

XR-Naltrexone: A Step-by-Step Guide

Step 1: Patient History

Initial Assessment (Naltrexone Readiness Form):

- Patient information
- Drug use: type, amount, route
- Treatment history: medications, response, adherence

Step 2: Medical Evaluation

Medical history:

- Complications (infections, overdoses, liver disease)
- Physical exam: vital signs, infections (abscesses, cellulitis)
- Labs: CBC, chemistry, UA, pregnancy, hepatitis panel, drug toxicology, breathalyzer

Step 3: Shared Decision-Making

Appropriateness for XR-Naltrexone:

- Provide information about patient's medical status and diagnosis
- Review consequences of opioid use
- Provide information about opioid use disorder and its treatment
- Review information on use and side effects of naltrexone (Naltrexone Education Form)
- Review diagnostic information (patient's medical status and diagnosis)



Step 4:

Assessment—Patient Readiness

Initial readiness assessment for XR-naltrexone

1. Vital signs
2. Urine toxicology (screen for all opioids including, buprenorphine, oxycodone and methadone)
3. Recent opioid use history
4. Pregnancy test
5. Assess for contraindications, e.g. active pain requiring opioids

NO USE

within past 10-14 days

- IF: Good evidence of opioid abstinence in past 2 weeks, no withdrawal symptoms, and opioid-negative toxicology.
- THEN: Proceed with the XR-naltrexone injection.

OR

USE

*within the past 14 days
but not in the past 7 days*

- Evaluate opioid withdrawal using Clinical Opiate Withdrawal Scale (COWS).

OR

USE

within past 7 days

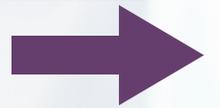
Patient may still be physically dependent even with opioid-negative toxicology.

- Treat withdrawal with adjunctive medication and postpone evaluation until at least 7 days of no opioid use (See **USE within 14 days**).
- In case of daily opioid use, recommend cessation and conduct buprenorphine-assisted withdrawal management.

If COWS >4
treat withdrawal with adjunctive medication and reevaluate in 1-2 days.

If COWS ≤4 AND
opioid-negative toxicology, perform i.m. naloxone challenge or p.o. naltrexone challenge.

Then proceed with the XR-naltrexone injection.



Step 5: Materials

- Refrigeration — Keep XR-naltrexone refrigerated at all times (36° to 46° F). Remove from refrigeration at least 30 minutes before administration. If not used, it can be returned to the refrigerator.
- IM injection setup (gloves, alcohol and/or betadine swab, sterile gauze pads, adhesive bandage, and sharps container)

Step 6: Drug/Patient Preparation

- Assess body habitus of patient – layer of fat over muscle not greater than length of injection needle (2”/usually BMI <40)
- Review medication preparation and injection via instructional [video](#) and/or package insert.

Step 7: Injection

- Proceed with dorsogluteal injection (upper outer quadrant, aspirate for blood)
- Alternate buttocks with subsequent injections
- Avoid injecting subcutaneously or into adipose
- If unable to inject because of clogged needle, withdraw, replace the needle and repeat procedure

Step 8: Observation

- Observe patient for 10 minutes for any immediate adverse reactions.
- Perform Medical Management Support for Opioid Dependence: [Initial Medical Management Form](#) (10 minutes)
- Remind patient to contact doctor/health care facility in case of any side effects.
- Patient should be given a [medication safety card](#) or bracelet to carry and present to caregiver to show in an emergency.

Step 9: Follow-up Visit

- Conduct active outreach to have patient return to the office for monthly injections (appointment reminders, family involvement)
- Unless contraindicated, administer injection of XR-Naltrexone every 4 weeks.
- Perform [Follow Up Medical Management session](#)
- If patient misses injection, administer injection only if no use or perform naloxone/naltrexone challenge (see Step 4)



Resources



Resources

Tools/Forms:

Clinical Opiate Withdrawal Scale (COWS)

- Intended to allow clinicians to rate common signs and symptoms of opiate withdrawal and monitor symptoms over time.

Naltrexone Readiness Form

- This form compiles information on patient history, lab information, drug use history, medical history, physical exam, and other pertinent information to assess patient readiness.

Naltrexone Education Form

- Provided to and reviewed with patient. Describes how naltrexone works, side effects, length of treatment, etc.

Initial Medication Management Form

- This template outlines the initial appointment in a series of appointments and is designed to support patients diagnosed with opioid dependence who are starting a course of medication to help them maintain abstinence.

Follow Up Medication Management Form

- This template outlines the follow-up appointments designed to help patients maintain abstinence.

Medication Safety Card

- Patient must carry this card with them at all times, to inform the caregiver of the relevant medical management considerations.

Additional Resources:

[ASAM National Practice Guideline](#)

[The Facts About Naltrexone](#)

[Opioid Detoxification and Naltrexone Induction Strategies: Recommendations for Clinical Practice](#)

[Primer on Antagonist-Based Treatment of Opioid Use Disorder in the Office Setting](#)

[Preparation and Injection of Extended-Release Naltrexone Video](#)

[VA/DoD Clinical Practice Guidelines for the Management of Substance Use Disorders](#)

[More Resources](#)

Resources

Clinical Protocols*:

Naloxone (i.m.) Challenge Procedure

- Obtain baseline COWS, if 4 or less proceed with the challenge
- Administer naloxone 0.4 mg (1 cc) i.m. to deltoid and observe for 20 minutes.
- If no change in COWS administer additional 0.8 mg (2 cc) to the other deltoid and monitor for additional 20 minutes
- Test is considered positive if there is a COWS increase of 2 or more from the pre-injection score
- In case of positive challenge, do not administer XR-naltrexone, wait 1-2 days and repeat the challenge
- If the test is negative, proceed with the XR-Naltrexone injection.

Naltrexone (p.o.) Challenge Procedure

- Obtain baseline COWS; if 4 or less proceed with the challenge
- Administer naltrexone 25 mg p.o. and observe for 90 minutes, if COWS increase is less than 2 proceed with XR-naltrexone injection
- In case of positive challenge, treat withdrawal with adjunctive medications and reschedule injection for next day
- Administer XR-naltrexone (no need for repeated challenge the next day unless there was a new episode of use)

Adjunctive Medications to treat Opioid Withdrawal

- Clonidine 0.1 mg every 4-6 hours (monitor for orthostatic hypertension, hold if SBP<100)
- Clonazepam 0.5 mg every 6-8 hours
- Trazodone 100 mg at night for insomnia

Buprenorphine-assisted withdrawal management

- Wait until the patient is in withdrawal (COWS > 6) and administer buprenorphine (4 mg bid on Day 1)
- Administer adjunctive medications as needed to alleviate residual withdrawal
- Continue adjunctive medication for at least 7 days after the last day of buprenorphine
- Perform naloxone/naltrexone challenge before administering XR-naltrexone

* The suggested protocols are off-label, based on the expert consensus and do not reflect the official position of SAMHSA.

