PURPOSE
This protocol specifies the criteria and procedures for pharmacists to initiate the dispensing and administration of naltrexone for medication assisted treatment to individuals for opioid use disorder recovery.

PHARMACIST EDUCATION AND TRAINING
Prior to initiating the dispensing and administration of naltrexone under this protocol, pharmacist(s) must have received education and training in opioid use disorders and naltrexone therapy, including review of American Society of Addiction Medicine’s National Practice Guideline for the use of medications in the treatment of addiction involving opioid use\(^1\), from a provider accredited by the Accreditation Council for Pharmacy Education, or by a comparable provider approved by the Kentucky Board of Pharmacy.

Provider of Training: _______________________________________

Date Training Completed: ________________________________

CRITERIA
Pharmacist(s) authorized to initiate the dispensing and administration of naltrexone will follow the most current American Society of Addiction Medicine, National Practice Guideline for the use of medications in the treatment of addiction involving opioid use.\(^1\)

Inclusion criteria:
Any individual, 18 years or older, with a diagnosis of opioid use disorder who meets the following criteria:

- evaluation of hepatic function within the past 14 days; pharmacist may order hepatic function laboratory tests or conduct point-of-care hepatic function testing and document results to satisfy this criterion
- adequately detoxified from opioids as verified by point-of-care urine drug screen
- has no signs or symptoms of withdrawal as verified by Clinical Opiate Withdrawal Scale (COWS) \{Appendix 1\}
- is able to provide informed consent

Exclusion criteria:
- Individuals who are pregnant are not eligible to receive therapies under this protocol and should be referred to their primary care or Ob/Gyn provider.
- Individuals who have contraindications (severe allergic reaction to naltrexone or any component of the extended-release injectable naltrexone formulation).

\(^1\) Available at: https://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf
• Individuals with acute hepatitis or liver failure or liver function tests >3 times the upper limits of normal (ULN).
• Individuals testing positive for opioids via a point-of-care urine drug screen

MEDICATIONS
This protocol authorizes pharmacists to initiate the dispensing and administration of the following medications as referenced in the manufacturer’s product information.2

1) Extended-release injectable naltrexone (Vivitrol®)
2) Oral naltrexone (ReVia®, Depade®), which is used solely for the initial withdrawal challenge

PROCEDURES FOR INITIATION OF THERAPY
Naltrexone will be initiated only in carefully selected individuals based on relevant medical and social history and consideration of contraindications and precautions of therapy as outlined in the pharmacologic product guide and identified through assessment and screening.2

Relevant Medical and Social History
• Past medical history, including an active diagnosis of opioid dependence disorder
• Current medications
• Allergies and hypersensitivities
• Previous medication assisted therapy attempts and failures
• Psychosocial counseling treatment plans

Contraindications and Precautions
• Hypersensitivity to naltrexone, or components of the naltrexone diluent
• Pregnancy
• Chronic opioid analgesics for chronic pain syndromes
• Current opioid dependence, including partial agonists
• Acute hepatitis or liver failure or liver function tests >3x ULN
• Positive urine drug screen for opioids
• Positive opioid withdrawal assessment- indicated by COWS score 5 or greater
  o Injection will not be provided to individuals with positive opioid withdrawal assessment. (Opioid withdrawal assessment will be repeated in 24 hours.)
• Any individual who has failed the naltrexone challenge test as evidenced by a change in COWS score of 2 or more
• Moderate to severe renal impairment
• History of thrombocytopenia or coagulation disorders

Assessment and Screening
• Individual confirmation of absence of opioid use for 7-10 days
• Negative urine drug screen for opioids
• Opioid withdrawal assessment as follows:
  o naltrexone 25mg oral x1 (1/2 of a 50mg tablet) with observation for 60 minutes for signs and symptoms of opioid withdrawal.

2 Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021897s015lbl.pdf
Prior to and following the 60-minute observation period, pharmacist will complete the Clinical Opiate Withdrawal Scale (COWS) {Appendix 1}.

• Negative urine pregnancy test in females of child-bearing potential

If all inclusion and assessment criteria are met, pharmacists will administer long acting injectable naltrexone (Vivitrol®) 380 mg IM according to the manufacturer’s product information. Individuals receiving therapy will be monitored for adverse reactions for a period of 15 minutes. In the unlikely event of a serious or life-threatening allergic reaction, pharmacists will implement the attached anaphylaxis protocol {Appendix 2}.

PROCEDURES FOR MONITORING AND CONTINUATION OF THERAPIES
Subsequent naltrexone will be dispensed and administered every 28 days (+/- 2 days) only in individuals who confirm absence of opioid use for 7-10 days and provide a negative urine drug screen for opioids. Individuals outside of 30 days since last injection will also require an opioid withdrawal assessment. Females of child-bearing potential must also have a negative urine pregnancy test.

Follow up monitoring and evaluation shall occur at a minimum at every 28 days (+/- 2 days) with each injection to determine effectiveness, adverse effects and individual progress with therapy, including participation in psychosocial treatment. If follow-up monitoring and evaluation indicates therapy continuation is warranted, naltrexone will be dispensed and administered every 28 days (+/- 2 days). Treatment periods longer than 12 months of continuous therapy are not authorized under this protocol without explicit approval from the authorizing practitioner.

Should follow-up evaluation and monitoring indicate continued therapy with extended-release injectable naltrexone is warranted, all procedures as outlined for initiation of therapies, including education, documentation and notification, will be followed.

EDUCATION REQUIREMENTS
Individuals receiving extended-release injectable naltrexone under the protocol will receive education regarding:

1) Benefits, including the mechanism of action of naltrexone
2) Alternatives to naltrexone
3) Requirement of opioid free period for at least 7-10 days to avoid precipitation of severe opioid withdrawal
4) Risk of opioid overdose at the end of duration of effect time period, if a dose is missed or treatment is discontinued, and in attempt to overcome blockade
5) Warnings and adverse effects possible with use of naltrexone
6) Expectation to carry and/or wear documentation of naltrexone treatment
7) Benefits of treatment shown only when used as part of a program that includes counseling and support
8) Use of rescue naloxone for emergency treatment of opiate overdose
naloxone rescue medication will be provided under pharmacist naloxone protocol if individual does not have naloxone available.

A written medication guide {Appendix 3} will be provided to each individual at initiation of therapy.

**DOCUMENTATION**
Pharmacists shall document via prescription record each individual who receives naltrexone under this protocol, including:

(a) Documentation as required in 201 KAR 2:170 for the dispensing of prescription medication
(b) Documentation that the individual receiving naltrexone was provided with the required education pursuant to this protocol
(c) Documentation of informed consent to receive treatment
(d) Documentation of the history and assessment, of the care plan implemented and follow-up evaluation and monitoring, including individual confirmation of continued opioid free period and negative urine drug screen; and if applicable, negative urine pregnancy test and/or results of oral naltrexone challenge, including COWS assessment
(e) Documentation of medication lot and expiration; location of injection; and initials or NPI of administering pharmacist

**NOTIFICATION**
Pharmacist(s) shall provide notification of the medications dispensed and administered under the protocol to the primary care provider within two (2) business days. Any individual affirmatively stating that he/she does not have a primary care provider will be referred for a medical evaluation prior to initiating therapies under this protocol.

Pharmacist(s) shall provide notification if medication is ceased by the individual, or if administration is not warranted under conditions of the protocol, to the primary care provider within two (2) business days.

[If directed by the authorizing practitioner] the pharmacist shall provide written notification via fax or other secure electronic means to the authorizing practitioner of persons receiving naltrexone therapy under this protocol within 7 days of initiating dispensing.

**TERMS**
This protocol is effective as of the date all parties execute the document. It shall remain in effect for a period of one year and shall automatically renew for successive one year periods unless otherwise terminated by any party, with or without cause. Any termination without cause shall require prior notice to all parties of no less than sixty days.
SIGNATURES

__________________________________   ____________________
Practitioner Name        Date

__________________________________
Practitioner Signature

__________________________________   ____________________
Pharmacist Name        Date

__________________________________
Pharmacist Signature
APPENDIX 1
Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

<table>
<thead>
<tr>
<th>Patient’s Name: __________________________</th>
<th>Date and Time ____________________________</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for this assessment: __________________________________________________________</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Resting Pulse Rate</strong>: _____ beats/minute</th>
<th><strong>GI Upset</strong>: over last 1/2 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured after patient is sitting or lying for one minute</td>
<td>0 no GI symptoms</td>
</tr>
<tr>
<td>0 pulse rate 80 or below</td>
<td>1 stomach cramps</td>
</tr>
<tr>
<td>1 pulse rate 81-100</td>
<td>2 nausea or loose stool</td>
</tr>
<tr>
<td>2 pulse rate 101-120</td>
<td>3 vomiting or diarrhea</td>
</tr>
<tr>
<td>4 pulse rate greater than 120</td>
<td>5 multiple episodes of diarrhea or vomiting</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Sweating</strong>: over past 1/2 hour not accounted for by room temperature or patient activity.</th>
<th><strong>Tremor</strong>: observation of outstretched hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no report of chills or flushing</td>
<td>0 no tremor</td>
</tr>
<tr>
<td>1 subjective report of chills or flushing</td>
<td>1 tremor can be felt, but not observed</td>
</tr>
<tr>
<td>2 flushed or observable moistness on face</td>
<td>2 slight tremor observable</td>
</tr>
<tr>
<td>3 beads of sweat on brow or face</td>
<td>4 gross tremor or muscle twitching</td>
</tr>
<tr>
<td>4 sweat streaming off face</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Restlessness</strong>: Observation during assessment</th>
<th><strong>Yawning</strong>: Observation during assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 able to sit still</td>
<td>0 no yawning</td>
</tr>
<tr>
<td>1 reports difficulty sitting still, but is able to do so</td>
<td>1 yawning once or twice during assessment</td>
</tr>
<tr>
<td>3 frequent shifting or extraneous movements of legs/arms</td>
<td>2 yawning three or more times during assessment</td>
</tr>
<tr>
<td>5 unable to sit still for more than a few seconds</td>
<td>4 yawning several times/minute</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Pupil size</strong>:</th>
<th><strong>Anxiety or Irritability</strong>:</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 pupils pinned or normal size for room light</td>
<td>0 none</td>
</tr>
<tr>
<td>1 pupils possibly larger than normal for room light</td>
<td>1 patient reports increasing irritability or anxiousness</td>
</tr>
<tr>
<td>2 pupils moderately dilated</td>
<td>2 patient obviously irritable or anxious</td>
</tr>
<tr>
<td>5 pupils so dilated that only the rim of the iris is visible</td>
<td>4 patient so irritable or anxious that participation in the assessment is difficult</td>
</tr>
</tbody>
</table>

| **Bone or Joint aches**: previously having pain
If patient was having pain, only the additional component attributed to opiates withdrawal is scored | **Gooseflesh skin**: |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td>0 skin is smooth</td>
</tr>
<tr>
<td>1 mild diffuse discomfort</td>
<td>3 piloerection of skin can be felt or hairs standing up on arms</td>
</tr>
<tr>
<td>2 patient reports severe diffuse aching of joints/muscles</td>
<td>5 prominent piloerection</td>
</tr>
<tr>
<td>4 patient is rubbing joints or muscles and is unable to sit still because of discomfort</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Runny nose or tearing</strong>: Not accounted for by cold symptoms or allergies</th>
<th><strong>Total Score</strong></th>
<th><strong>The total score is the sum of all 11 items</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 nasal stuffiness or unusually moist eyes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 nose running or tearing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 nose constantly running or tears streaming down cheeks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.
Appendix 2
Addendum for Management of Adverse Reactions to Naltrexone

All medications have the potential to cause an adverse reaction. In order to minimize adverse reactions, individuals must be carefully screened for precautions and contraindications before the medication is administered. Even with careful screening, reactions may occur. These reactions can vary from trivial and inconvenient (e.g. soreness, itching) to severe and life threatening (e.g. anaphylaxis). If reactions occur, the pharmacists must be prepared with procedures for their management.

Anaphylactic Reactions

Signs and symptoms of anaphylactic reaction include:
- the sudden or gradual onset of generalized itching, erythema (redness), or urticaria (hives);
- angioedema (swelling of the lips, face, or throat);
- bronchospasm (wheezing);
- shortness of breath;
- shock;
- abdominal cramping; or
- cardiovascular collapse.

The following procedures should be used to manage anaphylactic reactions following administration:

1) If itching and swelling are confined to the injection site, observe closely for at least 30 minutes, watching for the development of generalized symptoms.
2) If symptoms are generalized, activate the emergency medical system (e.g., call 911) immediately.
   a. Administer diphenhydramine for hives or generalized itching, either orally or by intramuscular injection.
      • The standard dose is 1-2 mg/kg every 4-6 hours, or 50 to 100 mg maximum single dose for adults. Do not attempt to give oral medications to an individual who is not fully alert and able to swallow safely.
3) Place individual in a recumbent position and elevate legs.
4) The first-line therapy in anaphylaxis is epinephrine. There are no contraindications to epinephrine in the setting of anaphylaxis.
   a. Administer aqueous epinephrine 1:1000 dilution intramuscularly, 0.01mL/kg/dose (adult dose ranges from 0.3mL to 0.5mL, with a maximum single dose of 0.5mL), as indicated:

<table>
<thead>
<tr>
<th>5) Weight (lbs)</th>
<th>6) Weight (kg)</th>
<th>7) Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>8) 45-88 lb</td>
<td>9) 21-40 kg</td>
<td>10) 0.3mg (or mL)</td>
</tr>
<tr>
<td>11) 89-110 lbs</td>
<td>12) 41-50 kg</td>
<td>13) 0.45mg (or mL)</td>
</tr>
<tr>
<td>14) &gt;110 lbs</td>
<td>15) &gt;51 kg</td>
<td>16) 0.5mg (or mL)</td>
</tr>
</tbody>
</table>
1. Prefilled devices (i.e., EpiPen or similar autoinjector):
2. Weight > 66 lbs or 30 kg – EpiPen 0.30mg
3. The site of injection can be gently massaged to facilitate absorption.
   b. If EMS has not arrived and symptoms are still present, the dose of epinephrine may be repeated every 5 to 15 minutes for up to 3 doses, depending on the individual's response.

For all adverse reactions the following procedures should be used:
   • Monitor the individual closely and check vital signs (blood pressure, pulse, and respirations) every 2 to 5 minutes.
   • Stay with individual until EMS arrives.
   • If necessary, perform cardiopulmonary resuscitation (CPR) and maintain airway.
   • Keep individual in supine position unless he or she is having breathing difficulty. If breathing is difficult, individual's head may be elevated, provided blood pressure is adequate to prevent loss of consciousness. If blood pressure is low, elevate legs.
   • Notify the authorizing practitioner and, if applicable the primary care practitioner as soon as possible.
Appendix 3: Vivitrol® Medication Guide

What is Vivitrol®?

Vivitrol® is a prescription injectable medication used to treat alcohol dependence. You should stop drinking before starting VIVITROL.

What is the most important information I should know about VIVITROL?

To be effective, treatment with VIVITROL must be used with other alcohol or drug recovery programs such as counseling. VIVITROL may not work for everyone.

It is not known if VIVITROL is safe and effective in children.

Who should not receive VIVITROL?

Do not receive VIVITROL if you:

- are using or have a physical dependence on opioid-containing medicines or opioid street drugs.

See “What is the most important information I should know about VIVITROL?”

To see whether you have a physical dependence on opioid-containing medicines or opioid street drugs, your healthcare provider may give you a small injection of a medicine called naloxone. This is called a naloxone challenge test. If you get symptoms of opioid withdrawal after the challenge, your healthcare provider will not start treatment with VIVITROL at that time. Your healthcare provider may repeat the test after you have stopped using opioids to see whether it is safe to start VIVITROL.

- are having opioid withdrawal symptoms. Opioid withdrawal symptoms may happen when you have been taking opioid-containing medicines or opioid street drugs regularly and then stop.

Symptoms of opioid withdrawal may include:

- anxiety, sleep problems, weakness, feeling sick, sweating, yawning, crying, watery eyes, sneezing, rhinorrhea, stuffy nose, constipation, diarrhea, sleep problems, or vomiting.

See “What is the most important information I should know about VIVITROL?”

Tell your healthcare provider if you have any of these symptoms before taking VIVITROL.

- are allergic to any of the ingredients in VIVITROL or the liquid used to mix VIVITROL (alcohol). See the end of this Medication Guide for a complete list of ingredients in VIVITROL and the alcohol.

What are the possible side effects of VIVITROL?

VIVITROL can cause serious side effects, including:

- See “What is the most important information I should know about VIVITROL?”
- Depressed mood: Sometimes this leads to suicide, violent thoughts, and suicidal behavior. Tell your family members and people close to you about the risk of these reactions, especially in children and adolescents. Tell them to watch for any of the following signs and symptoms of depression, suicide, agitation, or unusual behavior, especially if they are new, worse, or get better to go to the hospital.

- You or someone close to you should get emergency medical help right away if you:
  - have fast breathing
  - have or develop a rash or hives
  - have difficulty swallowing or breathing
  - have loose, watery stools (loose or liquid); diarrhea
  - have confusion
  - have a skin rash that is red and itchy
  - have problems with vision
  - have persistent nausea
  - have shortness of breath
  - have swelling of your face, lips, tongue, or throat
  - have unusual or severe pain in your chest
  - have a sudden or severe change in your behavior
  - have any of these other side effects that are not listed above, or that are unusual or unusual

Tell your healthcare provider if you have any side effects that bother you or that you think are not listed.

How will I receive VIVITROL?

VIVITROL is injected into your muscle by a healthcare provider. You will not need a needle.

What are the ingredients in VIVITROL?

Active ingredients: naltrexone injection, polyethylene glycol 400 (PEG), and polyethylene glycol 2000 (PEG).

This Medication Guide was approved by the U.S. Food and Drug Administration.

Manufactured and marketed by:

Alkermes, Inc.

619 Waterfront

Waltham, MA 02451-1120

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