MEDICATION ASSISTED TREATMENT FOR SUBSTANCE USE DISORDERS: EXTENDED-RELEASE NALTREXONE (XR-NTX; VIVITROL®)

David R Gastfriend MD
Chief Executive Officer
Treatment Research Institute

Disclosures: Dr Gastfriend is a shareholder and former employee of Alkermes, Inc.
Pathophysiology

**Interventions**

- Psychosocial Therapies
- 12 Step Programs
- Monitoring

**Cortex**

*Role:*
- Decision making
- Thinking
- Reasoning
- Learning

**Limbic Region**

*Role:*
- Basic Drives
- Experience of Reward, Euphoria

Healthy Opioid Receptor Activity

**Dopamine**
- Eating when hungry
- Drinking when thirsty
- Rewards survival behavior

**Endorphins**
- Pain relief
- Stress relief
- Emotional bonding

Oral Naltrexone Refills Fall Precipitously

HHS/SAMHSA study (2004)¹

- Pharmacy claims for NTX-PO in a plan with 1.5 million insureds for 3 yrs (‘00-'02)¹
- Guidelines recommend treatment from 3-6 months to 2 years¹
- Approximately 50% did not refill even once – despite having coverage¹
- Other independent studies obtained similar discontinuation rates²

Development of XR-NTX

• Problem of nonadherence was well understood by 1975¹

• The promise of naltrexone was undermined by nonadherence

• NIAAA and NIDA awarded grants that led to development of microencapsulated naltrexone (XR-NTX) technology

• XR-NTX uses the Medisorb®* extended-release technology, first introduced in RISPERDAL® CONSTA®†

* Medisorb is a registered trademark of Alkermes, Inc.
† Risperdal Consta are registered trademarks of Janssen Pharmaceutical.

Reference:
1. NIDA Monograph, Narcotic Antagonists: The Search for Long-acting Preparations
VIVITROL Technology

- Polylactide-co-glycolide (PLG) polymer allows extended release of the active ingredient, naltrexone
- Elimination: polymer eventually metabolized and eliminated as CO₂ and H₂O

Dean RL. *Front Biosci.* 2005;10:643-55.
VIVITROL Pharmacokinetics
Steady-State Naltrexone Concentration

*Predicted concentrations based on rapid achievement of steady state and literature evidence

Plasma concentrations do not necessarily correlate with clinical efficacy.
VIVITROL Pharmacokinetics

- Reduced first-pass hepatic metabolism vs naltrexone PO\textsuperscript{1}
- Systemic naltrexone exposure \(~4x\) greater than oral with less than \(1/3\) the monthly dose\textsuperscript{1}
  - 380mg of VIVITROL vs 1500mg of NTX-PO
- Initial peak: \(~2\) hours post injection, \(2^{\text{nd}}\) peak \(~3-4\) days\textsuperscript{2}
- Elimination via urine
  - Caution with moderate to severe renal impairment
  - Mild renal insufficiency (CrCl=50-80ml/min), no dosage adjustment necessary
  - Elimination not altered in mild-mod hepatic impairment
- Elimination Half-life: 5-10 days

\textsuperscript{1} Dunbar JL, et al. Alcohol Clin Exp Res. 2006; 30:480-490
\textsuperscript{2} VIVITROL Prescribing Information. Waltham, MA: Alkermes, Inc; rev October 2010
VIVITROL Mechanism of Action

- VIVITROL contains naltrexone:
  - Opioid antagonist, high affinity for μ-opioid receptor
  - Has little or no opioid agonist activity, and few (if any) intrinsic actions besides its opioid blocking properties
  - Some pupillary constriction (unknown mechanism)
  - Blocks β-endorphin binding, which may prevent excessive dopamine release
- Mechanism by which VIVITROL exerts its effects in alcohol-dependent patients is not entirely understood. However, involvement of the endogenous opioid system is suggested by preclinical data.
fMRI Cue Activation by Alcohol Images

Social Drinkers

Alcohol-Dependent Individuals

XR-NTX fMRI Signal Deactivation

In 31 XR-NTX Patients: 2 wks Post- vs. Pre-Treatment

XR-NTX attenuates BOLD signal activation to odor & visual cues in detoxified alcohol-dependent volunteers

• XR-NTX decreased (blue pixels) cue reactivity
• Reactivity to conditioned cues may play a role in relapse

(Penetar DM, et al., McLean Hospital/Harvard Medical School, Alkermes)
A RANDOM CONTROL TRIAL OF XR-NTX FOR ALCOHOL DEPENDENCE:
(JAMA 2005;293:1617-1625)

JC Garbutt¹, HR Kranzler², SS O‘Malley³, DR Gastfriend⁴, HM Pettinati⁵, BL Silverman⁴, JW Loewy⁴, EW Ehrich⁴ for the Vivitrex Study Group

¹ University of North Carolina School of Medicine, Chapel Hill, NC
² University of Connecticut School of Medicine, Farmington, CT
³ Yale University School of Medicine, New Haven, CT
⁴ Alkermes, Inc., Waltham, MA
⁵ University of Pennsylvania School of Medicine, Philadelphia, PA

Funding: Alkermes Inc.

Objective: To determine efficacy and tolerability of a long-acting intramuscular formulation of naltrexone in alcohol-dependence.
Percent Abstinent Over 6 Months

- Subset of patients who were abstinent for 4 days (N=81)
- Randomized to XR-NTX full-dose vs. half-dose vs. Placebo

VIVITROL for Alcohol Dependence

Adverse Events

• Most Common Adverse Event: Nausea, particularly day 1-3
• Serious adverse events (SAEs) occurred at a rate similar to patients receiving placebo injections
  • 5.4% on VIVITROL vs. 7.2% on placebo
• Most common SAE: inpatient hospitalization for detox
• Other SAEs seen with VIVITROL
  • 2 cases of pneumonia (1 confirmed as eosinophilic)
  • 1 case of injection site induration requiring excision
• No significant increase in mean AST or ALT levels

2. VIVITROL Prescribing Information. Waltham, MA: Alkermes, Inc; rev October 2010
## Pharmacotherapy for Alcohol Dependence

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Oral</th>
<th>Injectable</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIVITROL(^1) (2006)</td>
<td>-</td>
<td>✔️</td>
<td>380 mg</td>
<td>1/month</td>
</tr>
<tr>
<td>Acamprosate(^2) (2004)</td>
<td>✔️</td>
<td>-</td>
<td>333 mg</td>
<td>2 tabs, 3 times/day (180 tabs/month)</td>
</tr>
<tr>
<td>Naltrexone(^3) (1994)</td>
<td>✔️</td>
<td>-</td>
<td>50 mg</td>
<td>1 tab/day (30 tabs/month)</td>
</tr>
<tr>
<td>Disulfiram(^4) (1951)</td>
<td>✔️</td>
<td>-</td>
<td>500 mg (Initiation) 125 – 500 mg (Maintenance)</td>
<td>1 tab/day (30 tabs/month)</td>
</tr>
</tbody>
</table>

1. VIVITROL [full prescribing information]. Waltham, MA: Alkermes, Inc; rev October 2010.
2. Campral [full prescribing information]. Merck Santé s.a.s.
3. ReVia [full prescribing information]. Duramed Pharmaceuticals, Inc.
4. Disulfiram [full prescribing information]. Odyssey Pharmaceuticals, Inc.
Days on Meds vs. Subsequent Detox: Outcomes During 6 Months post Index

Persistence Days on Index Medication

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Persistence Days on Index Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>XR-NTX (N=661)</td>
<td>61.6</td>
</tr>
<tr>
<td>Oral-NTX (N=2391)</td>
<td>49.8</td>
</tr>
<tr>
<td>Disulfram (N=3492)</td>
<td>45.8</td>
</tr>
<tr>
<td>Acamprosate (N=8958)</td>
<td>42.6</td>
</tr>
</tbody>
</table>

Number of Days in a Detox Facility

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Number of Days in a Detox Facility</th>
</tr>
</thead>
<tbody>
<tr>
<td>XR-NTX (N=661)</td>
<td>227</td>
</tr>
<tr>
<td>Oral-NTX (N=2391)</td>
<td>361</td>
</tr>
<tr>
<td>Disulfram (N=3492)</td>
<td>429</td>
</tr>
<tr>
<td>Acamprosate (N=8958)</td>
<td>741</td>
</tr>
</tbody>
</table>

P-value vs. XR-NTX: *P<0.05; †P<0.01
VIVITROL: Clinical Trial Data In Opioid Dependence
XR-NTX FOR OPIOID DEPENDENCE:
A Double-Blind, Placebo-Controlled, Multicentre Randomised Trial
(The Lancet, 2011;377:1506-1513)

E Krupitsky¹, EV Nunes², W Ling³, A Illeperuma⁴,
DR Gastfriend⁴, BL Silverman⁴

¹ Bekhterev Research Psychoneurological Institute, St Petersburg State Pavlov Medical University, St Petersburg, Russia
² New York State Psychiatric Institute and Department of Psychiatry, Columbia University, New York, NY, USA
³ Department of Psychiatry and Biobehavioral Sciences, University of California Los Angeles, Los Angeles, CA, USA
⁴ Alkermes, Inc., Waltham, MA

Funding: Alkermes Inc.

Objective: To assess drug use, craving and retention with XR-NTX in opioid dependence after detox
Response Profile
Cumulative % of Participants at Each Rate of Weekly Confirmed Abstinence: XR-NTX 380 mg vs. Placebo

- Total abstinence (100% opioid-free weeks) during Weeks 5-24 was reported in 45 subjects (35.7%) with XR-NTX vs 28 (22.6%) with placebo (P=0.0224)
VIVITROL for Opioid Dependence
Secondary Endpoint – Treatment Retention

Placebo - Median days of treatment = 96
VIVITROL - Median days of treatment = 168

Log-rank P = 0.0042 (adjusted)

VIVITROL for Opioid Dependence
Secondary Endpoint – Opioid Craving Score

- Baseline craving scores: VIVITROL=18; Placebo=22
- VIVITROL patients had a 50% reduction from baseline in VAS-craving vs. no change for placebo

**VIVITROL for Opioid Dependence: Most Common Clinical Adverse Events**

<table>
<thead>
<tr>
<th>Adverse Event, N (%)</th>
<th>VIVITROL (N=126)</th>
<th>Placebo (N=124)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase increased</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>Gamma-glutamyltransferase increased</td>
<td>7%</td>
<td>3%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6%</td>
<td>1%</td>
</tr>
<tr>
<td>Influenza</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Toothache</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Headache</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>≥ 1 serious adverse event</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Discontinued due to serious adverse event</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

No overdose events or other severe adverse events were reported.

In the Placebo group, 4 patients reported 5 SAEs: 2 infectious, 1 drug dependence, 1 psychotic disorder and 1 peptic ulcer.
In the VIVITROL group, 3 patients reported 4 SAEs consisting of infectious processes, e.g., AIDS/HIV or other infection.
VIVITROL for Opioid Dependence: Conclusions

- VIVITROL + Counseling:
  - Decreased opioid use and facilitated sustained remission
  - Reduced opioid cravings
  - Decreased relapse to physical opioid dependence
  - Retained opioid dependent patients in treatment
  - Impacted recovery by promoting abstinence and improvement in clinical global index (exploratory endpoint)

- Safety findings: No overdoses, no deaths
  - Discontinuations: 2% in both groups due to AEs, 0% due to severe AEs

- Limitations: Russian opioid-dependent (heroin) population, placebo and counseling response may have reduced VIVITROL effect size

<table>
<thead>
<tr>
<th>Study &amp; Design Type</th>
<th>Location</th>
<th>Total</th>
<th>XR-NTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid Challenge Blockade RCT</td>
<td>USA</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>1-Year Open Label Safety RCT</td>
<td>USA</td>
<td>121</td>
<td>101</td>
</tr>
<tr>
<td>Phase III Efficacy &amp; Safety RCT</td>
<td>Russia</td>
<td>250</td>
<td>126</td>
</tr>
<tr>
<td>Open-label Study in Health Professionals</td>
<td>USA</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>Retrospective Comparison in CRC Rehab Units</td>
<td>USA</td>
<td>7,687</td>
<td>165</td>
</tr>
<tr>
<td>Rikers Island (NYC) Jail Re-entry RCT</td>
<td>USA</td>
<td>33</td>
<td>17</td>
</tr>
<tr>
<td>Retrospective Health Economic Analysis XR-NTX vs. All FDA-Approved Oral Agents</td>
<td>USA</td>
<td>10,513</td>
<td>156</td>
</tr>
<tr>
<td><strong>TOTAL SAMPLE SIZE:</strong></td>
<td><strong>18,669</strong></td>
<td><strong>630</strong></td>
<td></td>
</tr>
</tbody>
</table>
6-Month Retention on XR-NTX: 3 Studies

Study Retention Over a 24-Week Treatment Period

- Health Professionals (U.S.) (N=48)
- 1-Year Safety Study (U.S.) (N=101)
- Phase III (Russia, Heroin) (N=126)
## XR-NTX Reports in Opioid Dependence

- **Alkermes Sponsored/Funded Trials:** 7
  - Alkermes Provided Study Drug for Trials: 3
  - Studies Conducted Independent of Alkermes: 5

- **Total Studies:** 15

  - Total Patients Treated with XR-NTX: 1,683
  - Est’d Total XR-NTX Patient x Months: 5,719

- **Reported Overdoses on XR-NTX:** 4
- **Reported Deaths on XR-NTX:** 1
<table>
<thead>
<tr>
<th>Study &amp; Design Type</th>
<th>Location</th>
<th>Total</th>
<th>XR-NTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid Challenge Blockade RCT</td>
<td>USA</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>1-Year Open Label Safety RCT</td>
<td>USA</td>
<td>121</td>
<td>101</td>
</tr>
<tr>
<td>Phase III Efficacy &amp; Safety RCT</td>
<td>Russia</td>
<td>250</td>
<td>126</td>
</tr>
<tr>
<td>Open-label Study in Health Professionals</td>
<td>USA</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>Retrospective Comparison in CRC Rehab Units</td>
<td>USA</td>
<td>7,687</td>
<td>165</td>
</tr>
<tr>
<td>Rikers Island (NYC) Jail Re-entry RCT</td>
<td>USA</td>
<td>33</td>
<td>17</td>
</tr>
<tr>
<td>Retrospective Health Economic Analysis XR-NTX vs. All FDA-Approved Oral Agents</td>
<td>USA</td>
<td>10,513</td>
<td>156</td>
</tr>
</tbody>
</table>

**TOTAL SAMPLE SIZE:** 18,669 630
CRC’s Vivitrol Procedure (Chris Jaquis, CRC)

• **Admission**: Patients sign Alkermes Release form (to obtain verification that insurance will cover med)

• **History & Physical** (within 24 hours of admission)
  • Medical staff discusses Vivitrol & continuing care

• **Mid-stay**
  • Medical staff Vivitrol Lecture (in conjunction with continuing care)
  • Information posted within center to promote Vivitrol
  • Meet with designated staff members to verify benefit & continue authorization process

• **Just Prior to Discharge**
  • Medication shipped directly to center to facilitate injection prior to discharge
  • Continuing Care with provider in home area is set for follow up injections
## CRC’s Vivitrol Procedure

(Chris Jaquis, CRC)

### Enrollment

<table>
<thead>
<tr>
<th>Activity</th>
<th>Responsible Individual</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Review admissions each morning to identify appropriate candidates</td>
<td></td>
</tr>
<tr>
<td>☐ Begin discussion/training program with patient (review VIVITROL</td>
<td></td>
</tr>
<tr>
<td>☐ Medication Guide/VIVITROL Literature</td>
<td></td>
</tr>
<tr>
<td>☐ Fax enrollment form and co-pay backer to Touchpoints or directly to</td>
<td></td>
</tr>
<tr>
<td>☐ preferred specialty pharmacy</td>
<td></td>
</tr>
<tr>
<td>☐ Give co-pay card to patient</td>
<td></td>
</tr>
<tr>
<td>☐ Complete Prior Authorization or Letter of Medical Necessity, if needed</td>
<td></td>
</tr>
<tr>
<td>☐ State reason for patient not receiving Vivitrol:</td>
<td></td>
</tr>
</tbody>
</table>

### Product Acquisition

<table>
<thead>
<tr>
<th>Activity</th>
<th>Responsible Individual</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ With patient, call TP or SP as soon as possible prior to discharge to</td>
<td></td>
</tr>
<tr>
<td>☐ authorize shipment of VIVITROL</td>
<td></td>
</tr>
<tr>
<td>☐ Receive medication from supplier, log into inventory, store per</td>
<td></td>
</tr>
<tr>
<td>☐ Package Insert instructions</td>
<td></td>
</tr>
<tr>
<td>☐ NOTES:</td>
<td></td>
</tr>
</tbody>
</table>

### Injections & Discharge Planning

<table>
<thead>
<tr>
<th>Activity</th>
<th>Responsible Individual</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Administer first injection</td>
<td></td>
</tr>
<tr>
<td>☐ With patient, select injector for future doses, coordinate with</td>
<td></td>
</tr>
<tr>
<td>☐ Touchpoints</td>
<td></td>
</tr>
<tr>
<td>☐ Provide follow-on VIVITROL provider info to patient (name, address,</td>
<td></td>
</tr>
<tr>
<td>☐ phone, etc.)</td>
<td></td>
</tr>
<tr>
<td>☐ Educate patient on SP process for refills</td>
<td></td>
</tr>
<tr>
<td>☐ Describe patient response to Vivitrol:</td>
<td></td>
</tr>
</tbody>
</table>
VIVITROL: Storage, Preparation And Injection
The VIVITROL Kit

• One vial: microspheres
• One vial: diluent
• One 5-mL syringe
• One 1-inch 20-gauge preparation needle
• Two 1.5-inch 20-gauge administration needles with aqua needle protection device
• Two 2-inch 20-gauge administration needles with orange needle protection device
VIVITROL Storage & Prep

• VIVITROL should always be kept refrigerated at temperatures 2–8°C, 36–46°F, not frozen
• Unrefrigerated VIVITROL microspheres can be stored at temperatures not exceeding 25°C or 77°F for no more than 7 cumulative days prior to administration
• Remove the box and open for 45 min to reach room temp
• Warm the diluent vial by rolling it in the hand until it no longer feels cold to touch
• Must be prepared & administered by a health professional
  • Inspect visually for particulate matter and discoloration
• VIVITROL must not be injected using any other needles
VIVITROL Prep

- Use the prep needle to add diluent to the microspheres vial
- Mix the powder and diluent by shaking vial vigorously for ~1 minute, ensuring the dose is thoroughly suspended
- Withdraw the suspension immediately into the syringe using the same prep needle
- Replace the preparation needle with one of the administration needles provided (1.5 inches or 2 inches) based on patient’s body habitus
  - Use an alternate treatment when patient’s body habitus precludes IM gluteal injection with provided needles
- Prepare 4.2 mL of suspension to administer 4 mL immediately by deep intramuscular (IM) injection into the gluteal muscle, in the upper outer quadrant
VIVITROL Administration

- Identify the upper, outer quadrant of buttock
- Inject immediately after mixing & drawing up
- Dispose of items in proper waste containers
- Re-inject every 4 weeks, or once a month
  - Alternate buttock sides monthly
- Needle jams (not common):
  - Withdraw & replace with extra needle from the VIVITROL kit
  - Re-inject at a site adjacent to the original injection (same buttock side)
VIVITROL Injection Technique

• Position patient lying face down
• **Inject deep**: Do NOT administer IV, subcutaneously or into adipose
• Good IM technique:
  • Express air bubbles prior to insertion in muscle
  • Check for aspirated blood (avoid venous injecting microspheres)
  • Hold the needle vertically at a 90-degree angle to skin to obtain deep muscle injection
Labeled Warnings and Precautions Related to VIVITROL Administration

• Injection Site Reactions
  • Injection site reactions may be very severe
  • Some have required surgical intervention
  • Patients should be informed that they should report any concerning injection site reactions to their healthcare professional(s)
  • Local massage, ice packs & NSAIDs have been used

• Intramuscular Injections
  • VIVITROL should be administered with caution to patients with thrombocytopenia or coagulation disorders (e.g., hemophilia and severe hepatic failure)
Additional Important Safety Information

• **Contraindications**: acute hepatic disease, renal insufficiency
  • Pain conditions likely to require opioid analgesics

• **Warnings**
  • Eosinophilic Pneumonia
  • Hypersensitivity Reactions
  • Unintended Precipitation of Opioid Withdrawal
  • Opioid Overdose at the End of a Dosing Interval, After Missing a Dose and After Attempts to Overcome Blockade
  • Depression and Suicidality
  • Reversal of VIVITROL Blockade for Pain Management
  • Alcohol Withdrawal
  • Interference with Laboratory Tests

• **Pregnancy**: Class C – no studies
Protracted Withdrawal: “Naltrexone Flu”

- A possibility when starting XR-NTX just after detox
- Flu-like signs & symptoms
  - Somatic complaints: insomnia, GI distress, hyperalgesia, anergy
  - Anxiety, irritability, dysphoria, anhedonia
  - Can decrease risk by waiting, post detox (BUT risking risk of relapse)
- Management: Aggressive Symptomatic Care
  - Insomnia: Aolpidem, trazedoen, quetiapine
  - GI Distress: H2 blockers
  - Anxiety: clonazepam, clonidine
- Symptoms generally remit by 2-4 weeks
  - True prolonged symptoms are rare & likely reflect other psychophollogy

Bisaga A., et al. PCSS
Adverse Events

• Most frequent with alcohol dependence:
  • nausea, vomiting, injection site reactions (including induration, pruritis, nodules and swelling)
  • muscle cramps, dizziness or syncope
  • somnolence or sedation,
  • anorexia, decreased appetite or other appetite disorders

• Most frequent with opioid-dependence:
  • hepatic enzyme abnormalities
  • injection site pain
  • nasopharyngitis, insomnia and toothache
MEDICATION ASSISTED TREATMENT
FOR SUBSTANCE USE DISORDERS:
EXTENDED-RELEASE NALTREXONE
(XR-NTX; VIVITROL®)

David R. Gastfriend
MD
Chief Executive Officer
Treatment Research Institute

Disclosures: Dr Gastfriend is a shareholder and former employee of Alkermes, Inc.

VIVITROL: Evidence-Based Patient Selection
## Choosing Agonist vs. Antagonist Treatment

<table>
<thead>
<tr>
<th></th>
<th>Agonist</th>
<th>Antagonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain physiological dependence and potential for withdrawal</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Potential for tolerance development</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>Euphoric effects/abuse/diversion</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Compatible with ongoing illicit opioid use</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>May alter use of other drugs</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Extinction of heroin-reinforced behaviors/reversal of underlying neurobiology</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>indefinite</td>
<td>?</td>
</tr>
<tr>
<td>Cultural/ideological barriers to availability</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Professional/public opposition</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Bisaga A., et al. PCSS

*Not offering medication after they stop drug use puts patients at increased risk of overdose and death*
VIVITROL Evidence Base: Suitable for whom…? YES

- Alcohol Dependent patients? ✓
- Opioid Dependent patients? ✓
- Young adults ages 18-25? ✓
- Healthcare professionals? ✓
- Severe alcohol dependent patients? ✓
- Severe opioid dependent patients? ✓
- HIV+ and Hepatitis C+ patients? ✓ (HCV+ if stable)
- Probationers and parolees? ✓
- Patients with private insurance? ✓
- Patients with public coverage? ✓
- Patients preparing to leave rehab? ✓
- Patients who WANT VIVITROL? ✓
VIVITROL Evidence Base: Which patients WANT Vivitrol…?

- Patients who are…
- Young or not particularly severe
- Leaving detox
- Leaving jail or prison
- Unable to receive or not appropriate for agonist meds
- Finishing detox or already abstinent but at high relapse risk
- Unable (e.g., due to job) to use agonist meds – or unwilling
- Not stabilizing on methadone or buprenorphine
- Completing methadone or buprenorphine treatment
- Both alcohol and opioid dependent