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 Vivitrol (naltrexone for extended-release injectable suspension) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies.

Vivitrol (naltrexone for extended-release injectable suspension) is a long acting opioid antagonist given once monthly by intramuscular injection. It is approved by the Food and Drug Administration (FDA) for the following indications:

- Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to receiving treatment
- Prevention of relapse to opioid dependence following opioid detoxification

POLICY

I. Injectable extended-release naltrexone (Vivitrol™) is considered **not medically necessary** for all applications because there are less expensive treatment options available.

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 regards 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 retrospecitve 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: July 2022
Revised: July 2021
Effective Date: August 12, 2021