What Could Your Next Patient with Alcohol Dependence or Opioid Dependence Achieve with VIVITROL® and Counseling?

Vivitrol®
(naltrexone for extended-release injectable suspension) 380 mg/vial

INDICATIONS

VIVITROL is indicated for:

- The treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL. Patients should not be actively drinking at the time of initial VIVITROL administration.
- The prevention of relapse to opioid dependence, following opioid detoxification.

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

IMPORTANT SAFETY INFORMATION

VIVITROL is contraindicated in patients:

- Receiving opioid analgesics
- With current physiologic opioid dependence or in acute opioid withdrawal
- Who have failed the naloxone challenge test or have a positive urine screen for opioids
- Who have exhibited hypersensitivity to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent

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VIV-006441

1

Understanding DSM-IV-TR and DSM-5 criteria

The DSM-IV-TR (the diagnostic standard that preceded the DSM-5) defined substance abuse and substance dependence independently, rather than grouping them under substance use disorder with levels of severity as the DSM-5 does.[1]

VIVITROL® was approved utilizing DSM-IV-TR diagnostic criteria.[2]

DSM-IV-TR: Criteria for alcohol dependence and opioid dependence[3]

Substance dependence is defined as a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by 3 (or more) of the following occurring at any time in the same 12-month period:

- Tolerance, as defined by either of the following:
  - A need for markedly increased amounts of the substance to achieve intoxication or desired effect
  - Markedly diminished effect with continued use of the same amount of the substance
- Withdrawal, as manifested by either of the following:
  - The characteristic withdrawal syndrome for the substance
  - The same substance is taken to relieve or avoid withdrawal symptoms
- The substance is often taken in larger amounts or over a longer period than was intended
- There is a persistent desire or unsuccessful efforts to cut down or control substance use
- A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects
- Important social, occupational, or recreational activities are given up or reduced because of substance use
- The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance

References: **1.** Compton WM, Dawson DA, Goldstein RB, Grant BF. Crosswalk between DSM-IV and DSM-5 substance use disorders for opioids, cannabis, cocaine and alcohol. *Drug Alcohol Depend*. 2013;132:387-390. **2.** VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **3.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Text Revision. Washington, DC: American Psychiatric Association; 2000.

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2

Understanding DSM-IV-TR and DSM-5 criteria (cont'd)

DSM-5: Criteria for substance use disorder, including alcohol use disorder and opioid use disorder[1]

The American Psychiatric Association defines substance use disorder as a problematic pattern of substance use, as it relates to that substance, leading to clinically significant impairment or distress as manifested by at least 2 of the following in 1 year:

- The substance is often taken in larger amounts or over a longer period than was intended
- There is a persistent desire or unsuccessful efforts to cut down or control substance use
- A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects
- Craving or a strong desire or urge to use the substance
- Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home
- Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance
- Important social, occupational, or recreational activities are given up or reduced because of substance use
- Recurrent substance use in situations in which it is physically hazardous
- Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
- Tolerance, as defined by either of the following:
  - A need for markedly increased amounts of the substance to achieve intoxication or desired effect
  - A markedly diminished effect with continued use of the same amount of the substance
- Withdrawal, as manifested by either of the following:
  - The characteristic withdrawal syndrome for the substance
  - The substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms

Severity is specified as:

- Mild for 2 to 3 symptoms
- Moderate for 4 to 5 symptoms
- Severe for 6 or more symptoms

Reference: 1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC; American Psychiatric Association; 2013.

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3

Counseling and Medication Target Two Brain Regions Associated With Addiction

Cortex[1]

Responsible for:

- Decision-making
- Thinking
- Reasoning
- Planning

Counseling targets the cortex to help treat the psychological aspects of addiction.

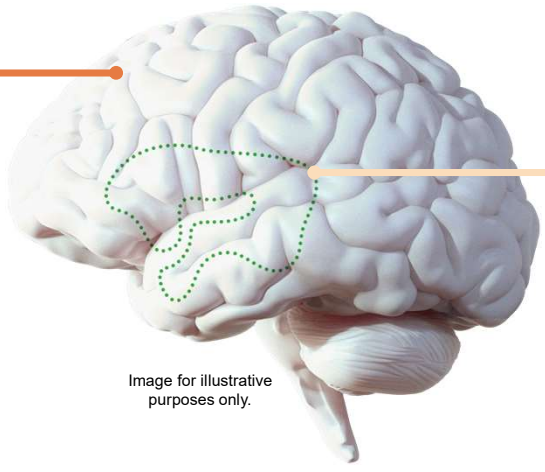

Image for illustrative purposes only.

Limbic System[1]

Responsible for:

- Basic drives or urges
- Rewards
- Pleasure

Medication targets the limbic region to help treat the physical effects of addiction.

Reference: 1. NIDA. Drugs, brains, and behavior: the science of addiction. NIH Publication No. 14-5605. https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction. Revised July 2014. Accessed August 3, 2022.

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4

Alcohol Use Disorder (AUD) in the US

According to the Substance Abuse and Mental Health Services Administration (SAMHSA):

An estimated **27.6 million** American adults had a past year AUD in 2020[1]

Few patients seek treatment[2]

According to a national epidemiologic survey, among those with 12-month AUD between April 2012 and June 2013, about 1 in 12 sought any type of psychosocial or medical treatment

4.9% of those with moderate AUD sought treatment*

21.3% of those with severe AUD sought treatment*

A 2013 survey of facilities providing substance abuse treatment found that fewer than **20%** provided medication-assisted therapy for alcohol abuse disorders[3]

*In the DSM-5, moderate AUD is defined as manifested by 4 to 5 symptoms, while severe AUD is defined by 6 or more symptoms.[4]

References: 1. SAMHSA. *Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health.* HHS Publication No. PEP21-07-01-003, NSDUH Series H-56. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2021. **2.** Grant BF et al. *JAMA Psychiatry.* 2015;72(8):757-766. **3.** SAMHSA. *National Survey of Substance Abuse Treatment Services (N-SSATS): 2013. Data on Substance Abuse Treatment Facilities.* Substance Abuse and Mental Health Services Administration; 2014. **4.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. Washington, DC; American Psychiatric Association; 2013.

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5

Alcohol Use Disorder (AUD) in the US (cont'd)

Participants in 3 National Institute on Alcohol Abuse and Alcoholism (NIAAA) study protocols were screened about their preference to seek treatment or not seek treatment for their alcohol dependence in clinical trials between 2008 and 2015 (n=791). The group differences in DSM-IV alcohol dependence criteria between nontreatment-seeking and treatment-seeking participants are presented.[1]

Criterion	Nontreatment-seeking participants (%)	Treatment-seeking participants (%)	P-value
Drinking more than planned	88.1%	86.3%	0.538
Unsuccessful attempts to cut down	59.5%	84.6%	<0.001
Spent much time in drinking	76.6%	84.8%	0.014
Missed activities because of drinking	42.8%	79.7%	<0.001
Psychological problems because of drinking	48.2%	87.6%	<0.001
Tolerance	83.3%	76.2%	0.05
Withdrawal	50.3%	73.2%	<0.001

Reference: 1. Rohn M, Lee M, Kleuter S, Schwandt M, Falk D, Leggio L. Differences between treatment-seeking and nontreatment-seeking alcohol-dependent research participants: an exploratory analysis. *Alcohol Clin Exp Res.* 2017;41(2):414-420.

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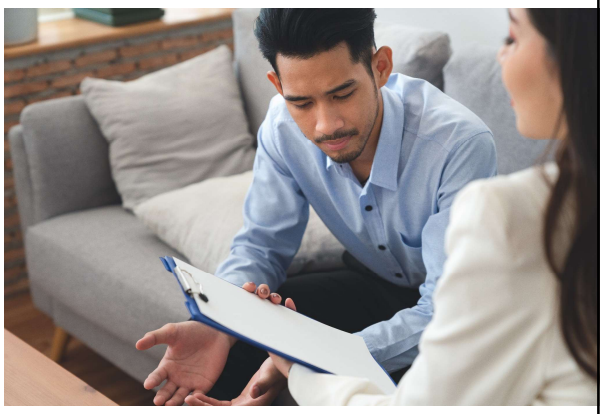
6

Medication-Assisted Treatment (MAT)

A 2009 government protocol from Substance Abuse and Mental Health Services Administration (SAMHSA) recommends MAT as part of an alcohol dependence treatment plan for appropriate patients[1]

- Research into alcohol dependence and treatment has shown that integrating counseling and an appropriate medication may improve treatment outcome
- Pharmacologic treatment for alcohol dependence should be used as an adjunct to, not a replacement for, psychosocial treatment
- SAMHSA suggests providers assess patient readiness before offering alcohol dependence treatment and develop a mutually agreed-upon intervention and treatment plan



MAT=medication-assisted treatment; SAMHSA=Substance Abuse and Mental Health Services Administration.

Reference: 1. Center for Substance Abuse Treatment. Incorporating alcohol pharmacotherapies into medical practice. Treatment Improvement Protocol (TIP) Series 49. HHS Publication No. (SMA) 09-4380. Printed 2009.

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7

Opioid Use Disorder in the US

In 2019, it is estimated that approximately

1.6 million

people in the US had an opioid use disorder in the past year[1]

2019 National Survey on Drug Use and Health, 2020

In 2021, it is estimated that approximately

1.27 million

people in the US received medication-assisted treatment for OUD[2]

US Department of Health and Human Services

OUD=opioid use disorder.

References: 1. US Department of Health and Human Services. *What is the US opioid epidemic?* https://www.hhs.gov/opioids/about-the-epidemic/index.html. Accessed August 3, 2022.
2. US Department of Health and Human Services. *Opioid crisis statistics.* https://www.hhs.gov/opioids/about-the-epidemic/opioid-crisis-statistics/index.html. Accessed August 3, 2022

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8

Counseling

Counseling is the foundation for a comprehensive treatment plan. Goals of counseling may include[1]:

- Addressing a client's motivation to change
- Replacing drug-using activities with constructive and rewarding activities
- Providing incentives for abstinence
- Building skills to resist drug use and prevent relapse
- Improving problem-solving skills
- Facilitating better interpersonal relationships

Reference: 1. National Institute on Drug Abuse. Principles of Drug Addiction Treatment. https://www.drugabuse.gov/sites/default/files/podat_1.pdf. Accessed August 3, 2022.

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9

How Does VIVITROL® Work?[1]

Mechanism of action: Naltrexone is an opioid antagonist with highest affinity for the mu opioid receptor; little or no opioid agonist activity

Pharmacodynamics: Naltrexone has few, if any, intrinsic actions besides its opioid blocking properties. However, it does produce some pupillary constriction by an unknown mechanism.

The administration of VIVITROL is not associated with the development of tolerance or dependence. In subjects physically dependent on opioids, VIVITROL will precipitate withdrawal symptomatology.

Occupation of opioid receptors by naltrexone may block the effects of endogenous opioid peptides. It markedly attenuates or completely blocks, reversibly, the subjective effects of exogenous opioids. The neurobiological mechanisms responsible for the reduction in alcohol consumption observed in alcohol-dependent patients treated with naltrexone are not entirely understood. However, involvement of the endogenous opioid system is suggested by preclinical data.

Naltrexone blocks the effects of opioids by competitive binding at opioid receptors. This makes the blockade produced potentially surmountable, but overcoming full naltrexone blockade by administration of opioids may result in non-opioid receptor-mediated symptoms such as histamine release.

VIVITROL is not aversive therapy and does not cause a disulfiram-like reaction either as a result of opioid use or ethanol ingestion.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

Reference: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021.

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10

Dosage and Administration[1]

- VIVITROL® must be prepared and administered by a healthcare provider
- Prior to initiation of VIVITROL, an opioid-free duration of a minimum of 7-10 days is recommended for patients, to avoid precipitation of opioid withdrawal that may be severe enough to require hospitalization
- The recommended dose of VIVITROL is 380 mg delivered intramuscularly as a gluteal injection, every 4 weeks or once a month, alternating buttocks for each subsequent injection, using the carton components provided
- VIVITROL must ONLY be administered as a deep intramuscular gluteal injection
- Pretreatment with oral naltrexone is not required before using VIVITROL
- See Full Prescribing Information for complete Directions for Use

Vivitrol®
(naltrexone for extended-release injectable suspension) 380 mg/vial

Reference: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021.

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11

VIVITROL® in the Treatment of Alcohol Dependence

Vivitrol®
(naltrexone for extended-release injectable suspension) 380 mg/vial

INDICATION

VIVITROL is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL. Patients should not be actively drinking at the time of initial VIVITROL administration. VIVITROL should be part of a comprehensive management program that includes psychosocial support.

IMPORTANT SAFETY INFORMATION

VIVITROL is contraindicated in patients:

- Receiving opioid analgesics
- With current physiologic opioid dependence or in acute opioid withdrawal
- Who have failed the naloxone challenge test or have a positive urine screen for opioids
- Who have exhibited hypersensitivity to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent

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12

Pivotal Clinical Trial

The Efficacy of VIVITROL® in the Treatment of Alcohol Dependence Was Evaluated in a 24-Week, Placebo-Controlled, Multicenter, Double-blind, Randomized Trial of Patients With Alcohol Dependence (DSM-IV Criteria) in an Outpatient Setting[1]

- Patients met the DSM-IV criteria for alcohol dependence and had a minimum of 2 episodes of heavy drinking per week in the 30 days before screening
  - Heavy drinking was defined as ≥5 standard drinks per day for men and ≥4 standard drinks per day for women
- Participants received an IM injection every 4 weeks in an outpatient setting for a total of 6 injections over 24 weeks, along with psychosocial support (defined as biweekly counseling)

Primary Endpoint: Event Rate of Heavy Drinking Over 24 Weeks of Treatment
- Defined as the number of heavy drinking days divided by the number of days at risk for heavy drinking

DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th edition.

Reference: 1. Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

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Pivotal Clinical Trial

Patient Disposition[1,2]

- 417 outpatients randomized to receive VIVITROL® 380 mg* (n=208) or placebo (n=209)
  - 3 patients did not receive any treatment due to enrollment failures based on investigator decision, leaving 205 patients included in the primary analysis and safety evaluation for the VIVITROL 380 mg group
- Oral naltrexone was not administered prior to the initial or subsequent injections of study medication

*In the clinical study, multiple dosages were tested, but only 380 mg data is presented here, as it is the only strength approved by the FDA.
†17 patients abstained for 7 days prior to treatment.
‡19 patients abstained for 7 days prior to treatment.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **2.** Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625.

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Pivotal Clinical Trial

Demographics and Clinical Baseline Characteristics in Alcohol Dependence Pivotal Trial[1]

	VIVITROL group (n=205)*	Placebo group (n=209)
Mean age in years†	45.0 (±10.1)	44.7 (±10.8)
White	172 (83.9%)	180 (86.1%)
Mean weight in kg†	84.2 (±20.7)	81.6 (±17.0)
Employed ≥20 hours/week	144 (70.2%)	151 (72.2%)
Other drug use		
Current smoker†	99 (48.3%)	88 (42.1%)
Antidepressants	62 (30.2%)	61 (29.2%)
Drinking behavior		
Patient treatment goal of total abstinence	90 (43.9%)	90 (43.1%)
Abstinence for 7 days before randomization	17 (8.3%)	19 (9.1%)
Self-help group attendance†	24 (11.7%)	23 (11.0%)
Mean % heavy drinking days in 30 days before randomization	64.0% (±25.9)	65.2% (±24.8)

*Three of 208 patients did not receive their first injection based on investigator decision.
†$P<0.05$ (significant difference between men and women in the overall study population).
Data are mean (SD) or number (%).

Reference: 1. Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625.

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15

Pivotal Clinical Trial

Study Limitations[1,2]

- Men and women in this study differed on a number of important variables, including the prevalence of smoking and antidepressant use, weight, and commitment to abstinence
- The men and women in this sample may have differed on other variables that may positively influence naltrexone response but were not assessed in this study, such as family history of alcoholism
- The study was not designed to answer whether naltrexone may or may not work for women
- The women who participated may not be representative of women with alcohol dependence in the general population, and the number of women studied was small
- Clinical trials may enroll patients with a greater degree of motivation for change than is seen among patients who are treated in traditional outpatient settings
- Although treatment attendance was relatively high in this study, dropouts reduce the extent to which the findings generalize to all of those with alcohol dependence
- Drinking data for dropouts were not obtained once they left the study, so it is not known how these drinking outcomes would have affected the results
- Analyses of group central tendencies (median, mean) do not reflect the experience of individual patients

References: 1. Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625. 2. O'Malley SS et al. *J Clin Psychopharmacol*. 2007;27(5):507-512.

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Pivotal Clinical Trial

In Patients Treated in the VIVITROL® Group vs the Placebo Group* Heavy Drinking Days Were Reduced

25% ↓ **FEWER HEAVY DRINKING DAYS PER MONTH VS PLACEBO**

VIVITROL 380 mg (n=205) vs placebo (n=209; HR=0.75 [0.60-0.94]; *P*=0.02).

*Patients in the VIVITROL group received VIVITROL 380 mg with psychosocial support. Patients in the placebo group received a placebo with psychosocial support.

HR=hazard ratio.

Reference: 1. Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625.

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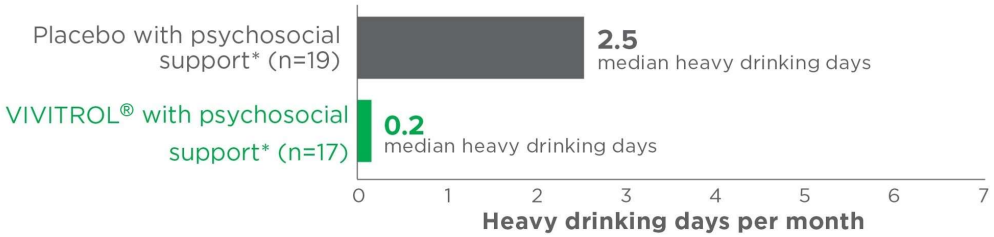
17

Pivotal Clinical Trial

In the subset population

Heavy drinking days[1]

Median heavy drinking days: ≥7-day abstinent subset (n=53) over 6 months[2]



At baseline: median 7-day abstinent patient had 15.2 drinking days and 15.2 abstinent days per average month (30.4 days).

A predefined subpopulation of lead-in abstinent patients (n=53, or 8% of the total study population) was defined as those who reported no drinking during the 7 consecutive days preceding the first injection.

*Psychosocial support was defined as biweekly counseling.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **2.** Data on file. Alkermes, Inc. Waltham, MA.

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18

Pivotal Clinical Trial

In the subset population
Any drinking days[1]

Median any drinking days per month: ≥7-day abstinent subset (n=53) over 6 months[2]

At baseline: median 7-day abstinent patient had 15.2 drinking days and 15.2 abstinent days per average month (30.4 days).

A predefined subpopulation of lead-in abstinent patients (n=53, or 8% of the total study population) was defined as those who reported no drinking during the 7 consecutive days preceding the first injection.

*Psychosocial support was defined as biweekly counseling.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **2.** Data on file. Alkermes, Inc. Waltham, MA.

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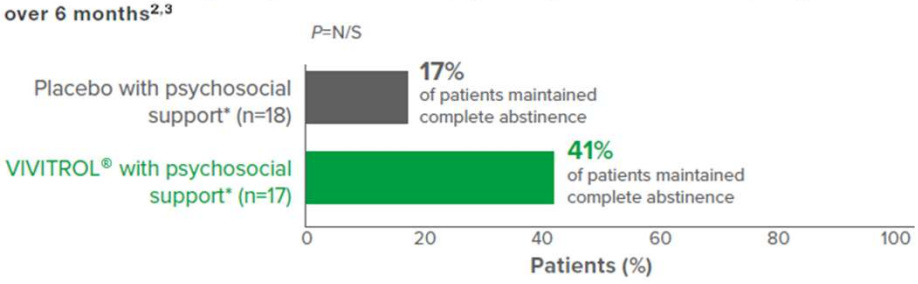
19

Pivotal Clinical Trial

In the subset population
Complete abstinence throughout treatment[1]

Patients maintaining complete abstinence (%): ≥7-day abstinent subset (n=53) over 6 months[2,3]



A predefined subpopulation of lead-in abstinent patients (n=53, or 8% of the total study population) was defined as those who reported no drinking during the 7 consecutive days preceding the first injection.

*Psychosocial support was defined as biweekly counseling.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **2.** Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625. **3.** Data on file. Alkermes, Inc. Waltham, MA.

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20

Pivotal Clinical Trial

Subset Analysis: Patients Who Completely Abstained From Drinking for ≥7 Days Before Treatment

Subset analysis limitations[1,2]:

- Due to the small numbers, this analysis should be interpreted with caution
- The same treatment effects were not evident among the subset of patients (n=571, 92% of the total study population) who were actively drinking at the time of treatment initiation
- Secondary data analysis. No adjustments were made for multiple comparisons; therefore, treatment differences could represent chance findings

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **2.** Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625.

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21

Post hoc Analysis

A post hoc analysis of a subset of patients in the pivotal trial who were able to abstain completely from drinking for the 4 consecutive days prior to first injection[1]

Median heavy drinking* days per month: ≥4-day abstinent subset (n=82)[1]

- VIVITROL® 380 mg with psychosocial support† (n=28): **0.2 heavy drinking days**
- Placebo with psychosocial support† (n=28): **2.9 heavy drinking days**

Median number of days to first heavy drinking event: ≥4-day abstinent subset population (n=82)[1,2]

Placebo with psychosocial support† (n=28)	20 days
VIVITROL with psychosocial support† (n=28)	181 days

At baseline, patients in both groups had a median of 14 heavy drinking days per month.

*Heavy drinking was defined as a self-report of ≥5 standard drinks consumed on a given day for male patients and ≥4 drinks for female patients.

†Psychosocial support was defined as biweekly counseling.[3]

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

References: 1. O'Malley SS et al. J Clin Psychopharmacol. 2007;27(5):507-512. **2.** Data on file. Alkermes, Inc. Waltham, MA.

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22

Pivotal Clinical Trial

Adverse Reactions

Treatment-emergent adverse reactions that occurred in ≥5% of patients with alcohol dependence treated with VIVITROL® and that occurred more frequently in the VIVITROL group vs the placebo group[1]

	VIVITROL 380 mg with psychosocial support* (n=205)	Placebo with psychosocial support* (n=214)
Any ISR	69%	50%
Injection site tenderness	45%	39%
Injection site induration	35%	8%
Nausea	33%	11%
Headache	25%	18%
Asthenic conditions	23%	12%
Injection site pain	17%	7%
Other ISR (primarily nodules, swelling)	15%	4%
Insomnia, sleep disorder	14%	12%
Vomiting NOS	14%	6%
Anorexia, appetite decreased NOS, appetite disorder NOS	14%	3%
Diarrhea	13%	10%

	VIVITROL 380 mg with psychosocial support* (n=205)	Placebo with psychosocial support* (n=214)
Dizziness, syncope	13%	4%
Anxiety	12%	8%
Arthralgia, arthritis, joint stiffness	12%	5%
Pharyngitis	11%	11%
Abdominal pain	11%	8%
Injection site pruritus	10%	0%
Depression	8%	4%
Muscle cramps	8%	1%
Injection site ecchymosis	7%	5%
Back pain, back stiffness	6%	5%
Rash	6%	4%
Dry mouth	5%	4%
Somnolence, sedation	4%	1%

*Psychosocial support was defined as biweekly counseling.
ISR=injection site reaction; NOS=not otherwise specified.

Reference: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021.

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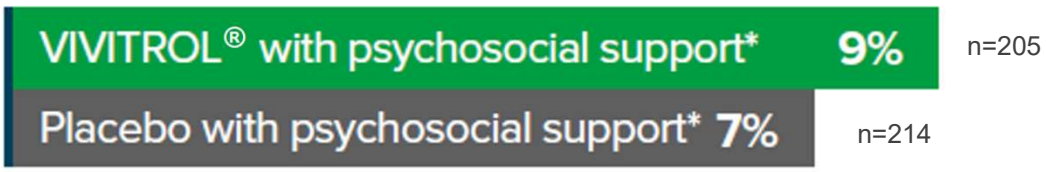
Pivotal Clinical Trial

Discontinuation Rates Due to Adverse Events[1]

Alcohol dependence controlled clinical trial of ≤6 months



*Psychosocial support was defined as biweekly counseling.

Reference: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

24

Important Safety Information

Vulnerability to Opioid Overdose:

- After opioid detoxification, patients are likely to have a reduced tolerance to opioids. VIVITROL® blocks the effects of exogenous opioids for approximately 28 days after administration. As the blockade wanes and eventually dissipates completely, use of previously tolerated doses of opioids could result in potentially life-threatening opioid intoxication (respiratory compromise or arrest, circulatory collapse, etc). Cases of opioid overdose with fatal outcomes have been reported in patients who used opioids at the end of a dosing interval, after missing a scheduled dose, or after discontinuing treatment.
- Patients and caregivers should be told of this increased sensitivity to opioids and the risk of overdose.
- Although VIVITROL is a potent antagonist with a prolonged pharmacological effect, the blockade produced by VIVITROL is surmountable. The plasma concentration of exogenous opioids attained immediately following their acute administration may be sufficient to overcome the competitive receptor blockade. This poses a potential risk to individuals who attempt, on their own, to overcome the blockade by administering large amounts of exogenous opioids.
- Any attempt by a patient to overcome the VIVITROL blockade by taking opioids may lead to fatal overdose. Patients should be told of the serious consequences of trying to overcome the opioid blockade.
- Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver, at the initial VIVITROL injection and with each subsequent injection. Strongly consider prescribing naloxone for the emergency treatment of opioid overdose.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

25

Important Safety Information (Cont'd)

Injection Site Reactions:

- VIVITROL® must be prepared and administered by a healthcare provider and must ONLY be administered as a deep intramuscular gluteal injection.
- Inadvertent subcutaneous/adipose layer injection of VIVITROL may increase the likelihood of severe injection site reactions. Select proper needle size for patient body habitus and use only the needles provided in the carton.
- VIVITROL injections may be followed by pain, tenderness, induration, swelling, erythema, bruising, or pruritus; however, in some cases injection site reactions may be very severe.
- Injection site reactions not improving may require prompt medical attention, including, in some cases, surgical intervention.
- In the clinical trials, one patient developed an area of induration that continued to enlarge after 4 weeks, with subsequent development of necrotic tissue that required surgical excision.
- Patients should be informed that any concerning injection site reactions should be brought to the attention of their healthcare provider.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Important Safety Information (Cont'd)

Precipitation of Opioid Withdrawal:

- When withdrawal is precipitated abruptly by administration of an opioid antagonist to a patient with opioid dependence, the resulting withdrawal syndrome can be severe. Some cases have been severe enough to require hospitalization and/or management in the ICU.
- To prevent occurrence of precipitated withdrawal, patients with opioid dependence, including those being treated for alcohol dependence, should be opioid-free (including tramadol) before starting VIVITROL® treatment:
  - An opioid-free interval of a minimum of 7–10 days is recommended for patients previously dependent on short-acting opioids.
  - Patients transitioning from buprenorphine or methadone may be vulnerable to precipitated withdrawal for as long as 2 weeks.
- If a more rapid transition from agonist to antagonist therapy is deemed necessary and appropriate by the healthcare provider, monitor the patient closely in an appropriate medical setting where precipitated withdrawal can be managed.
- Patients should be made aware of the risk associated with precipitated withdrawal and be encouraged to give an accurate account of last opioid use, as precipitated opioid withdrawal has been observed in patients with alcohol dependence in circumstances where the prescriber had been unaware of the additional use of opioids or co-dependence on opioids.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

27

Important Safety Information (Cont'd)

Hepatotoxicity:

- Cases of hepatitis and clinically significant liver dysfunction have been observed in association with VIVITROL®. Warn patients of the risk of hepatic injury and advise them to seek help if experiencing symptoms of acute hepatitis. Discontinue VIVITROL in patients who exhibit signs and symptoms of acute hepatitis.

Depression and Suicidality:

- Patients with alcohol dependence or opioid dependence taking VIVITROL should be monitored for depression or suicidal thoughts. Alert families and caregivers to monitor and report the emergence of symptoms of depression or suicidality.

When Reversal of VIVITROL Blockade Is Required for Pain Management:

- For VIVITROL patients in emergency situations, suggestions for pain management include regional analgesia or use of non-opioid analgesics. If opioid therapy is required to reverse the VIVITROL blockade, patients should be closely monitored by trained personnel in a setting staffed and equipped for CPR.

Eosinophilic Pneumonia:

- Patients who develop dyspnea and hypoxemia should seek medical attention immediately. Consider the possibility of eosinophilic pneumonia in patients who do not respond to antibiotics.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

28

Important Safety Information (Cont'd)

Hypersensitivity Reactions including Anaphylaxis:

- Patients should be warned of the risk of hypersensitivity reactions, including anaphylaxis, and should be advised to seek immediate medical attention in a healthcare setting prepared to treat anaphylaxis should a hypersensitivity reaction occur. The patient should not receive any further treatment with VIVITROL®.

Intramuscular Injections:

- As with any intramuscular injection, VIVITROL should be administered with caution to patients with thrombocytopenia or any coagulation disorder.

Alcohol Withdrawal:

- Use of VIVITROL does not eliminate nor diminish alcohol withdrawal symptoms.

Interference with Laboratory Tests:

- VIVITROL may be cross-reactive with certain immunoassay methods for the detection of drugs of abuse (specifically opioids) in urine. For further information, reference to the specific immunoassay instructions is recommended.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

29

Important Safety Information (Cont'd)

Adverse Reactions

- The adverse events seen most frequently in association with VIVITROL® therapy for alcohol dependence (occurring in ≥5% and at least twice as frequently with VIVITROL than placebo) include nausea, vomiting, injection site reactions (including induration, pruritus, nodules, and swelling), arthralgia, arthritis, or joint stiffness, muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders.
- The adverse events seen most frequently in association with VIVITROL in patients with opioid dependence (occurring in ≥2% and at least twice as frequently with VIVITROL than placebo) include hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache.

You are encouraged to report side effects to the FDA.
Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

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VIVITROL® in the Treatment of Opioid Dependence

Vivitrol®
(naltrexone for extended-release injectable suspension) 380 mg/vial

INDICATION

VIVITROL is indicated for prevention of relapse to opioid dependence, following opioid detoxification. VIVITROL should be part of a comprehensive management program that includes psychosocial support.

IMPORTANT SAFETY INFORMATION

VIVITROL is contraindicated in patients:

- Receiving opioid analgesics
- With current physiologic opioid dependence or in acute opioid withdrawal
- Who have failed the naloxone challenge test or have a positive urine screen for opioids
- Who have exhibited hypersensitivity to naltrexone, polylactide-co-glycolide (PLG), carboxymethylcellulose, or any other components of the diluent

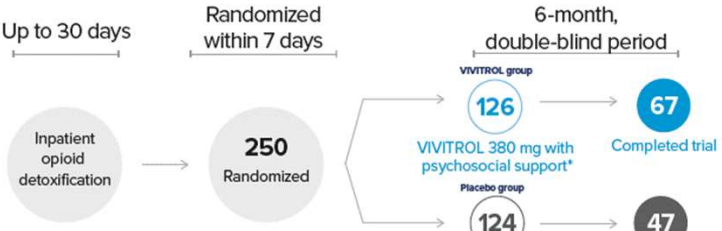
Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

31

Pivotal Clinical Trial

The Efficacy of VIVITROL® in the Treatment of Opioid Dependence Was Evaluated in a 24-Week, Placebo-Controlled, Multicenter, Double-blind, Randomized Trial of patients With Opioid Dependence (DSM-IV Criteria) in an Outpatient Setting Who Were Completing or Had Recently Completed Detoxification[1]

- Prior to treatment initiation, patients were voluntarily seeking treatment, completing ≤30 days of inpatient opioid detoxification, and not taking opioids for ≥7 days.
- Participants received VIVITROL or placebo, with a urine drug test (UDT) every week, psychosocial support every 2 weeks, and treatment injection every 4 weeks.
  - Psychosocial support consisted of biweekly sessions of individual drug counseling, adapted for opioid dependence.



*Psychosocial support was defined as biweekly counseling.

Reference: 1. Krupitsky E et al. *Lancet.* 2011;377(9776):1506-1513.

Vivitrol®
(naltrexone for extended-release injectable suspension) 380 mg/vial

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Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

32

Pivotal Clinical Trial

The Efficacy of VIVITROL® in the Treatment of Opioid Dependence Was Evaluated in a 24-Week, Placebo-Controlled, Multicenter, Double-blind, Randomized Trial of patients With Opioid Dependence (DSM-IV Criteria) in an Outpatient Setting Who Were Completing or Had Recently Completed Detoxification[1]

- Patients randomized to VIVITROL (n=126) or placebo (n=124)
- After randomization: 4-week period for treatment engagement during which opioid use, if it occurred, was allowed (not included in analysis)
- Subjects provided additional self-report of opioid use

Endpoints

Primary endpoint was confirmed opioid abstinence during Weeks 5 - 24

- Confirmed abstinence or "opioid-free" defined as negative UDT for opioids and no self-reported opioid use
- Weeks 1 - 4 were omitted from endpoint to allow for stabilization of abstinence

Secondary endpoints were self-reported opioid-free days, opioid craving scores, treatment retention days, and relapses to physiologic opioid dependence

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

UDT=urine drug test.

Reference: 1. Krupitsky E et al. *Lancet.* 2011;377(9776):1506-1513.

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Pivotal Clinical Trial

Demographics and Clinical Baseline Characteristics[1]

- Duration of opioid dependence ranged from 1 to 26 years, with more patients in the VIVITROL® group reporting shorter duration
  - For example, <10 years' duration of use was 47% for the VIVITROL group vs 36% for the placebo group

	VIVITROL® 380 mg with psychosocial support (n=126)	Placebo with psychosocial support (n=124)
Age in years	29.4 (±4.8)	29.7 (±3.6)
Men	113 (90%)	107 (86%)
White	124 (98%)	124 (100%)
Duration of opioid dependence in years	9.1 (±4.5)	10.0 (±3.9)
Days of prestudy inpatient detoxification	18 (±9)	18 (±7)
Opioid craving scale	18 (±23)	22 (±24)
HIV serology positive	51 (40%)	52 (42%)
Hepatitis C positive	111 (88%)	117 (94%)

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Data are mean (SD) or number (%).

Reference: 1. Krupitsky E et al. *Lancet.* 2011;377(9776):1506-1513.

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Pivotal Clinical Trial

Study Limitations[1]

- Retention in placebo group might have been reduced by recognition, upon opioid use, that one was on placebo
  - Or, among patients in placebo group who had relapsed to regular opioid use, by reluctance to return to clinic and face a withdrawal reaction from a naloxone challenge test
- Placebo group showed a substantial retention and response profile and a markedly higher rate of positive naloxone challenge tests
- High retention rate might have been influenced by:
  - Inclusion criterion that patients have someone available to supervise attendance
  - Provision of individual counseling
  - Absence of alternative treatments in Russia
  - Promise of active VIVITROL® treatment for all patients after 6 months, in subsequent open-label extension safety study
- Analyses of group central tendencies (median, mean) do not reflect experience of individual patients

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Reference: 1. Krupitsky E et al. *Lancet*. 2011;377(9776):1506-1513.

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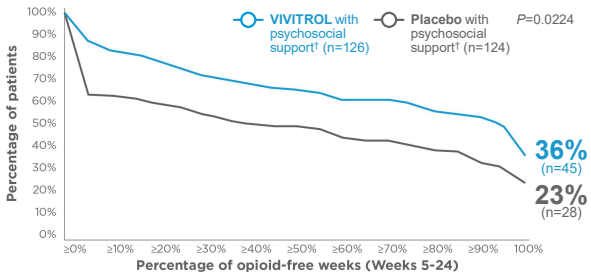
Pivotal Clinical Trial

With VIVITROL® and Counseling, 36% of Patients in the Pivotal Trial Maintained Complete Abstinence for Weeks 5 - 24 vs 23% With Placebo and Counseling[1,2]

Subjects sustaining varying percentages of opioid-free weeks*



- Data were not collected during Weeks 1 - 4 of the trial to allow for stabilization of abstinence.
- Median of VIVITROL group had confirmed abstinence for 90% of weeks in evaluation period vs 35% for median of placebo group[2]
- Number of patients with positive naloxone challenge at end of 24 weeks: 1 VIVITROL patient vs 17 placebo patients[2]

*Confirmed abstinence or "opioid-free" was defined as a negative UDT for opioids and no self-reported opioid use.
†Psychosocial support consisted of biweekly counseling sessions of individual drug counseling, adapted for opioid dependence.
Data represented as the median.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **2.** Krupitsky E, et al. *Lancet*. 2011;377(9776):1506-1513.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
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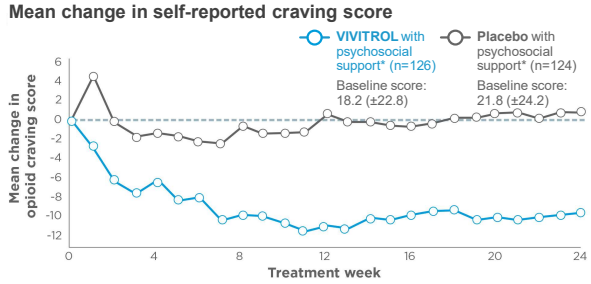
Pivotal Clinical Trial

Secondary Endpoint: Mean Change in Opioid Craving[1]

Mean change in self-reported craving score



- Patients in the VIVITROL® group had a -10.1 mean change in craving visual analog scale (VAS) score, while patients in the placebo group had a +0.7 change in craving VAS score (P<0.0001)†
- Patients in the VIVITROL group had a 55% lower mean craving score at 24 weeks than the mean score at baseline. Patients in the placebo group had a 3% higher mean craving score at 24 weeks than the mean score at baseline.[2]

*Psychosocial support consisted of biweekly sessions of individual drug counseling, adapted for opioid dependence.
†Craving (described as a "need for opioids") was self-reported weekly according to a VAS of 0 to 100, with 0 being "not at all" and 100 being "very much so." Adjusted for multiplicity by the Bonferroni-Holm method to preserve family-wise type 1 error at 0.05.
VAS=visual analog scale.

References: 1. Krupitsky E et al. *Lancet.* 2011;377(9776):1506-1513. **2.** Data on file. Alkermes, Inc. Waltham, MA.

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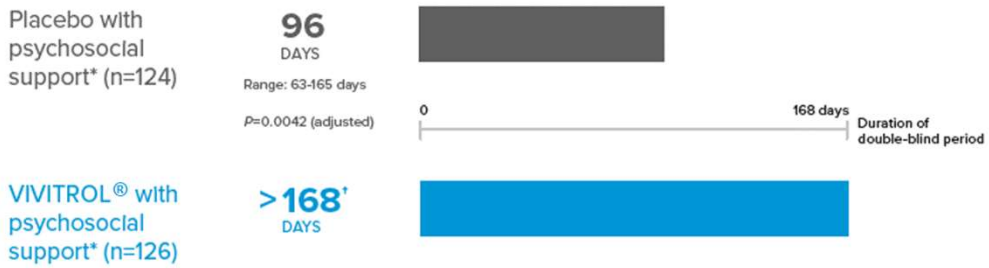
Pivotal Clinical Trial

Secondary Endpoint: Number of days of retention[1,2]



*Psychosocial support consisted of biweekly counseling sessions of individual drug counseling, adapted for opioid dependence.
†Median number of days of retention >168 days for patients (n=67) who continued into the open-label long-term extension study.

References: 1. Krupitsky E, Nunes EV, Ling W, Gastfriend DR, Memisoglu A, Silverman BL. Injectable extended-release naltrexone (XR-NTX) for opioid dependence: long-term safety and effectiveness. Addiction. 2013;108(9):1628-1637. **2.** Krupitsky E et al. *Lancet.* 2011;377(9776):1506-1513.

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

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Pivotal Clinical Trial

Adverse Reactions

Treatment-emergent clinical adverse reactions (events in ≥2% of patients with opioid dependence treated with VIVITROL® and occurring more frequently in the VIVITROL group than in the placebo group)[1]

Events	VIVITROL 380 mg with psychosocial support* (n=126)	Placebo with psychosocial support* (n=124)
Alanine aminotransferase increased	13%	6%
Aspartate aminotransferase increased	10%	2%
Gamma-glutamyltransferase increased	7%	3%
Nasopharyngitis	7%	2%
Insomnia	6%	1%
Influenza	5%	4%
Hypertension	5%	3%
Injection site pain	5%	1%
Toothache	4%	2%
Headache	3%	2%

Please see the complete list of adverse reactions in the VIVITROL Prescribing Information.

Reference: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Pivotal Clinical Trial

Discontinuation Rates Due to Adverse Events[1,2]

Opioid dependence pivotal trial

VIVITROL® with psychosocial support*	2%
Placebo with psychosocial support*	2%

*Psychosocial support consisted of biweekly counseling sessions of individual drug counseling, adapted for opioid dependence.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. **2.** Krupitsky E et al. *Lancet.* 2011;377(9776):1506-1513.

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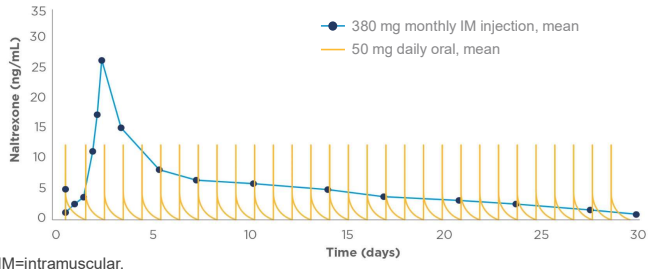
VIVITROL® Is a Once-Monthly Treatment Option

Extended-release, microsphere formulation of naltrexone, administered by deep IM gluteal injection every 4 weeks or once a month[1]

- Transient initial naltrexone plasma concentration peak ~2 hours after injection, followed by second peak in ~2 days
- Concentrations slowly decline beginning ~14 days after dosing, with measurable levels for >1 month
- Compared to daily oral dosing with naltrexone 50 mg over 28 days, total naltrexone exposure is 3- to 4-fold higher following administration of a single dose of VIVITROL 380 mg. Steady state is reached at the end of the dosing interval following the first injection

Plasma naltrexone concentration[2,3]*



*Data for oral naltrexone beyond Day 5 have been extrapolated from a study of normal healthy volunteers (n=14) given oral naltrexone 50 mg daily for 5 days.[2,3] Plasma concentrations do not necessarily correlate with clinical efficacy.

IM=intramuscular.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. 2. Dunbar JL et al. *Alcohol Clin Exp Res*. 2006;30(3):480-490. 3. Dean RL. *Front Biosci*. 2005;10:643-655.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Important Safety Information

Vulnerability to Opioid Overdose:

- After opioid detoxification, patients are likely to have a reduced tolerance to opioids. VIVITROL® blocks the effects of exogenous opioids for approximately 28 days after administration. As the blockade wanes and eventually dissipates completely, use of previously tolerated doses of opioids could result in potentially life-threatening opioid intoxication (respiratory compromise or arrest, circulatory collapse, etc). Cases of opioid overdose with fatal outcomes have been reported in patients who used opioids at the end of a dosing interval, after missing a scheduled dose, or after discontinuing treatment.
- Patients and caregivers should be told of this increased sensitivity to opioids and the risk of overdose.
- Although VIVITROL is a potent antagonist with a prolonged pharmacological effect, the blockade produced by VIVITROL is surmountable. The plasma concentration of exogenous opioids attained immediately following their acute administration may be sufficient to overcome the competitive receptor blockade. This poses a potential risk to individuals who attempt, on their own, to overcome the blockade by administering large amounts of exogenous opioids.
- Any attempt by a patient to overcome the VIVITROL blockade by taking opioids may lead to fatal overdose. Patients should be told of the serious consequences of trying to overcome the opioid blockade.
- Discuss the availability of naloxone for the emergency treatment of opioid overdose with the patient and caregiver, at the initial VIVITROL injection and with each subsequent injection. Strongly consider prescribing naloxone for the emergency treatment of opioid overdose.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Important Safety Information (Cont'd)

Injection Site Reactions:

- VIVITROL® must be prepared and administered by a healthcare provider and must ONLY be administered as a deep intramuscular gluteal injection.
- Inadvertent subcutaneous/adipose layer injection of VIVITROL may increase the likelihood of severe injection site reactions. Select proper needle size for patient body habitus and use only the needles provided in the carton.
- VIVITROL injections may be followed by pain, tenderness, induration, swelling, erythema, bruising, or pruritus; however, in some cases injection site reactions may be very severe.
- Injection site reactions not improving may require prompt medical attention, including, in some cases, surgical intervention.
- In the clinical trials, one patient developed an area of induration that continued to enlarge after 4 weeks, with subsequent development of necrotic tissue that required surgical excision.
- Patients should be informed that any concerning injection site reactions should be brought to the attention of their healthcare provider.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Important Safety Information (Cont'd)

Precipitation of Opioid Withdrawal:

- When withdrawal is precipitated abruptly by administration of an opioid antagonist to a patient with opioid dependence, the resulting withdrawal syndrome can be severe. Some cases have been severe enough to require hospitalization and/or management in the ICU.
- To prevent occurrence of precipitated withdrawal, patients with opioid dependence, including those being treated for alcohol dependence, should be opioid-free (including tramadol) before starting VIVITROL® treatment:
  - An opioid-free interval of a minimum of 7–10 days is recommended for patients previously dependent on short-acting opioids.
  - Patients transitioning from buprenorphine or methadone may be vulnerable to precipitated withdrawal for as long as 2 weeks.
- If a more rapid transition from agonist to antagonist therapy is deemed necessary and appropriate by the healthcare provider, monitor the patient closely in an appropriate medical setting where precipitated withdrawal can be managed.
- Patients should be made aware of the risk associated with precipitated withdrawal and be encouraged to give an accurate account of last opioid use, as precipitated opioid withdrawal has been observed in patients with alcohol dependence in circumstances where the prescriber had been unaware of the additional use of opioids or co-dependence on opioids.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

44

Important Safety Information (Cont'd)

Hepatotoxicity:

- Cases of hepatitis and clinically significant liver dysfunction have been observed in association with VIVITROL®. Warn patients of the risk of hepatic injury and advise them to seek help if experiencing symptoms of acute hepatitis. Discontinue VIVITROL in patients who exhibit signs and symptoms of acute hepatitis.

Depression and Suicidality:

- Patients with alcohol dependence or opioid dependence taking VIVITROL should be monitored for depression or suicidal thoughts. Alert families and caregivers to monitor and report the emergence of symptoms of depression or suicidality.

When Reversal of VIVITROL Blockade Is Required for Pain Management:

- For VIVITROL patients in emergency situations, suggestions for pain management include regional analgesia or use of non-opioid analgesics. If opioid therapy is required to reverse the VIVITROL blockade, patients should be closely monitored by trained personnel in a setting staffed and equipped for CPR.

Eosinophilic Pneumonia:

- Patients who develop dyspnea and hypoxemia should seek medical attention immediately. Consider the possibility of eosinophilic pneumonia in patients who do not respond to antibiotics.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

45

Important Safety Information (Cont'd)

Hypersensitivity Reactions including Anaphylaxis:

- Patients should be warned of the risk of hypersensitivity reactions, including anaphylaxis, and should be advised to seek immediate medical attention in a healthcare setting prepared to treat anaphylaxis should a hypersensitivity reaction occur. The patient should not receive any further treatment with VIVITROL®.

Intramuscular Injections:

- As with any intramuscular injection, VIVITROL should be administered with caution to patients with thrombocytopenia or any coagulation disorder.

Alcohol Withdrawal:

- Use of VIVITROL does not eliminate nor diminish alcohol withdrawal symptoms.

Interference with Laboratory Tests:

- VIVITROL may be cross-reactive with certain immunoassay methods for the detection of drugs of abuse (specifically opioids) in urine. For further information, reference to the specific immunoassay instructions is recommended.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

46

Important Safety Information (Cont'd)

Adverse Reactions

- The adverse events seen most frequently in association with VIVITROL® therapy for alcohol dependence (occurring in ≥5% and at least twice as frequently with VIVITROL than placebo) include nausea, vomiting, injection site reactions (including induration, pruritus, nodules, and swelling), arthralgia, arthritis, or joint stiffness, muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders.
- The adverse events seen most frequently in association with VIVITROL in patients with opioid dependence (occurring in ≥2% and at least twice as frequently with VIVITROL than placebo) include hepatic enzyme abnormalities, injection site pain, nasopharyngitis, insomnia, and toothache.

You are encouraged to report side effects to the FDA.
Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Help Appropriate Patients Reach for the Next Stage in Their Recovery Journey With VIVITROL® and Counseling

VIVITROL and Counseling—A Proven Treatment Option for Appropriate Patients With Alcohol Dependence[1,2]

In outpatients with alcohol dependence able to abstain in an outpatient setting, the VIVITROL group vs the placebo group demonstrated:

- Greater reduction in the rate of heavy drinking over 24 weeks (primary endpoint)

In a subset of outpatients from the pivotal trial able to completely abstain for 7 consecutive days prior to first injection (n=53, 8%):

- A reduced number of drinking days over 24 weeks was observed in the VIVITROL group vs the placebo group*
- Increased likelihood of maintaining complete abstinence from alcohol over 24 weeks

VIVITROL—A Proven Treatment Option to Prevent Relapse to Opioid Dependence, Following Opioid Detoxification, When Used With Counseling[1,3]

In patients with opioid dependence treated with VIVITROL and counseling, the following were observed:

- A sustained complete abstinence from opioids (primary endpoint)
  - Complete abstinence sustained by 36% of subjects in VIVITROL group vs 23% in placebo group from Weeks 5 to 24
- A mean change in self-reported opioid craving score from baseline (secondary endpoint)

*Secondary data analysis. No adjustments were made for multiple comparisons; therefore, treatment differences could represent chance findings. The same treatment effects were not evident among the subset of patients (n=571, 92% of the total study population) who were actively drinking at the time of treatment initiation.

References: 1. VIVITROL [prescribing information]. Waltham, MA: Alkermes, Inc; rev March 2021. 2. Garbutt JC et al. *JAMA*. 2005;293(13):1617-1625. 3. Krupitsky E et al. *Lancet*. 2011;377(9776):1506-1513.

Vivitrol (naltrexone for extended-release injectable suspension) 380 mg/vial

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Vivitrol®
(naltrexone for extended-release injectable suspension) 380 mg/vial

Vivitrol2gether® Patient Support Services and the VIVITROL® Co-pay Savings Program

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Vivitrol2gether® Patient Support Services

Fulfillment Support

- Support for fulfillment of VIVITROL® through specialty pharmacies
- Information, education, and resources to assist with filling VIVITROL prescriptions when working with the specialty pharmacy

Transition of Care

- Transition of care support services
- Using the Provider Locator tool, coordinators can help identify potential follow-on providers based on patient's transition destination

Call 1-800-VIVITROL for assistance with Provider Locator.

Direct Contact With Enrolled Patients

- A Vivitrol2gether coordinator* can talk to the patient to explain and help facilitate the shipment of VIVITROL
- Coordinators can also text and call the patient for monthly appointment and refill reminders

Additional Resources and Programs

- iAssist patient enrollment portal can help with the prescription process through digital prescriptions
- Insurance and Pharmacy Navigator can help to access applicable pharmacy information using healthcare provider location and patient insurance plans

Enroll patients at
VIVITROLhcp.com/enroll

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*A coordinator does not provide medical advice or individualized patient care.

Please see Important Safety Information on slides 42-47.
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The VIVITROL® Co-pay Savings Program Can Help Eligible Patients With the Cost of Their VIVITROL Prescription

Co-pays and deductibles

- Program offers up to $500/month of insurance co-pay or deductible expenses to eligible patients with a VIVITROL prescription. Terms and Conditions apply*

91% **of eligible patients using the co-pay savings program had no out-of-pocket expenses for VIVITROL**

Claims data derived from insured patients enrolled in program from January through December 2020. Data not state-specific.

Self-pay

- Eligible patients without insurance coverage may save up to $500 on purchase price of VIVITROL. Terms and Conditions apply*

For more information, visit **VIVITROLCopay.com**

*Terms and Conditions

Eligibility for Alkermes-Sponsored Co-pay Savings. This offer is only available to patients 18 years or older, with a prescription consistent with the Prescribing Information and the patient is not enrolled in, or covered by, any local, state, federal or other government program that pays for any portion of medication costs, including but not limited to Medicare, including Medicare Part D or Medicare Advantage plans; Medicaid, including Medicaid Managed Care and Alternative Benefit Plans under the Affordable Care Act; Medigap; VA; DOD; TRICARE; or a residential correctional program.

Additional Terms of Use: This offer is not conditioned on any past, present, or future purchase, including refills. Alkermes reserves the right to rescind, revoke, or amend this offer, program eligibility, and requirements at any time without notice. This offer is limited to one per patient, may not be used with any other offer, is not transferable and may not be sold, purchased or traded, or offered for sale, purchase or trade. Void where prohibited by law. Program Administrator or its designee will have the right upon reasonable prior written notice, during normal business hours, and subject to applicable law, to audit compliance with this program.

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Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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Vivitrol®
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Discussion

Please see Important Safety Information on slides 42-47.
Prescribing Information and Medication Guide will be furnished during this program.

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