



# Increasing Issues of Polypharmacy and Off-Label Drug Use in Psychiatric Care

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# Speaker Introductions

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# Overview

- Issues related to polypharmacy and off-label use of psychiatric medications
- Latest FDA-approved indications for Provigil (modafinil), Buprenex and Subutex (buprenorphine HCl), Suboxone (buprenorphine HCl and naloxone HCl), and Vivitrol (naltrexone for extended-release injectable suspension)
- Most common off-label uses of these medications
- Polypharmacy issues associated with these medications, including contraindications and potential for medication interactions and addiction

# Common Prescribing Practices in Psychiatric Care

- Polypharmacy
  - Evidence for added benefit of polypharmacy with psychiatric medications remains limited
  - Growing evidence that some medication combinations are unnecessary and produce increased adverse events
- Off-label prescribing
  - May produce more pronounced side effects or adverse events
  - Increases risk for unforeseen circumstances

# Reducing Inappropriate or Unnecessary Prescribing: **Critical Actions**

- Obtain accurate medication and medical history
- Link each prescribed medication to a disease state
- Identify medications treating side effects
  - Discontinuing one drug that is causing a side effect can lead to the discontinuation of several drugs

# Provigil (Modafinil)

# Modafinil: FDA-Approved Indications

- Modafinil is a wake-promoting quasi-stimulant that is indicated to improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy, obstructive sleep apnea, and shift work disorder
  - In patients with obstructive sleep apnea, modafinil is indicated as an adjunct to standard treatment(s) for the underlying obstruction

# Modafinil: Off-Label Uses

- Treatment of cognitive dysfunction in some psychiatric disorders
- Nonmedical use by healthy individuals as a way to help extend alertness, reduce the need for sleep, and improve cognitive reinforcement
- Small studies have evaluated its use in schizophrenia, ADHD, and cocaine dependence and withdrawal, and as an adjunct to antidepressants for depression
- Most health plans do not cover modafinil for these off-label uses, which are considered experimental, investigational, or unproven

# Modafinil: Potential for Abuse

- Low likelihood for abuse in individuals who do not abuse drugs
- Debate surrounds its potential for abuse
- Modafinil has been shown to:
  - Increase dopamine levels in the brain, which is associated with the potential for abuse
  - Produce psychoactive and euphoric effects that are typically associated with CNS stimulant drugs such as Ritalin (methylphenidate), which is commonly abused

# Modafinil: Polypharmacy & Contraindications

- Modafinil may be combined with antidepressants (clomipramine, protriptyline) for patients suffering from narcolepsy with cataplexy
- Patients should not take modafinil if they have a history of:
  - Left ventricular hypertrophy or ischemic ECG changes, chest pain, arrhythmia, or other clinically significant manifestations of mitral valve prolapse associated with the use of CNS stimulants
  - Severe mental illness

**Buprenorphine Formulations:  
Buprenex or Subutex (Buprenorphine HCl),  
and  
Suboxone (Buprenorphine HCl and  
Naloxone HCl)**

# Buprenorphine Formulations:

## FDA-Approved Indications

- Buprenex is a partial opioid agonist indicated for the relief of moderate to severe pain
- Subutex and Suboxone are approved for the treatment of opiate dependence
  - Subutex is intended for detoxification and is given during the first few days of treatment
  - Suboxone is used during the maintenance phase of treatment
- Buprenorphine is a controlled substance that can easily be abused
  - In 2002, the U.S. Drug Enforcement Administration (DEA) classified buprenorphine and any products containing buprenorphine as Schedule III drugs

# Buprenorphine Formulations: Off-Label Uses

- Buprenex
  - Used off-label for opioid dependence before Suboxone and Subutex were approved in 2002
  - FDA now recommends that Buprenex not be used to treat opioid addiction and that the drug not be administered to those living with or recovering from addiction
- Suboxone and Subutex
  - Sometimes used off-label for the treatment of depression or pain (limited study data)
  - FDA does not recommend the use of Suboxone or Subutex for pain, especially for opioid-naïve patients

# Buprenorphine Formulations: Potential for Abuse

- Buprenex injection is more likely to be diverted and abused than Suboxone and Subutex, which are taken sublingually
  - Both Suboxone and Subutex contain buprenorphine HCl, but Suboxone also contains naloxone, which was added to discourage intravenous misuse of buprenorphine
- Use of Buprenex by individuals addicted to narcotics can result in withdrawal symptoms
- All buprenorphine formulations have the potential for abuse and produce dependence of the opioid type
- Associated with lower risk for overdose compared with short-acting opioids such as hydrocodone

# Buprenorphine Formulations: Polypharmacy and Contraindications

- Many patients with addiction disorders also have some type of mental health disorder, requiring polypharmacy
- Buprenorphine formulations should not be combined with CNS antidepressants, benzodiazepines, and other opioids
  - The synergistic effects of these combinations could lead to overdose

# Vivitrol (Naltrexone XR Inj) (Monthly Injection)

# Vivitrol: FDA-Approved Indications

- Vivitrol, which is an opioid-receptor antagonist administered by intramuscular injection once per month, is indicated for the:
  - Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to the initiation of treatment with Vivitrol (patients should not be actively drinking at the time of initial Vivitrol administration)
  - Prevention of relapse to opioid dependence, following opioid detoxification
- Vivitrol should be part of a comprehensive program that includes psychosocial support

# Vivitrol (Naltrexone): Off-Label Uses

- Low dose naltrexone (LDN) has been studied for the treatment of pain in a wide range of diseases, including HIV/AIDS, multiple sclerosis, Parkinson's disease, and certain cancers
  - Trials have largely been pilot studies and do not provide scientific evidence to justify clinical use
  - Larger, more rigorous studies are needed to thoroughly assess the effects and safety of LDN for treating pain

# Vivitrol: Potential for Abuse

- Unlike other anti-addiction medications such as methadone and buprenorphine, Vivitrol is not an opioid and does not have addictive properties

# Vivitrol: Polypharmacy & Contraindications

- Concurrent opioid and alcohol dependence is common, but **Vivitrol should not be taken in combination with buprenorphine**
- Vivitrol should not be used for patients:
  - Receiving opioid analgesics
  - With concurrent physiologic opioid dependence
  - In acute opioid withdrawal

# Polypharmacy & Off-Label Drug Use in Psychiatric Care: **The Role of Independent Review**

- An independent medical review:
  - Looks at whether or not a specific procedure was medically necessary
  - Facilitates effective psychiatric care, which requires an in-depth understanding of developments in psychopharmacology so that disease management can be individualized for each patient
- Independent review organizations provide specialty match
  - Especially important in psychiatric care due to the high rates of polypharmacy and off-label medication use, which often result from comorbid mental and substance use disorders and physical health problems
  - Board-certified physician specialists who work with IROs keep up-to-date with the latest medical literature, the latest standard of care, and continually evolving therapies

# Conclusions

- Polypharmacy
  - An effective clinical intervention in some cases, depending on the medications used and the characteristics of the individual patient
  - Increases risk for medication-related adverse events
  - Often creates the need for additional medication
- Off-label prescribing
  - Legal and beneficial for some patients
  - Often little or no scientific support

# Conclusions

- Independent medical reviews
  - Provide unbiased evaluation of medical need in psychiatric care
  - Facilitate effective psychiatric care, which is often complicated by comorbid conditions and polypharmacy
- Independent review organizations
  - Provide ready access to specialists, which healthcare plans may lack internally
  - Allow for timely determination of whether the requested treatment falls under medical necessity guidelines and the latest standard of care

# Questions and Answers

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