Naltrexone Formulations in Correctional Settings

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Patients may enter your facility on injectable naltrexone (Vivitrol) for treatment of Opioid Use Disorder.

Must you keep them on this expensive formulation, or can you switch them to oral naltrexone during incarceration?

This brief provides clinical, financial, and administrative information prisons and jails can use in deciding whether to keep detainees on extended release naltrexone (XR-NTX, or the brand Vivitrol) or switch them to oral naltrexone tablets in instances where detainees have been prescribed XR-NXT prior to incarceration. This brief does NOT cover comparative effectiveness of naltrexone to other FDA-approved medications for opioid use disorder.

FDA APPROVED INDICATIONS FOR NALTREXONE

Extended Release Naltrexone (XR-NTX) intramuscular injection is approved by the Food and Drug Administration (FDA) for "prevention of relapse to opioid dependence following opioid detoxification" and "for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment."

Oral naltrexone is approved by the FDA for "the blockade of the effects of exogenously administered opioids," i.e., a one-time dose to block an opioid, and is also approved for the "treatment of alcohol dependence." The use of oral naltrexone for treating opioid use disorder (OUD) is not explicitly approved by the FDA and therefore its use for OUD is "off-label."

Why is oral naltrexone not approved for treatment of OUD?

In a Cochrane review[1] of oral naltrexone for OUD compared to placebo or nonpharmacological treatments, there was a significant decrease in recidivism for those on oral naltrexone but there was not improvement in retention in treatment or abstinence[2]. There was a very high drop-out rate in these studies, which is consistent with other oral naltrexone studies. For example, in a study of commercially insured patients[3]:

- 70% of individuals given oral naltrexone discontinued treatment within thirty days
- 52% of patients given long-acting injectable naltrexone discontinued treatment within thirty days

Significantly improved retention in treatment with injectable long-acting naltrexone compared to oral formulation has led the FDA to approve only long acting formulations of naltrexone for OUD.

AMERICAN SOCIETY FOR ADDICTION MEDICINE POSITION ON ORAL NALTREXONE FOR OUD

In its March/April 2020 update to its National Practice Guideline for the Treatment of Opioid Use Disorder[4], the American Society of Addiction Medicine (ASAM) specifies that *"except under special circumstances, evidence does not support the use of oral naltrexone as an effective treatment for prevention of opioid use disorder relapse."* Special circumstances are noted to include *"(1) for highly compliant and motivated patients such as safety sensitive workers (e.g. police, firefighters, and healthcare professionals) or other individuals with high levels of monitoring and knowledge of negative consequences for nonadherence; (2) patients who wish to take an opioid receptor antagonist but are unable to take extended-release naltrexone (e.g. patients who may need an opioid analgesic within the next month); and (3) patients who may benefit from medication to prevent return to illicit drug use but cannot or will not take extended-release naltrexone and do not wish to be treated with (or do not have access to) opioid agonists."*

The Executive Summary of the Focused Update of the ASAM National Practice Guideline[5] further states that *"oral naltrexone seems to be most useful when there is a support person to administer and supervise the medication."*

Both "high levels of monitoring" and "a support person to administer and supervise the medication" are conditions present in correctional settings, making the use of oral naltrexone for OUD in jails and prisons clinically acceptable.

RESEARCH ON NALTREXONE FOR JUSTICE INVOLVED POPULATIONS

For justice-involved populations, XR-NTX is supported by data showing reduced opioid use when administered pre-release from incarceration and to those under criminal justice supervision[6].

A systematic review and meta-analysis[7] looking at oral and XR-NTX combined found:

- Oral naltrexone did not significantly improve retention in treatment, and injectable naltrexone approached statistical significance in retention in treatment.
- Oral naltrexone significantly decreased re-incarceration rates.
- XR-NXT produced a significant reduction in relapse.

This study concluded "XR-NTX has been shown to be an effective treatment for OUD and has been more accepted in criminal justice settings. In general, oral naltrexone is not considered a first-line recommendation for individuals with OUD—except in a controlled environment—because it is too easily discontinued."[8]

This study, too, supports the concept of oral naltrexone for OUD in the "controlled environment" of a jail or prison.

INTERPRETING RECOMMENDATIONS FOR ORAL NALTREXONE FOR OUD IN CORRECTIONAL SETTINGS

The decision to continue naltrexone treatment for OUD in prisons and jails is unequivocal in terms of medical practice. The detainee has been diagnosed with a chronic opioid addiction that is a protected condition under the Americans with Disabilities Act, and has been prescribed an FDA-approved treatment that complies with treatment guidelines.

There is no specific research that creates a clear precedent for switching a patient from XR-NTX to oral naltrexone. Nonetheless, the cost differential between the oral and injectable medications and the clinical appropriateness based on the controlled environment for medication administration makes this a reasonable consideration in many prisons and jails.

Termination of naltrexone treatment for OUD deviates from the standard of care and places the facility at risk of legal action for failure to treat. It also places the detainee at serious risk of relapse, overdose, and death both if opioids are accessed in the facility and/or if a precipitous release occurs.

Medi-Cal cost for a 380 mg XR-NTX injection in March 2020 was $1,265.

Medi-Cal cost for 28 days of treatment with 50 mg of oral naltrexone was $22.12.[9]

Switching a detainee from XR-NTX to oral naltrexone is an off-label use of this medication. Additionally, if naltrexone is determined to the most appropriate medication based on clinical evaluation to treat an individual for OUD, starting this detainee on oral naltrexone would also be an off-label use of oral naltrexone. However, it is clear that so long as the administration of oral naltrexone in a prison or jail is closely supervised, observed, and monitored, the "controlled environment" exists in which oral naltrexone is effective and acceptable for treating OUD. This satisfies the concerns of the FDA and ASAM.

Administration of 100 mg of oral naltrexone provides nearly 100% blockade of 25 mg of intravenous heroin for 48 hours.[10] The duration of effect of 50 mg dosing, which is the common dose in the U.S., has not been well researched.

Oral naltrexone provides an affordable and clinically appropriate option for continued treatment in a supervised correctional setting.

JUSTICE SYSTEM CONSIDERATIONS FOR SWITCHING FROM XR-NTX TO ORAL NALTREXONE

When a detainee enters a jail or prison and has received XR-NTX in the community or prior correctional setting, the facility is posed with a number of considerations.

When was the last injection/when is the next injection due?

The answer determines how much time the facility has to develop a plan of action. Of note, research shows and clinical practice supports that naltrexone levels begin to drop 21 days after XR-NTX injection.[8] In clinical practice, injections are often given 21-28 days after the prior dose.

How long is the detainee likely to be incarcerated?

This informs the facility's plan. For example:

- If the next injection is due in 17 days and the detainee is expected to be released within 3-5 days, no action is needed *except* to flag the medical record for health care staff to re-evaluate the plan if the detainee remains in the facility.
- If the next injection is due in 6 days and the detainee is likely to remain incarcerated beyond that, the health care team must make arrangements for continuation of naltrexone treatment. The medical record must be flagged, and a workflow must be identified to initiate oral naltrexone on or before the day the injection would have been due. As noted above, 21-28 days following the last injection is generally considered acceptable.
- If the facility provides XR-NTX in preparation for release, the facility may be able to cover one or more XR-NTX injections using the release resources if the anticipated release date is close to the next injection date.

Do facility medication practices constitute an effective "controlled environment" that supports oral over XR-NTX for treatment of OUD?

The effectiveness of oral naltrexone is contingent on daily use. A facility's medication practices *must sufficiently account for these factors:*

- Interpreting the ASAM clinical guidelines as applied to correctional settings, oral naltrexone should never be given as "keep on person." Observed therapy through a medication line or cell-side administration is essential.
- Ingestion of oral naltrexone must be sufficiently observed to assure that detainee "cheeking" or other forms of diversion are not employed.
- Missed doses of oral naltrexone are immediately flagged and acted upon.

For both diversion and missed doses, a nurse, SUD counselor, or mental health counselor must confer with the patient within 24 hours and refer to the prescriber for an urgent evaluation if indicated. Patient education about the risk of relapse and overdose following cessation of oral naltrexone is essential.

JUSTICE SYSTEM CONSIDERATIONS FOR MAINTAINING XR-NTX

There are reasonable considerations for prisons and jails to continue detainees on XR-NTX.

- Importantly, XR-NTX removes the need for the detainee to decide each day if he/she wishes to take the naltrexone as ordered. Anecdotally, detainees frequently comment on the value of removing daily temptations in their sobriety. Where opioids are available in prisons and jails, this is a real concern.
- When an inmate is on no other medications requiring direct observation, the use of XR-NTX would mean that an inmate needs a brief health care encounter one time every 28 days rather than a daily visit to the medication line.
- There are significant personnel costs for nursing and custody in daily medication administration.
- Safety factors in inmate movement 30 times a month (for daily medication administration) versus once (for a monthly medication administration) should also be considered.
- Prisons and jails should weigh these factors against the cost differential of the medication formulations.
- Prisons and jails should also consider the community practice and whether XR-NTX is covered by Medicaid and/or widely used in the community. There may be compelling reasons for prison or jail addiction treatment practices to align with the practices in the community.

SUMMARY STATEMENTS

Licensed physicians are allowed to prescribe medications for “off-label” use. Rules for off-label use by non-physician prescribers vary by state. ASAM supports off-label use of lower-cost oral naltrexone for treatment of OUD when monitored. ASAM enumerates conditions of an appropriate “controlled environment” in which oral naltrexone is an acceptable treatment for OUD, and correctional settings can provide that environment.

Correctional settings may safely and economically treat OUD with oral naltrexone so long as the controlled environment is assured. Consideration of off-label use of oral naltrexone for OUD include patient-specific, patient preference, facility space and transport, expected duration of incarceration, community practices, and other factors.

AUTHORS

Shannon Robinson
MD, FASAM
Principal
srobinson@healthmanagement.com

Donna Strugar-Fritsch
BSN, MPA, CCHP
Principal
dstrugarfritsch@healthmanagement.com

Scott Haga
MPAS, PA-C
Senior Consultant
shaga@healthmanagement.com

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