Naltrexone (Extended-Release Naltrexone [XR-NTX]) primer for MAT mentors

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Joshua Lee, Disclosures

- Grants: NIDA, NIAAA, Alkermes-ISS
- No other conflicts (no advisory, speaking, consulting, etc.)
- Free study drug: Reckitt Benkiser, Alkermes

- Vivitol®:
  - Alkermes, Inc – sole manufacturer
  - Developed with NIH (NIDA, NIAAA) funding

The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.
Educational Objectives

• At the conclusion of this activity participants should be able to:
  ▪ Explain the rationale for XR-NTX treatment of:
    – Alcohol use disorders
    – Opioid use disorders
  ▪ Teach practical approaches to XR-NTX:
    – Induction
    – Maintenance
  ▪ Summarize the evidence base for XR-NTX
Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.
- This webinar has been tailored for lead mentors, mentors, and administrative staff.
Extended-Release Naltrexone

• aka, “sustained-release injectable” (SRI) naltrexone
  ▪ Mu opioid receptor full antagonist
  ▪ 30+ day (monthly) injectable formulation
  ▪ polylactide-co-glycolide (PLG) biodegradable matrix (same as Risperdal Consta)

• Labeled for alcohol dependence:
  ▪ “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 (1.1).

• Label for opioid dependence:
  ▪ “VIVITROL is indicated for the prevention of relapse to opioid dependence, following opioid detoxification (1.2).
Extended-Release Naltrexone

- Monthly intramuscular injection
- Given by nurse, PA, MD
- Non-narcotic, no abuse
- Prescribed by MD/DO/NP

Exclusions:
- Pregnancy
- Severe liver disease
- Chronic pain requiring opioids
Case Vignettes: Heroin

• 44 yo male unable to stop heroin, using 10 bags IN daily
  ▪ Meets criteria for opioid use disorder, severe (heroin dependence)
  ▪ Living at home, unemployment, supportive spouse, no kids, no other medical/psyche history, NKDA, no meds, HCV/HIV-

• Motivated for XR-NTX vs. BUP-NX and methadone

• Admitted to detox unit
  ▪ 3-day methadone taper, standing clonidine q6hr, PO fluids, clonazepam BID, tylenol/motrin
  ▪ Day 5 of detox given 12.5mg oral naltrexone, day 6 25mg
  ▪ Day 7 50mg oral naltrexone, naloxone challenge negative, XR-NTX injection #1
  ▪ Post-injection week 1: poor sleep, some GI (mild), given trazodone HS
Month 1: 3 days of IN heroin use
  ▪ Reported no effects, didn’t get high
Individual counseling twice a week
Continues XR-NTX 3 months…no heroin misuse, urines are negative
Declines injection #4…2 weeks later he is still opioid negative and in counseling
Counseled explicitly about lowered tolerance and OD/death risk related to any usual opioid misuse
How will he do now?
XR-NTX for Opioid Relapse Prevention: Krupitsky, Lancet, 2011

- 13-site Russian RCT N=250: XR-NTX vs. TAU post-detox
- Higher rates of ‘median’ XR-NTX opioid abstinence: 90% vs. 30%
XR-NTX  Opioid Treatment: Evidence-base

- Good efficacy data post-detox…in Russia
- US effectiveness studies on-going:
  - NIDA 5-site XR-NTX vs. TAU CJS outpatient
  - NIDA CTN-0051 X:BOT, XR-NTX vs. BUP-NX
- The great challenge is a successful detox/induction
- Very good alcohol/opioid and HCV/HIV liver safety data: XRNTX appears very safe
XR-NTX Practical Considerations

• Which opioid users need XR-NTX?
  – Anyone considering ‘drug-free’ recovery
  – Intolerant to bup-nx or methadone
  – Cannot access bup-nx or methadone

• There is no evidence that XR-NTX vs. agonists if better, worse, same, etc.
  – Head-to-head XR-NTX vs. BUP-NX is on-going (CTN-0051 X:BOT)
XR-NTX Practical Considerations

• How do I get XR-NTX for a patient?
  – Adequate insurance or program coverage
    • Out-of-pocket XR-NTX is $1100/dose
    • Covered by most commercial insurance
    • MA coverage for outpatients variable

• How is it delivered?
  – Shipped to MD/office
  – Refrigerated until dosing visit
XR-NTX Opioid Treatment: Induction

• Patient already detoxed (jail, rehab, etc.)?
  – Check opioid urine and self-report (negative)
  – Naloxone challenge (0.8mg IM, SC, or IV)
  – XR-NTX injection #1 immediately after challenge
XR-NTX  Opioid Treatment: Induction

• Patient actively using opioids?
  – 1. Opioid/clonidine detox until urine is completely opioid negative
  – 2. Early low-dose oral naltrexone challenge
    • Both approaches rely on liberal use of clonidine and ‘comfort’ meds, benzos/sleep, NSAIDs, GI agents
XR-NTX Practical Considerations

• Side Effects?
  – Injection site pain: common
  – HA, nausea, flu-like: common with 1st injection
  – Opioid blockade – acute pain mgt: universal
XR-NTX Practical Considerations

• How long should I treat for?
  – Unknown
  – Pivotal trial 6 months of XR-NTX, then an open-label extension phase
  – Reimbursement for 6-24+ months is standard

• When XR-NTX stops?
  – Return to non-antagonized, low tolerance
  – Resume ‘baseline’ risk of relapse, overdose
  – No evidence of otherwise higher OD risk
Case Vignettes: Alcohol

- 44 yo male unable to stop drinking, using 10 beers daily
  - Meets criteria for alcohol use disorder, severe (alcohol dependence)
  - Living at home, unemployment, supportive spouse, no kids, no other medical/psyche history, NKDA, no meds, no seizure history.
- Not interested in in-patient treatment; can stop drinking for a few days with no adverse events;
- Interested in XR- vs. oral medical management (MM) options
- Family Practice physician conducts NIAAA Clinician’s Guide based MM
  - Orders Vivitrol, delivered to medical office
  - Patient encouraged to stop drinking immediately, pursue AA, professional counseling, and consider IOP: none completed by the patient at week 1
• Vivitrol injection #1, 1 week after initial visit, patient still drinking
• Patient with decreased heavy drinking days and increased days abstinent at week 4, given injection #2...at 6 months till drinking 2-5 days/month, but no heavy drinking days.
• States he doesn’t like the taste of beer anymore, but finding it hard to completely change his routines
• MD urges him to reconsider AA, IOP, and individual counseling
• AEs: HA w initial injection, IM soreness
• Vivitrol seems to be working, MD continues injections another 6 months
Pivotal XR-NTX Alcohol Study: Garbutt J, JAMA, 2005

- XR-NTX 380mg vs. 190mg vs. Placebo
- N=415
- 25% reduction in heavy drinking days
- Placebo arm did quite well
XR-NTX Alcohol Treatment in Primary Care

- XR-NTX + MM in Primary Care x 12 weeks
- N=72 enrolled
  - 56% (n=40) retained at week 12
  - 29% (n=19) enrolled in a 1-year extension study
    - Median time in extended treatment: 38 weeks (8 injections; range 16-72 weeks)

- Drinking reductions were sustained in treatment

- No data on drop-outs

LeeJD, JSAT, 2008, 2011
XR-NTX Alcohol Treatment: Evidence-base

- Good efficacy data on reduced heavy drinking
- Feasible in primary care Med Mgt
- Retrospective cost effectiveness data is favorable
- Not clear how to best combine with oral naltrexone
- Not clear what optimal length of treatment is
- Combines with any counseling: not clear what is best mix
PCSSMAT is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with: American Osteopathic Academy of Addiction Medicine (AOAAM), American Psychiatric Association (APA) and American Society of Addiction Medicine (ASAM).

For More Information: [www.pcssmat.org](http://www.pcssmat.org)

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References


