Vivitrol
(naltrexone for extended-release injectable suspension)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

This policy document describes the status of medical technology or treatment at the time the document was developed. Since that time, new technology or treatment may have emerged or new medical literature may have been published. This policy will be reviewed regularly and be updated as scientific and medical literature becomes available.

DESCRIPTION

The intent of the policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Vivitrol (naltrexone for extended-release injectable suspension) is a long acting opioid antagonist given once monthly by intramuscular injection.

Vivitrol is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to receiving treatment. Patients should not be actively drinking at the time of initial Vivitrol administration.

Vivitrol is indicated for the prevention of relapse to opioid dependence following opioid detoxification.

Vivitrol should be part of a comprehensive management program that includes psychosocial support.

POLICY

Required Documentation

Submission of the following is necessary to initiate the prior authorization review for initial requests:

1. Chart notes, medical records or laboratory values documenting results of urine screen within 7 days and/or naltrexone oral challenge within 7 days
2. Chart notes or medical records documenting participation in and adherence to a comprehensive rehabilitation program that includes psychosocial support
3. For Alcohol Use Disorder: chart notes, medical records or claims history documenting failed adherence to oral naltrexone, disulfiram, or acamprosate therapy

Prescriber Specialties

The requested medication must be prescribed by or in consultation with one of the following:

1. Addiction medicine specialist
2. Psychiatrist

Criteria for Initial Approval

Alcohol Use Disorder

Vivitrol may be considered medically necessary when ALL of the following criteria are met:

1. Patient is 18 years of age or older
2. Patient is currently in treatment for alcohol dependence or alcohol use disorder
3. Patient is not receiving concurrent treatment with opioid analgesics for any indication
4. Patient has had an opiate and opioid-free duration of a minimum of seven days prior to treatment initiation including but not limited to buprenorphine, methadone, tramadol, and mitragyna speciosa korth (Kratom)
5. Patient is not experiencing acute opioid withdrawal
6. Patient has a recent (within 7 days) negative urine screen for opioids OR the patient has recently (within 7 days) passed a naloxone challenge test
7. Patient does not have acute hepatitis or liver failure (e.g., Child-Pugh C)
8. Patient is not actively using alcohol at the time of Vivitrol administration
9. Patient has failed to adhere to oral naltrexone, disulfiram, or acamprosate therapy
10. Documented participation in and adherence to a comprehensive rehabilitation program that includes psychosocial support
11. Patient will not exceed a maximum dose of 380 mg intramuscularly every 28 days

Approval duration of 6 months

Opioid Use Disorder

Vivitrol may be considered medically necessary when ALL of the following criteria are met:

1. Patient is 18 years of age or older
2. Patient is currently being treated for opioid addiction, opioid dependence, or opioid use disorder
3. Patient has successfully completed an opioid detoxification program and is not experiencing acute opioid withdrawal
4. Patient has had an alcohol, opiate and opioid-free duration of a minimum of seven days prior to treatment initiation including but not limited to buprenorphine, methadone, tramadol, and mitragyna speciosa korth (Kratom)
5. Patient has a recent (within 7 days) negative urine screen for opioids OR the patient has recently (within 7 days) passed a naloxone challenge test
6. Patient does not have acute hepatitis or liver failure (e.g., Child-Pugh C)
7. Patient is not actively using opioids at the time of Vivitrol administration
8. Patient has, or is anticipated to have, difficulty adhering to daily oral naltrexone

9. Documented participation in and adherence to a comprehensive rehabilitation program that includes psychosocial support
10. Patient will not exceed a maximum dose of 380 mg intramuscularly every 28 days

Approval duration of 6 months

Continuation of Therapy
Patient continues to meet the initial criteria listed in the Criteria for Initial Approval, has demonstrated clinical benefit and there is no evidence of unacceptable toxicity from the requested medication.

For patients requesting the medication for Opioid Use Disorder, clinical benefit is defined by complete abstinence from opioids.

Approval duration of 12 months

Other
Vivitrol (naltrexone) is considered **not medically necessary** for members who do not meet the criteria set forth above.

CLINICAL RATIONALE

Background
Naltrexone is an opioid antagonist reported to reduce the cravings for opioids and alcohol in dependent patients; it does not diminish or prevent withdrawal symptoms. It also does not ensure abstinence from alcohol and opioids; it may, however, decrease patients' motivation to continue utilizing these substances by blocking some of their reinforcing effects.

The Guidelines for Psychosocially Assisted Pharmacological Treatment of Opioid Dependence recommend naltrexone in the prevention of relapse following detoxification. Consensus guidelines from the National Institute on Alcohol Abuse and Alcoholism and the National Institute of Health indicate treatment with naltrexone decreases relapses to heavy drinking by curbing alcohol consumption.

Vivitrol, an extended-release injectable formulation of naltrexone, was developed in an effort to address the non-adherence that occasionally occurs with daily oral pharmacotherapy. However, there is no evidence demonstrating significant improvements in remission rates for both opioid and alcohol dependence in patients receiving the injectable formulation in comparison to those receiving the oral formulations.

Opioid Dependence/Opioid Use Disorder
One of the largest and longest US studies comparing extended-release naltrexone (XR-NTX) to buprenorphine-naloxone (BUP-NX) included 570 participants with a follow-up period of 36 weeks post-treatment completion. Participants were randomized to receive XR-NTX every 28 days or BUP-NX sublingual film daily for a duration of 24 weeks. Detoxification protocols varied by site and were included in the analysis. The primary outcome was time to a relapse event, with both intention-to-treat and per-protocol analyses performed. Secondary outcomes included successful induction, adverse events including overdose, opioid use, and opioid craving.

For the intention-to-treat population, BUP-NX was favored over XR-NTX in regard to relapse-free survival, successful induction, and proportion of opioid-relapse events. 18 overdoses occurred in the group of participants assigned to receive XR-NTX, compared to 10 for BUP-NX. 8 of the XR-NTX overdoses occurred in individuals that failed induction, compared to 1 of the BUP-NX overdoses. The per-protocol analysis found no statistical difference between the two treatment groups for any of the outcomes, other than adverse events, in which participants receiving XR-NTX experienced injection site reactions.

Successful induction onto XR-NTX treatment occurred more frequently for participants that completed detoxification at an extended-stay, opioid-free program. Of those participants initiated onto treatment, no difference in death or overdose events was observed between the two treatments.

Another randomized trial comparing XR-NTX and BUP-NX took place in Norway and included 159 patients discharged from detoxification units, inpatient treatment, or prison. The primary outcomes included retention in the study, urine drug tests without illicit opioids, and number of days of use of illicit opioids and heroin. Retention rates were similar between treatment groups, and no significant difference was found between treatment groups for proportion of opioid-negative urine drug tests or illicit opioid and heroin use.

Finally, a Final Evidence Report completed by the Institute for Clinical and Economic Review (ICER) demonstrated that Vivitrol (naltrexone for extended-release injectable suspension) produces marginally fewer quality-of-life years (QALYs) and similar life years to generic sublingual buprenorphine/naloxone while providing inferior effectiveness at higher drug costs and similar nondrug costs. Further, ICER's report concluded that Vivitrol (naltrexone for extended-release injectable suspension) produces outcomes equivalent to those associated with buprenorphine/naloxone in the treatment of opioid use disorder.

Overall, current evidence has not demonstrated superiority of Vivitrol over alternative treatments for opioid use disorder. For study participants successfully completing detoxification, outcomes between treatments are comparable. In addition, extended-release naltrexone requires an individual to be opioid-free for 7-10 days before starting treatment. These detoxification requirements have resulted in poor treatment induction rates, and a subsequent increase in overdoses for study participants assigned to receive XR-NTX.

Alcohol Dependence/Alcohol Use Disorder

To date, there have been very few high-quality studies (i.e., randomized controlled trials, systematic reviews, etc.) conducted that have evaluated clinical outcomes in patients with alcohol dependence who have been treated with XR-NTX versus oral naltrexone (ONTX), acamprosate, or disulfiram. Currently, there is an ongoing, large-scale randomized controlled trial being conducted at Bellevue Hospital Center in New York, New York that will examine the effectiveness of XR-NTX vs. ONTX in producing a Good Clinical Outcome, defined as abstinence or moderate drinking (< 2 drinks/day, men; < 1 drink/day, women; and < 2 heavy drinking occasions/month) during the final 20 of 24 weeks of primary care-based Medical Management treatment for alcohol dependence. Secondary aims will estimate the cost effectiveness of XR-NTX vs. ONTX, in conjunction with primary-care-based Medical Management for both groups. This large scale randomized controlled trial is the first of its kind.

Of the high-quality studies conducted that have evaluated the effectiveness of XR-NTX vs. other oral pharmacotherapies on clinical outcomes in the treatment of alcohol dependence, most have been in HIV-positive populations. In 2020, a systematic review was completed and evaluated 7 relevant, high-quality studies in this population. In summary, both XR-NTX and ONTX led to reduced alcohol use, improved viral suppression, unchanged antiretroviral treatment (ART) adherence and did not have any significant adverse events in this population. However, the evaluation of the efficacy of XR-NTX vs. ONTX, acamprosate, or disulfiram was not possible either due to a lack of head-to-head comparisons or conflicting data between studies.

Additional studies that have evaluated the effectiveness of XR-NTX vs. ONTX, acamprosate, or disulfiram on clinical outcomes in the treatment of alcohol dependence have primarily been retrospective, consisted of a large degree of heterogeneity, or have had conflicting results. In 2014, a meta-analysis of 4 retrospective studies that evaluated cost and utilization outcomes between XR-NTX and other oral pharmacotherapies for the treatment of alcohol and opioid dependence in the general population showed that XR-NTX was associated with longer medication persistence compared to other oral pharmacotherapies, but patients treated with XR-NTX vs. other oral pharmacotherapies did not

demonstrate significant differences in total days in a detox facility, emergency department utilization, or total healthcare costs. In addition, 3 retrospective studies and one proof-of-concept study in a veteran sub-population all demonstrated no significant differences in clinical outcome measures for XR-NTX vs. other oral pharmacotherapies used in the treatment of alcohol dependence.

Due to inconsistent study data and a lack of high-quality study design, researchers have been largely unable to draw firm conclusions on the clinical outcomes for patients with alcohol dependence who are treated with XR-NTX vs. other oral pharmacotherapies.

Overall, current evidence has not demonstrated superiority of Vivitrol over alternative treatments for opioid use disorder. For study participants successfully completing detoxification, outcomes between treatments are comparable. In addition, extended-release naltrexone requires an individual to be opioid-free for 7-10 days before starting treatment. These detoxification requirements have resulted in poor treatment induction rates, and a subsequent increase in overdoses for study participants assigned to receive XR-NTX.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J2315 Injection, naltrexone, depot form, 1mg.

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POLICY HISTORY

Policy #: 05.01.13
Original Effective Date: September 2006
Reviewed: June 2025
Revised: August 2021
Effective Date: October 17, 2024