharmacy claims for SUD medications were for oral buprenorphine/naloxone (1,300 claims), followed by oral buprenorphine (334 claims), oral naltrexone (209 claims), extended-release subcutaneous buprenorphine injection (21 claims) and extended-release naltrexone injection (10 claims). Similar trends were observed in the second quarter of 2019. In the first quarter of 2020 (January through April) there were approximately 3500 physician administered claims for oral buprenorphine/naloxone (2,449 claims), extended-release naltrexone injection (11 claims) and oral buprenorphine (978 claims). Physician administered claims include physician offices and SUD clinics.

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this literature scan is available in Appendix 3, which includes dates, search terms and...
limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

**New Systematic Reviews:**

**The Impact of Varenicline on Alcohol Consumption in Subjects with Alcohol Use Disorders**

A moderate-quality 2019 systematic review and meta-analyses aimed to ascertain whether varenicline improves drinking-related outcomes in subjects with AUDs. Literature was searched through August 2019 for randomized, placebo-controlled trials in humans. Although varenicline has been shown to be safe and effective in improving abstinence in tobacco smokers, results from trials using varenicline for AUDs are inconsistent. Ten randomized, placebo-controlled studies (n=731, 66.6% male, 55.1% smokers) that examined studies of subjects with heavy drinking or alcohol dependence/AUD and reported alcohol use-related outcomes met inclusion criteria. Overall risk of bias was low for all 10 RCTs. The primary outcome of interest was percentage of heavy drinking days. Secondary outcomes included the number of drinks per drinking day, percentage of days abstinent, and change in alcohol craving.

In the meta-analyses, no significant differences in percentage of heavy drinking days (n=597; WMD =-1.09; 95% CI, -4.86 to 2.69; I²=22%), number of drinks per drinking day (n=570; WMD =-0.71; 95% CI, -1.44 to 0.03; I²=0%), or percentage of days abstinent (n=439; WMD=3.89; 95% CI, -1.25 to 9.02; I²=0%) were noted with varenicline 2 mg once daily. A statistically significant decrease in craving was observed (n=436; SMD =-1.44 to 0.03; I²=0%). In summary, varenicline was shown to reduce alcohol craving but not improve drinking-related outcomes in subjects with AUDs.

**Pharmacotherapy for the Treatment of Cannabis Use Disorder**

A systematic review funded by the VA in 2020 reviewed the benefits and risks for the treatment of CUD. Literature was searched from January 2014 through September 2019. Fourteen new RCTs and 12 RCTs from a previous 2014 Cochrane review met inclusion criteria. Because populations, duration, and concurrent interventions were heterogeneous among studies, the authors did not pool their findings, nor did they pool data across drug classes. Overall, the evidence base is limited because of the small number of studies investigating most drug classes, small sample sizes, nearly universal high attrition rates, and other methodological flaws in approximately half of the trials.

Four trials with low risk of bias (ROB) and 2 high-ROB trials evaluated the use of antidepressants (escitalopram, fluoxetine, bupropion, nefazodone, venlafaxine, and vilazodone) to treat CUD. Overall, low-strength evidence showed that selective serotonin reuptake inhibitors (SSRIs) did not reduce cannabis use (as assessed by negative urinalysis results) and that neither SSRIs nor bupropion improved treatment adherence. Most studies had high rates of attrition (as high as 60%), which increased risk of bias in these trials.

The authors found insufficient evidence for the effectiveness of antipsychotics in treating CUD. One high-ROB head-to-head RCT compared ziprasidone and clozapine (n=30) in adults with CUD and a psychotic spectrum disorder. Findings indicated no difference between groups in cannabis use changes or treatment adherence. Results suggest that clozapine may be associated with more adverse events and that ziprasidone may be associated with better drug tolerance and psychotherapy adherence.
Low-strength evidence from 1 low-ROB and 1 unclear-ROB RCT showed that buspirone has no benefit over placebo for treatment retention (calculated risk ratio, 0.92 [95% CI, 0.61 to 1.26]). Two RCTs with mood stabilizers; 1 with low ROB (lithium) and the other with high ROB (divalproex), provide insufficient evidence from which to form conclusions about their respective efficacy in CUD treatment. These trials found no difference between valproex or lithium and placebo in cannabis abstinence, changes in frequency or quantity of cannabis use, or treatment adherence. Regarding withdrawal symptoms, divalproex did not differ from placebo in craving or irritability. Lithium and placebo were similar in reported withdrawal severity. However, lithium was more effective for attenuating nightmares, loss of appetite, and stomach aches.

Three low-ROB RCTs and 3 RCTs with unclear ROB examined the use of cannabinoids (nabilone, dronabinol, and nabiximol) in treating CUD. Dronabinol is FDA-approved for treatment of adults with anorexia associated with Acquired Immunodeficiency Syndrome (AIDS) or for nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond to conventional antiemetic treatments. Nabilone is FDA-approved for treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Nabiximol is an investigational product containing tetrahydrocannabinol (THC) and cannabidiol (CBD) that is not FDA-approved. It is available as an oral spray in the European Union for the treatment of spasticity due to multiple sclerosis. One small RCT (n=18) comparing nabilone with placebo found no difference in any outcome of interest. Two other trials, 1 comparing dronabinol and the other comparing a combination of dronabinol and lofexidine with placebo, found no difference in the achievement of abstinence, reduction in cannabis use, cannabis craving, or harms. Findings were mixed for the effect of dronabinol on withdrawal symptoms and treatment retention.

Two small RCTs with unclear ROB provide insufficient evidence about the effects of gabapentin and topiramate on all outcomes of interest because of small sample sizes, high attrition, and methodological issues. Participants receiving gabapentin (n=50), but not those receiving topiramate (n=66), substantially decreased their cannabis use compared with those receiving placebo. In addition, gabapentin was associated with a decrease in depressive symptoms, better neurocognitive performance, and treatment retention and was more effective than placebo in mitigating withdrawal symptoms. Participants receiving topiramate had poorer depressive and neurocognitive outcomes and higher rates of attrition than those receiving placebo.

In summary, this systematic review examined 26 trials of pharmacotherapies to treat CUD. Low- to moderate-strength evidence shows that buspirone, cannabinoids, and SSRIs are ineffective for decreasing cannabis use or improving abstinence. Insufficient evidence is available to draw conclusions about the effectiveness of other drug classes in managing CUD including mood stabilizers, antipsychotics, and anticonvulsants.

**Interventions for Substance Use Disorders in Adolescents**

In May 2020, AHRQ published a systematic review evaluating behavioral, pharmacologic and combined interventions for adolescents aged 12 to 20 years with problematic SUD. The literature search was conducted through November 2019. One hundred eighteen studies met inclusion criteria. Most studies enrolled adolescents with some combination of alcohol and cannabis use. The most commonly reported outcomes included frequency of use and abstinence. Very few studies evaluated users of opioids, methamphetamine, or substances other than alcohol or cannabis. Studies often combined different types of interventions, making comparisons of specific interventions difficult. The available studies did not consistently report a common set of outcomes, which limited the ability to combine information from potentially relevant studies. For most outcomes, individual studies were deemed to have moderate risk of bias, most commonly due to incomplete outcome data, poor compliance, and a lack of blinding of participants, study personnel, and outcome assessors.
Motivational interviewing reduced heavy alcohol use days by 0.7 days/month (low SoE, alcohol use days by 1.2 days/month (moderate SoE), and overall substance use problems with a SMD of 0.5 days (low SoE), compared with treatment as usual. Brief MI did not reduce cannabis use days (net mean difference of 0; moderate SoE). Across multiple intensive interventions, family focused therapy was most effective, reducing alcohol use days by 3.5 days/month compared with treatment as usual (low SoE). No intensive interventions reduced cannabis use days (low SoE). Pharmacologic treatment of OUD led to a more than 4 times greater likelihood of abstinence with extended courses (2 to 3 months) of buprenorphine compared to short courses (14 to 28 days; low SoE). More research is needed to understand the role of medications in treatment of alcohol and cannabis use disorders and of pharmacological treatments typically used for comorbid psychiatric illnesses.

After review, 10 systematic reviews were excluded due to poor quality, wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). New Guidelines: High Quality Guidelines: Medications for Opioid Use Disorder
In January 2020, SAMHSA published an updated Treatment Improvement Protocol focused on medications for OUD. Improving access is crucial to closing the wide gap between the need for treatment with OUD medications and the availability of such treatment, given the strong evidence of OUD medications’ effectiveness. Pertinent changes to the protocol include:

- Updating the expanded list of “other qualifying practitioners" who are eligible to apply for a waiver to prescribe buprenorphine (i.e., clinical nurse specialists, certified registered nurse anesthetists, and certified nurse midwives).
- Clarifying that buprenorphine is available in an extended-release injection formulation.
- Adding information about the use of subdermal formulations of buprenorphine (i.e., Probuphine and Sublocade).
- Adding information about possible clinical interactions between formulations of buprenorphine and naltrexone with various other medications and products.
- Improving the language to make clear the importance of testing for HIV and hepatitis C.
- Updating recommendations from the USPSTF on performing drug screening for adults in primary care settings.

Of note, prior to the COVID-19 pandemic, an in-person evaluation was required to initiate treatment with buprenorphine or methadone and daily visits were often required to pick up methadone doses. While an in-person evaluation is still required to initiate methadone treatment, the Drug Enforcement Agency (DEA) and SAMHSA are allowing buprenorphine to be prescribed via telehealth or over the phone. For both medications, the temporary SAMHSA guidelines allow treatment centers and programs to dispense up to 28 doses for clinically stable patients and up to 14 doses for less clinically stable patients.

Screening for Unhealthy Drug Use
In June 2020, the USPSTF updated its 2008 recommendations for screening for unhealthy drug use in adults and adolescents. Screening refers to asking questions about unhealthy drug use, not testing biological specimens. This recommendation statement applies to adults 18 years or older, including pregnant and postpartum persons, and adolescents aged 12 to 17 years in primary care settings. This statement does not apply to adolescents or adults who have a currently diagnosed drug use disorder or are currently undergoing or have been referred for drug use treatment. This statement applies to settings and populations for which services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. In adults, the USPSTF concludes with moderate
certainty that screening by asking questions about unhealthy drug use has moderate net benefit when services for accurate diagnosis of unhealthy drug use or drug use disorders, effective treatment, and appropriate care can be offered or referred. In adolescents, because of the lack of evidence, the USPSTF concludes that the benefits and harms of screening for unhealthy drug use are uncertain and that the balance of benefits and harms cannot be determined. The USPSTF recommends screening by asking questions about unhealthy drug use in adults 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred (B recommendation).

Additional Guidelines for Clinical Context:

Primary Care-Based Interventions to Prevent Illicit Drug Use in Children, Adolescents, and Young Adults

Illicit drug use is associated with many negative health, social, and economic consequences and is a significant contributor to 3 of the leading causes of death among young persons (aged 10-24 years): unintentional injuries including motor vehicle crashes, suicide, and homicide. To update its 2014 recommendation, the USPSTF commissioned a 2020 review of the evidence on the potential benefits and harms of interventions to prevent illicit drug use in children, adolescents, and young adults. This recommendation applies to children (11 years and younger), adolescents (aged 12-17 years), and young adults (aged 18-25 years), including pregnant persons. Only 1 study reported on harms and 2 studies reported an increase in illicit drug use after drug prevention interventions. Because of limited and inadequate evidence. The USPSTF concludes that the benefits and harms of primary care-based interventions to prevent illicit drug use in children, adolescents, and young adults are uncertain, that the evidence is insufficient to assess the balance of benefits and harms, and that more research is needed (Class I Statement).

After review, 1 guideline was excluded due to poor quality.

New Formulations: No new formulations have been marketed since the last review.

New FDA Safety Alerts:

Table 1. Description of New FDA Safety Alerts

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Month / Year of Change</th>
<th>Location of Change (Boxed Warning, Warnings, CI)</th>
<th>Addition or Change and Mitigation Principles (if applicable)</th>
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<tbody>
<tr>
<td>Naloxone</td>
<td>Narcan</td>
<td>July 2020</td>
<td>Drug Safety Communication^22</td>
<td>For all patients who are prescribed opioid pain relievers, health care professionals should discuss the availability of naloxone, and consider prescribing it to patients who are at increased risk of opioid overdose. Such patients include those who are using concomitant benzodiazepines or other medicines that depress the central nervous system, who have a history of OUD, or who have experienced a previous opioid overdose. Health care professionals should also consider prescribing naloxone if the patient has household members, including children, or other close contacts who are at risk for accidental ingestion or opioid overdose.</td>
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</tbody>
</table>
References:


## Appendix 1: Current Preferred Drug List

<table>
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<td>ACAMPROSATE CALCIUM</td>
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<td>IMPLANT</td>
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**Appendix 2: New Comparative Clinical Trials**

A total of 102 citations were manually reviewed from the initial literature search. After further review, 102 citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).

**Appendix 3: Medline Search Strategy**

Ovid MEDLINE(R) without Revisions 1996 to August Week 1 2020 and Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations 1946 August 14, 2020

```
1 acamprosate.mp. 809
2 exp Disulfiram/ 951
3 exp Naltrexone/ 5107
4 exp Alcoholism/ 32020
5 exp Substance-Related Disorders/ 165191
6 exp Alcohol Deterrents/ 6593
7 Buprenorphine 4081
8 Buprenorphine, Naloxone Drug combination 281
9. lofexidine 120
10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 170861
10 limit 9 to (English language and humans and yr="2019-Current" and (clinical trial, all or clinical trial or comparative study or controlled clinical trial or meta-analysis or multicenter study or practice guideline or pragmatic clinical trial or randomized controlled trial or systematic reviews)) 102
```
**Buprenorphine and Buprenorphine/Naloxone**

**Goals:**
- Prevent use of high-dose transmucosal buprenorphine products for off-label indications.

**Length of Authorization:**
- Up to 6 months

**Requires PA:**
- Transmucosal buprenorphine products that exceed an average daily dose of 24 mg per day

**Covered Alternatives:**
- Current PMPDP preferred drug list per OAR 410-121-0030 at [www.orpdl.org](http://www.orpdl.org)
- Searchable site for Oregon FFS Drug Class listed at [www.orpdl.org/drugs/](http://www.orpdl.org/drugs/)

### Approval Criteria

<table>
<thead>
<tr>
<th>Step</th>
<th>Question</th>
<th>Yes: Go to #2</th>
<th>No: Pass to RPh. Deny; not funded by OHP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Is the diagnosis funded by the OHP?</td>
<td>Yes: Go to #2</td>
<td>No: Pass to RPh. Deny; not funded by OHP</td>
</tr>
<tr>
<td>2.</td>
<td>Is the prescription for opioid use disorder (opioid dependence or addiction)?</td>
<td>Yes: Go to #3</td>
<td>No: Pass to RPh. Deny; medical appropriateness</td>
</tr>
<tr>
<td>3.</td>
<td>Is the prescription for a transmucosal formulation of buprenorphine (film, tablet) with an average daily dose of more than 24 mg (e.g., &gt;24 mg/day or &gt;48 mg every other day)?</td>
<td>Yes: Pass to RPh. Deny; medical appropriateness</td>
<td>No: Go to #4</td>
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# Approval Criteria

<table>
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<th>Yes: Approve for anticipated length of treatment or 6 months, whichever is less.</th>
<th>No: Go to #5</th>
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<tbody>
<tr>
<td></td>
<td>Note: Notify prescriber concomitant naloxone is recommended if not present in claims history.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Will the prescriber switch to a preferred product?</th>
<th>Yes: Inform prescriber of covered alternatives in class.</th>
<th>No: Approve for anticipated length of treatment or 6 months, whichever is less.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note: Preferred products are reviewed for comparative safety and efficacy by the Oregon Pharmacy and Therapeutics Committee.</td>
<td>Note: Notify prescriber concomitant naloxone is recommended if not present in claims history.</td>
<td></td>
</tr>
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## Lofexidine

### Goal(s):
- Encourage use of substance use disorder medications on the Preferred Drug List.
- Restrict use of lofexidine under this PA to ensure medically appropriate use of lofexidine based on FDA-approved indications.

### Length of Authorization:
- Up to 14 days

### Requires PA:
- Lofexidine 0.18mg tablets

### Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at [www.orpdl.org](http://www.orpdl.org)
• Searchable site for Oregon FFS Drug Class listed at [www.orpdl.org/drugs/](http://www.orpdl.org/drugs/)

## Approval Criteria

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<tbody>
<tr>
<td>1. What diagnosis is being treated?</td>
<td>Record ICD10 code.</td>
<td></td>
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<tr>
<td>2. Is this an FDA approved indication? (Mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults)</td>
<td><strong>Yes</strong>: Go to #3</td>
<td><strong>No</strong>: Pass to RPh. Deny; medical appropriateness</td>
</tr>
<tr>
<td>3. Will the prescriber consider a change to a preferred product?</td>
<td><strong>Yes</strong>: Inform prescriber of covered alternatives in class.</td>
<td><strong>No</strong>: Approve for up to 14 days of total therapy.</td>
</tr>
</tbody>
</table>

- Message:
  - Preferred products do not require a PA. Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Oregon Pharmacy & Therapeutics Committee.

*P&T/DUR Review: 12/20 (DM); 11/19 (DM); 1/19
Implementation: 3/1/19*