Substance Use Disorder Series

MODULE 5

Pharmacological Treatment Options for Substance Use Disorders

Casey Fitzpatrick, PharmD, BCPS

Advisory Board

- Casey Fitzpatrick, PharmD, BCPS
- Brittany Riley, PharmD, BCPS, MS
- Charles “CK” Babcock, PharmD, CDE, BCACP
- Kimberly Broedel-Zaugg, RPh, MBA, PhD

Disclosures

- Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

Objectives

1. Recommend pharmacological treatment options for substance use disorder (SUD) patients
2. Compare treatment options for various SUDs
3. Discuss treatment options for pregnant and postpartum women with SUD

Goals of Treatment

- Prevent:
  - Overdoses and overdose deaths
  - Medical complications
  - Psychosocial decline
  - Transition to injection drug use
  - Injection-related infectious diseases including skin and soft tissue infections, endocarditis, hepatitis C and HIV

Opioid Use Disorder (OUD)

Chronic/Maintenance Treatment Options

MARSHALL
SCHOOL OF PHARMACY

Medication-Assisted Treatment (MAT)

- MAT is the use of medications, in combination with counseling and behavioral therapies, to treat substance use disorders
  - Counseling and behavioral therapies are discussed in depth in Module 4
- Three drugs approved by the Food and Drug Administration (FDA) for the treatment of opioid dependence includes:
  - Methadone
  - Buprenorphine
  - Naltrexone

OUD Treatment Statistics

- 2017 National Survey of Substance Abuse Treatment Services (N-SSATS)
  - Buprenorphine was provided by only 29% of substance use treatment facilities
    - 24% of facilities provided injectable naltrexone
  - In treatment programs that offer MAT, only about one-third of clients receive them
    - 28% received methadone
    - 8% received buprenorphine
    - 2% received naltrexone

Drug Addiction Treatment Act of 2000 (DATA 2000)

- Permits prescribers who meet certain requirements to prescribe narcotic medications, including buprenorphine, for patients with OUD
- Waivers can be obtained from the Substance Abuse and Mental Health Services Administration (SAMHSA) by physicians after satisfying 8 hours of required training
  - Prescribers will have a special Drug Enforcement Administration (DEA) number starting with X

"Become a buprenorphine Waivered Practitioner." Substance Abuse and Mental Health Services. https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner. Accessed June 28, 2020.

Drug Addiction Treatment Act of 2000 (DATA 2000) continued

- Prescribers can treat 30 patients initially
  - Can request to increase patient limit to 100 patients after year one and 275 patients after year two
  - SUPPORT Act
    - Qualified practitioners can treat up to 100 patients in first year
    - Extended prescribing privileges to midlevel practitioners

"Become a buprenorphine Waivered Practitioner." Substance Abuse and Mental Health Services. https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner. Accessed June 28, 2020.

Buprenorphine

MARSHALL
SCHOOL OF PHARMACY

Buprenorphine Overview

- A mixed agonist-antagonist opioid receptor modulator
  - Partial agonist at the μ-opioid receptor
  - Antagonist at the κ-opioid receptor
- Has a "ceiling effect" at higher doses for respiratory depression, sedation, and subjective measures such as euphoria
- Commonly combined with the opioid antagonist naloxone to deter misuse
  - In theory, if injected, the naloxone may precipitate withdrawal in an opioid-dependent individual (not clinically significant)

Lutfy K, Cowan A. *Curr Neuropharmacol.* 2004;2(4):394-402.
Mello NK, Mendelson JH. *Drug Alcohol Depend*. 1985;14(3-4):283-303.
Virani AS, Bezchlibnyk-Butler KZ, Jeffries JJ, Procyshyn RM. (2012). Clinical Handbook of Psychotropic Drugs. 19th ed. Bern: Hogrefe & Huber Publishers

Rationale for Use

- Buprenorphine has ↑ binding affinity compared to full opioid agonists at the μ-opioid receptor with a lower intrinsic activity
  - Blocks the effect of exogenous opioids
    - Deterrent for illicit opioid use
  - Provides a fraction of effect that levels out with higher doses – "ceiling effect"
    - Minimizes functional impairment
    - Reduces potential for overdose
- Has been shown to be more effective than oral naltrexone or placebo therapy in decreasing opioid consumption and prolonging time to relapse

Ling W, Mooney L, Torrington M. *Pain Manag.* 2012;2(4):345-350
Schottenfeld RS, Chawarski MC, Mazlan M. *Lancet*. 2008;371(9631):2192-2200

Formulations for OUD

- Buprenorphine alone
  - Probuphine® – implant for subdermal administration
  - Sublocade® – extended-release injection for subcutaneous use
  - Subutex® – sublingual (SL) tablet
- Buprenorphine and naloxone combinations
  - Bunavail®- buccal film
  - Cassipa® – SL film
    - FDA-approved in September 2018 but currently unavailable
  - Suboxone® - SL film or tablet for SL or buccal use
    - Some states
  - Zubsolv – SL tablets

Corresponding Dosages of Buprenorphine and Naloxone Combination Products

Suboxone SL Film	Zubsolv SL Tablet	Bunavail Buccal Film
N/A	0.7 mg/0.18 mg	N/A
2 mg/0.5 mg*	1.4 mg/0.36 mg	N/A
4 mg/1 mg*	2.9 mg/0.71 mg	2.1 mg/0.3 mg
8 mg/2 mg*	5.7 mg/1.4 mg	4.2 mg/0.7 mg
12 mg/3 mg*	8.6 mg/2.1 mg	6.3 mg/1 mg
N/A	11.4 mg/2.9 mg	N/A

*Generic available

Safety/Monitoring

Notable Adverse Effects	Boxed Warnings (not all inclusive)	Drug Interactions
• Headache (13-36%) • Constipation (3-13%) • Nausea (5-20%) • Vomiting (4-9%) • Drowsiness (1-13%) • Sleep disturbances (1-21%) • Depression (1-6%) • Anxiety (1-5%)	• Risk of serious or fatal respiratory depression • Accidental exposure can be fatal (especially in children) • Addiction, abuse, and misuse potential • CNS depression with other CNS depressants • Life-threatening neonatal withdrawal with prolonged use during pregnancy	• Caution with CNS depressants (increased sedation, dizziness, and confusion) • Avoid use with other QT-prolonging agents or patients with an increased risk of arrhythmia

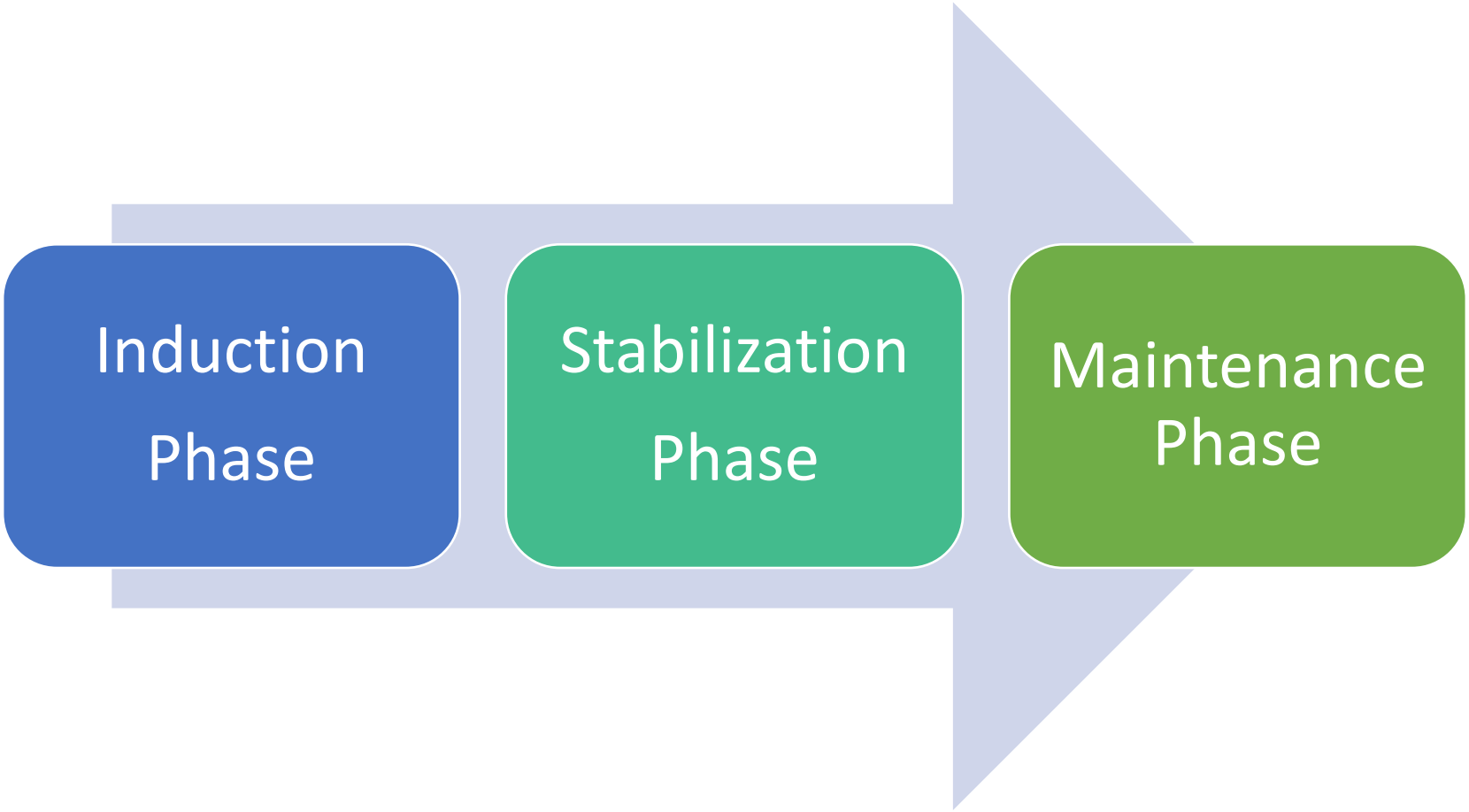
Ling W, Mooney L, Torrington M. *Pain Manag.* 2012;2(4):345-350

Concerns

- Diversion and noncompliance remain troublesome issues among clinicians
  - Efforts to thwart these issues include performing random film/tablet counts as well as random urine drug screens
    - Attempts to hold patients accountable
  - The use of long-acting formulations (implant and extended-release injection for subcutaneous use) are promising solutions to diversion and noncompliance

Ling W, Mooney L, Torrington M. *Pain Manag.* 2012;2(4):345-350

Treatment with Buprenorphine



"Buprenorphine." Substance Abuse and Mental Health Services. https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine Accessed June 28, 2020.

Induction Phase

- Find the lowest dose that that minimizes cravings for opioids while preventing withdrawal symptoms
  - Example:
    - First sublingual dose (2-4 mg) should be given after ~12-24 hours since the last use of opioids to ensure patient is in the early stages of opioid withdrawal
      - May be titrated by 2-4 mg every 2 hours as needed for ongoing withdrawal symptoms
      - Consider a dose of up to 8-16 mg on day 1, 8-16 mg on day 2, and 12-24 mg on day 3

"Buprenorphine." Substance Abuse and Mental Health Services. https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine Accessed June 28, 2020.

Stabilization Phase

- Reached when the patient is:
  - Without withdrawal symptoms
  - Not experiencing adverse effects
  - No longer has uncontrollable cravings for opioids

"Buprenorphine." Substance Abuse and Mental Health Services. https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine Accessed June 28, 2020.

Maintenance Phase

- Minimum dose needed to maintain abstinence is continued
  - Dosing regimens range from three-times per week to once (most common) or twice daily
  - Length of therapy is tailored for each patient
    - May be indefinite

"Buprenorphine." Substance Abuse and Mental Health Services. https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine Accessed June 28, 2020.

Discontinuing Buprenorphine

- No perfect tapering schedule exists
  - Can range from days to months
- Discontinuation should be considered if the patient is:
  - Psychologically and medically stable
  - Able to maintain a drug-free lifestyle

AND

  - No longer feels the drug is necessary to remain abstinent

Methadone

MARSHALL
SCHOOL OF PHARMACY

Methadone Overview

- μ-opioid agonist that prevents opioid intoxication and reduces withdrawal risk
- Used as maintenance therapy for OUD as well as a detoxification agent
- Long elimination half-life (24-36 hours)
- Can only be dispensed through an opioid treatment program (OTP) certified by Substance Abuse and Mental Health Services Administration (SAMHSA)
  - Referred to as methadone maintenance treatment (MMT)

Stotts AL, Dodrill CL, Kosten TR. *Expert Opin Pharmacother*. 2009;10(11):1727-1740.

Rationale For Use

- In setting of MAT, methadone is associated with reductions in:
  - Intravenous drug use
  - Criminal activity
  - HIV transmission
  - Mortality
- Less diversion potential compared to buprenorphine

Dole VP, et al. *N Engl J Med*. 1969;280(25):1372-1375
Gowing, et al. *J Gen Intern Med*. 2006;21(2):193-195
Gronbladh L, Ohlund LS, Gunne LM. *Acta psychiatrica Scanindanvica*. 1990;82(3):223-227
Newman RG, Whitehill WB. *Lancet*. 1979;2(8141):485-488

Safety/Monitoring

Notable Adverse Effects	Boxed Warnings (not all inclusive)	Drug Interactions
• Cardiovascular (ECG changes, QT prolongation, bradycardia, cardiac arrhythmia) • Constipation • Confusion • Dizziness • Euphoria • Somnolence • Decreased testosterone • Weight gain	• Life-threatening QT prolongation and arrhythmias including torsades de pointes • Life-threatening respiratory depression • Neonatal opioid withdrawal syndrome	• Caution with CNS depressants (increased sedation, dizziness, and confusion) • Avoid use with other QT-prolonging agents or patients with an increased risk of arrhythmia • Caution with serotonergic agents (increased risk of serotonin syndrome)

Treatment with Methadone

- Initial dose should be between 10-30 mg and continued for 3 days
- If patient experiencing withdrawal, increase dose by 5-10 mg every three days (max of 20 mg per week)
- Adequate maintenance dose usually ranges from 60-120 mg/day
  - May be higher or lower depending on withdrawal symptoms and side effects
- When switching to buprenorphine, patients should be on a dose ≤40 mg/day

Stotts AL, Dodrill CL, Kosten TR. *Expert Opin Pharmacother*. 2009;10(11):1727-1740.

Methadone Concerns for OUD

- Diversion and/or misuse remain an issue
- Patients are required to attend clinic daily for dosing unless special arrangements are made
- Overdose is possible, particularly in the initial stages of treatment or during dose titrations
- Short- or long-term pain management and surgical needs can be problematic
- Methadone maintenance therapy patients experience prejudice, stereotypes and discrimination

Earnshaw V, Smith L, Copenhaver M. *Int J Ment Health Addict*. 2013;1(1):110-122.

Naltrexone

MARSHALL
SCHOOL OF PHARMACY

Naltrexone Overview

- An opioid-receptor antagonist that blocks the effects of exogenous opioids
  - Essentially a longer acting formulation of naloxone
- Available as daily pill (Revia®) or once monthly intramuscular injection (Vivitrol®)
- Patients must be opioid-free (typically 7-10 days) prior to starting therapy
- Also approved for alcohol dependence

Safety/Monitoring

Formulation	Notable Adverse Effects	Miscellaneous (not all inclusive)
Tablet (IR): Revia® IM Injection (ER): Vivitrol®	• Syncope (13%) • Headache (3 to 25%) • Dizziness (4 to 13%) • Nausea (10 to 33%) • Vomiting (3 to 14%) • Insomnia (3 to 14%) • Increased serum AST/ALT (2-13%) • Injection site reactions (IM formulation)	Monitoring • Obtain liver enzymes at baseline and periodically • Monitor for withdrawal symptoms upon initiation Drug Interactions • Opioid agonists (decreased effects)

Example Dosing Strategy

- Oral (Revia®)
  - After 7-10 opioid free days, initiate 25 mg (one-half tablet). If tolerated, give another 25 mg 1 hour later.
  - Target dose = 50 mg/day or 350 mg/week
    - Alternative dosing strategies include:
      - 50 mg a day during the week and 100 mg (two tablets) on Saturday; or
      - 100 mg every other day; or
      - 150 mg every 3 days
- IM (Vivitrol®)
  - 380 mg every 4 weeks
    - Some physicians will give an initial 25-50 mg oral dose to ensure patient tolerates

Rationale for Use

- No potential for misuse or diversion
- Do not get the negative adverse events associated with opioid-based alternatives
- In clinical trials, has been shown to:
  - Increase opioid abstinent weeks
  - Decrease cravings for opioids
  - Decrease the risk of overdose

Nunes EV, et al. *J Addict Med*. 2015;9(3)238-243.

Naltrexone Concerns in OUD

- Adherence for oral naltrexone is typically poor which limits it effectiveness
- Effective pain management, particularly for acute and/or severe pain, can be difficult to achieve
- Detoxified opioid-dependent patients, after treatment with naltrexone, have an increased risk of overdose in the event of a relapse
- Injection may wear off early in some individuals
- Mortality rate in treatment of OUD substantially higher than for methadone and buprenorphine

Wolfe D, et al. *Lancet*. 2011;377(9776):1468-1470.
Gibson, A. and Degenhardt, L. (2005) *Mortality related to naltrexone in the treatment of opioid dependence: A comparative analysis,* Sydney: National Drug and Alcohol Research Centre.

Pregnancy Considerations

- Opioid dependent pregnant women should receive maintenance therapy during pregnancy and continued during labor and delivery
  - Buprenorphine and methadone are safe and effective treatment options for OUD during pregnancy
    - Neonatal abstinence syndrome (NAS) may still occur in babies whose mothers received these medications
- When buprenorphine is selected, it is generally recommended to be used alone (i.e., without naloxone) due to safety concerns with naloxone
- If a patient becomes pregnant while receiving naltrexone, it should be discontinued if the risk for relapse is low
  - If concerns for relapse exist, consideration for methadone or buprenorphine should be given

National Institute on Drug Abuse, 2017. https://www.drugabuse.gov/publications/treating-opioid-use-disorder-during-pregnancy/treating-opioid-use-disorder-during-pregnancy Accessed June 28, 2020.

Alcohol Use Disorder (AUD)

Chronic/Maintenance Treatment Options

MARSHALL
SCHOOL OF PHARMACY

Goals of Treatment

- Should be individualized depending on patient's preference and may include:
  - Abstinence from alcohol
  - Reduction or moderation of alcohol use
  - Eliminate drinking in high-risk situations (e.g., work or before driving)
  - Prevent long-term complications associated with chronic alcohol use (e.g., cirrhosis of the liver)
  - Improve relationships with friends and family

Treating Alcohol Use Disorder

- Medications are underused in the treatment of AUD
- Medications should be prescribed as part of a comprehensive treatment program that involves counseling and social supports
- FDA-approved medications for the management of alcohol dependence or the prevention of relapse include:
  - Acamprosate (Campral®)
  - Oral naltrexone (Revia®)
  - Extended-release injectable naltrexone (Vivitrol®)
  - Disulfiram (Antabuse®)

Acamprosate (Campral®)

- Exact mechanism is unclear but may act by modulating glutamate
- May reduce “cravings” for alcohol
- Concerns exist regarding adherence
  - Must be taken three times daily
- Excellent safety and tolerability profile
- Preferred in patients with severe hepatic impairment
- Use is contraindicated in patients with severe renal impairment (CrCl ≤ 30 ml/min) and should be used with caution in patients with moderate renal impairment (30 to 50 ml/min).

“Medication for the Treatment of Alcohol Use Disorder.” National Institute on Alcohol Abuse and Alcoholism. https://store.samhsa.gov/system/files/sma15-4907.pdf Accessed June 28, 2020.

Acamprosate Prescribing Information

Dosing	Notable Adverse Effects	Miscellaneous
• 666 mg by mouth three times a day = 1998 mg/day • 333 mg three times a day for patients with impaired renal function	• Diarrhea 17% (most common side effect) • Intestinal cramps • Headache • Insomnia • Muscle weakness • Depression • Anxiety	• There are no known drug interactions • Renal concerns exist

"Medication for the Treatment of Alcohol Use Disorder." National Institute on Alcohol Abuse and Alcoholism. https://store.samhsa.gov/system/files/sma15-4907.pdf Accessed June 28, 2020.

Naltrexone

- Opioid receptor blocker (exact mechanism for alcohol dependence is not well understood)
- May reduce “cravings” for alcohol
  - Also shown to reduce the likelihood of return to drinking and fewer drinking days overall
- Available as daily pill or once monthly long-acting intramuscular injection (Vivitrol®)
- Has been shown to be ineffective in patients who are drinking at treatment initiation
- May lead to reduced effectiveness of opioids taken for analgesia

“Medication for the Treatment of Alcohol Use Disorder.” National Institute on Alcohol Abuse and Alcoholism. https://store.samhsa.gov/system/files/sma15-4907.pdf Accessed June 28, 2020.

Naltrexone Prescribing Information

Dosing	Notable Adverse Effects	Miscellaneous (not all inclusive)
• Oral: 50 mg/day • IM: 380 mg every four weeks	• Syncope (13%) • Headache (3 to 25%) • Dizziness (4 to 13%) • Nausea (10 to 33%) • Vomiting (3 to 14%) • Insomnia (3 to 14%) • Increased serum AST/ALT (2-13%) • Injection site reactions (IM formulation)	Monitoring • Obtain liver enzymes at baseline and periodically • Monitor for withdrawal symptoms upon initiation Drug Interactions • Opioid agonists (decreased effects) and can precipitate opioid withdrawal in opioid dependent patients

"Medication for the Treatment of Alcohol Use Disorder." National Institute on Alcohol Abuse and Alcoholism. https://store.samhsa.gov/system/files/sma15-4907.pdf Accessed June 28, 2020.

Disulfiram (Antabuse®)

- Disrupts the normal metabolism of alcohol by inhibiting the enzyme aldehyde dehydrogenase
  - Results in a buildup of acetaldehyde
- Acts as an alcohol deterrent (negative feedback)
  - If alcohol is consumed while taking disulfiram, a patient will develop symptoms that include nausea/vomiting, flushing of the face and hands, and headache, among others
  - Contraindicated for patients actively using alcohol
- Adherence is critical and usually reserved for patients with considerable motivation for adherence
- Does not reduce cravings for alcohol

"Medication for the Treatment of Alcohol Use Disorder." National Institute on Alcohol Abuse and Alcoholism. https://store.samhsa.gov/system/files/sma15-4907.pdf Accessed June 28, 2020.

Disulfiram Prescribing Information

Dosing*	Notable Adverse Effects	Drug Interactions
• Initial and maintenance dose is 250 mg /day (may range from 125-500 mg/day)	• Acneiform eruption • Headache • Impotence • Fatigue • Garlic-like aftertaste • Mild increases in hepatic enzymes	• Avoid use with alcohol, metronidazole, ritonavir, and sertraline • Caution with rifampin, benzodiazepines, isoniazid, and oral anticoagulants

*Should not be administered until abstaining from alcohol for at least 12 hours

"Medication for the Treatment of Alcohol Use Disorder." National Institute on Alcohol Abuse and Alcoholism. https://store.samhsa.gov/system/files/sma15-4907.pdf Accessed June 28, 2020.

Alternative Agents

MARSHALL
SCHOOL OF PHARMACY

Topiramate

- An anticonvulsant with activity at several cellular targets
- Multiple brand names
- Most commonly used for epilepsy and migraines
- Studies indicate significant reductions in the percent of heavy drinking days, percent of drinking days, “cravings” for alcohol, and abstinence from alcohol

Paparrigopoulos T, et al. *BMC. Psychiatry*. 2011, 11:41.

Topiramate Prescribing Information

Dosing	Notable Adverse Effects	Miscellaneous
200-300 mg/day	• Weight loss (4 to 21%) • Memory dysfunction (3 to 12%) • Dizziness (4 to 25%) • Paresthesia (1 to 51%) • Gastrointestinal issues (2 to 11%) • Nephrolithiasis • Metallic taste	• For CrCl < 70 ml/min, reduce normal dose by 50% • Do not discontinue abruptly due to the possibility of withdrawal seizures; taper dose gradually • Use during pregnancy can cause cleft lip and/or palate

Gabapentin (Neurontin®)

- An anticonvulsant and GABA analogue
- Most commonly used for neuropathy, post-herpetic neuralgia, and fibromyalgia
- Concerns for addiction and dependence exist
- Studies suggest at doses between 900 and 1800 mg/day, use was associated with increased abstinence rates, reductions in heavy drinking days, and “cravings” for alcohol

Mason BJ, et al. *JAMA Intern Med*. 2014;174(1):70-77.

Gabapentin (Neurontin®) Prescribing Information

Dosing	Notable Adverse Effects	Miscellaneous
Initial: 300 mg/day Target: 600 mg three times daily	• Fatigue (23%) • Insomnia (18%) • Headache (14%) • Dizziness (11 to 28%) • Gastrointestinal complaints (1 to 8%) • Weight gain (2 to 3%)	• Renally eliminated: Reduce doses at a CrCl <60 ml/min • Caution for additive CNS effects with CNS depressants

Selection of Pharmacotherapy

- Naltrexone and acamprosate have shown the most promise in clinical trials and should be considered for initial treatment (1B)
  - Patient preferences should be considered such as costs, side effect profile, and ease of administration
    - For patients with hepatic disease (e.g., acute hepatitis or hepatic failure) consider acamprosate while naltrexone should be considered in patients with renal dysfunction
- Disulfiram, topiramate, or gabapentin are second-line agents (2C)
  - Consider if patient has preference to one of these medications or are intolerant to or have not responded to naltrexone and acamprosate

"Guideline Statements and Implementation." American Psychiatric Association. https://psychiatryonline.org/doi/full/10.1176/appi.books.9781615371969.alcohol04 Accessed June 28, 2020.

Duration of Treatment

- There are no specific recommendations for duration of treatment for the previously mentioned drugs
- Decisions regarding duration of treatment should by individualized for each patient based on:
  - Disorder severity
  - History of relapses
  - Clinical response
  - Tolerability

Pregnancy and Postpartum Considerations

- Pharmacotherapies for AUD **have not** been shown in clinical trials to be absolutely safe for pregnant or nursing women
  - These medications should only be used during pregnancy and breastfeeding when, in the judgement of the physician, the benefits outweigh the risks
  - Non-pharmacologic interventions are recommended preferentially
- Pregnant women with AUD should be referred to an addiction specialist or a specialist in managing high-risk pregnancies

"Guideline Statements and Implementation." American Psychiatric Association. https://psychiatryonline.org/doi/full/10.1176/appi.books.9781615371969.alcohol04 Accessed June 28, 2020.

Stimulant Use Disorder

Chronic/Maintenance Treatment Options

MARSHALL
SCHOOL OF PHARMACY

Stimulants

- Includes:
  - Amphetamine-type substances
    - Amphetamine
    - Methamphetamine
    - MDMA (ecstasy)
    - Pseudoephedrine
    - Ephedrine
    - Methylphenidate
  - Cocaine

Treating Stimulant Use Disorder

- There are no Food and Drug Administration (FDA) maintenance medications approved to treat stimulant use disorder
- There is insufficient evidence for or against the use of any pharmacotherapy for the treatment of stimulant use disorder
- Initial treatment should include psychosocial interventions depending on patient preference and provider training/competence (see module 4)
  - May include:
    - Cognitive behavioral therapy
    - Recovery-focused behavioral therapy/motivational incentives

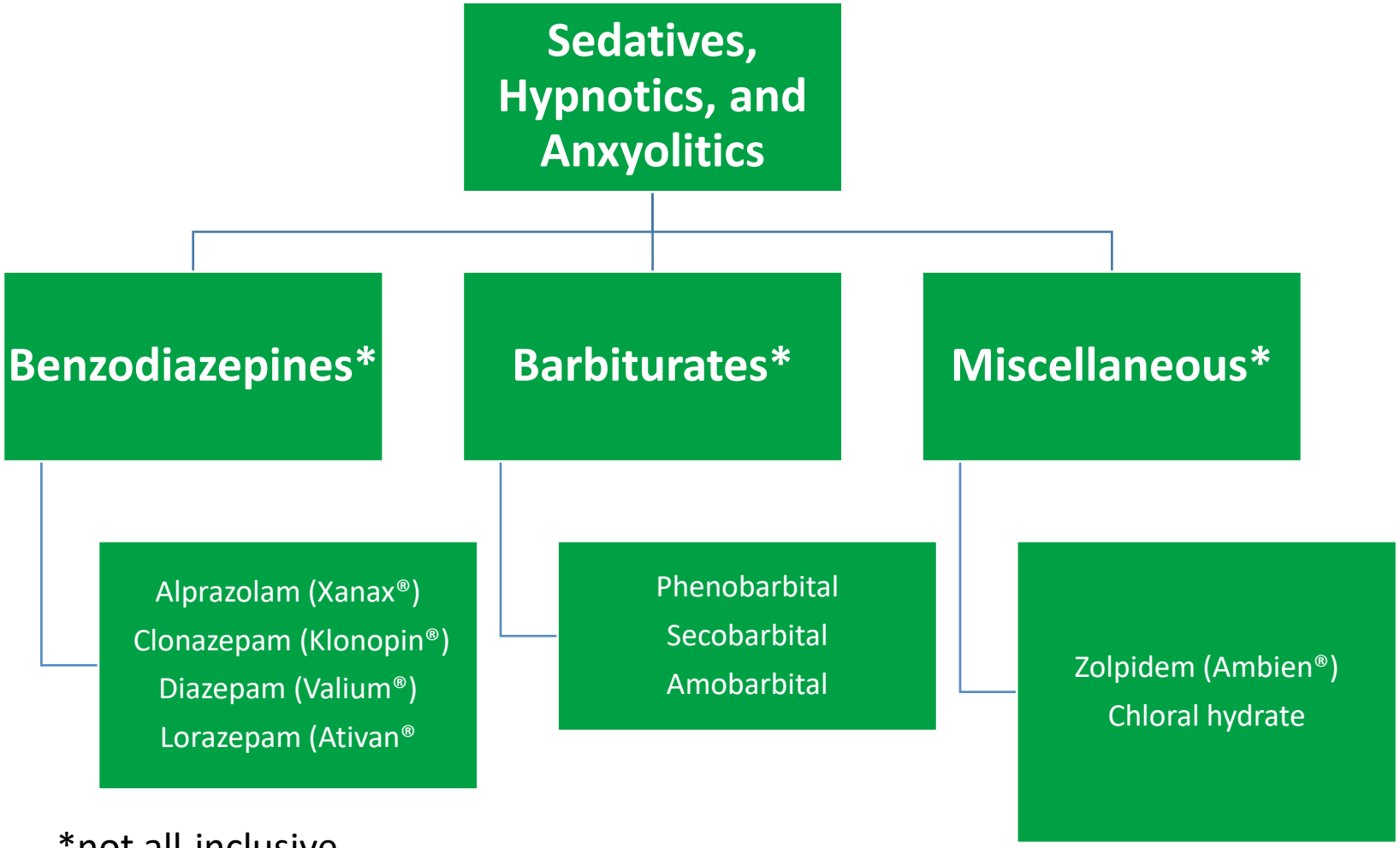
"VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders." Department of Veteran Affairs. https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPGRevised22216.pdf Accessed June 28, 2020.

Sedative, Hypnotic, or Anxiolytic Use Disorder

Chronic/Maintenance Treatment Options

MARSHALL
SCHOOL OF PHARMACY

Sedatives, Hypnotics, and Anxiolytics



*not all-inclusive

Treating Sedative, Hypnotic, or Anxiolytic Use Disorder

- There are no FDA-approved medications for treating patients with a sedative, hypnotic, or anxiolytic use disorder
- The first goal of treatment is detoxification (see Module 7)
  - Patients can be at risk for life-threatening seizures with abrupt discontinuation (particularly with benzodiazepines and barbiturates)
- A comprehensive evaluation (medical, psychological and social) should be performed to identify underlying issues
- Counseling, behavioral therapies, and group programs may be beneficial (see Module 4)

Hallucinogens
Treatment Options

MARSHALL
SCHOOL OF PHARMACY

Hallucinogens

- Includes:
  - Phencyclidine (PCP)
    - Can also act as a stimulant
  - Lysergic acid diethylamide (LSD)
  - Ketamine
  - Peyote (mescalamine)
  - Psilocybin (magic mushrooms)

Hallucinogen Use

- Not typically associated with physical dependence
- There are no FDA-approved medications indicated for the treatment of hallucinogen use
- Behavioral treatments, such as cognitive behavioral therapy, may be beneficial (see Module 4)

Cannabis Use Disorder

Treatment Options

MARSHALL
SCHOOL OF PHARMACY

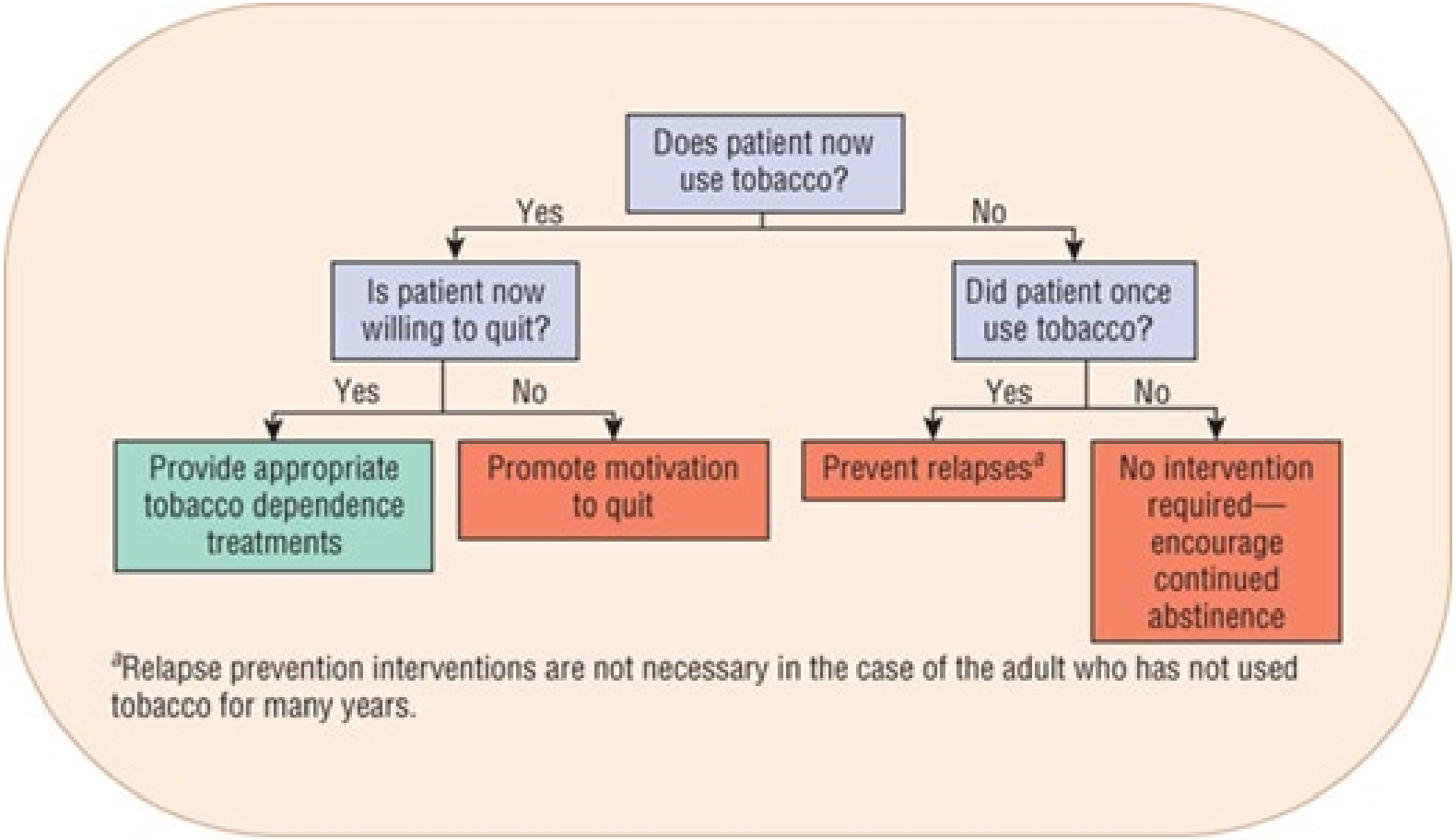
Treating Cannabis Use Disorder

- There are no FDA-approved medications indicated for the treatment of cannabis use disorder
- No medication has been shown to be effective in assisting patients in cutting down or abstaining from marijuana use
- Initial treatment should include psychosocial interventions depending on patient preference and provider training/competence (see Module 4)
  - May include:
    - Cognitive behavioral therapy
    - Recovery-focused behavioral therapy

Tobacco Use Disorder
Maintenance Treatment Options

MARSHALL
SCHOOL OF PHARMACY

Algorithm for Treating Tobacco Dependence



DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Pharmacologic Agents

- First-line
  - Nicotine replacement therapy (NRT)
    - Nicotine gum
    - Nicotine inhaler
    - Nicotine lozenge
    - Nicotine nasal spray
    - Nicotine patch
  - Sustained-release (SR) bupropion (Zyban®)
  - Varenicline (Chantix®)
- Second-line
  - Clonidine (Catapres®)
  - Nortriptyline (Pamelor®)

Nicotine Replacement Therapy

- All forms are equally efficacious
  - Can combine nicotine products
- Patients should be advised to stop smoking completely before initiating
- Nicotine was previously a pregnancy category D
- Initial dose depends on smoking history
- Associated with relatively few side effects
  - Headache, insomnia, tachycardia
  - Often formulation specific
    - Skin irritation → patch
    - Mouth irritation/throat irritation → nasal spray/inhaler
    - Jaw pain → gum

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Form	How supplied	Counseling points
Patch	7, 14, and 21 mg	• For patients who smoke > 10 cigarettes a day, start with the 21 mg/day patch and follow tapering regimen • Those who smoke 10 or less, start with 14 mg/day patch and follow tapering regimen
Gum	2 and 4 mg	• Should be chewed until a “peppery” or flavored taste develops and then parked between the cheek and gum to facilitate buccal absorption • At least 9 pieces of gum daily should be used to increase the chances of quitting
Lozenge	2 and 4 mg	• Patients who smoke within 30 minutes of waking should use 4 mg; otherwise, the 2mg is used • At least 9 lozenges should be used initially to increase chances of quitting
Inhaler	Each cartridge delivers 80 inhalations; each inhalation is 4 mg	• Available by prescription only • Recommended dose = 6-16 cartridges per day
Nasal spray	Bottle contains 100 doses; each dose is 0.5 mg	• Available by prescription only • One to two doses should be used hourly, up to five doses; maximum of 40 doses in 24 hours

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Bupropion SR (Zyban®)

- MOA: Primarily inhibits dopamine and norepinephrine reuptake
- Should be initiated 7 days before quit date and treatment should last for at least 8 weeks
  - Treatment can continue for up to 6 months to increase chances of quitting
- Can be combined with nicotine patch if needed

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Bupropion SR Safety/Monitoring

- Adverse effects: increased risk of seizures, decreased appetite, insomnia, irritability, headache
- Contraindications:
  - Current or past seizure disorder
  - History of monoamine oxidase inhibitor use in last 14 days
  - History of anorexia nervosa or bulimia
- FDA boxed warning for risk of serious neuropsychiatric symptoms
  - Includes depressed mood, agitation, anxiety, hostility, suicidal thoughts, and attempted suicide

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Varenicline (Chantix®)

- MOA: Nicotine receptor partial agonist
- Should be continued for a total of 12 weeks; can be continued for an additional 12 weeks if patient successful at smoking cessation
- Can be combined with bupropion, but combining it with NRT increases adverse events

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Varenicline Safety/Monitoring

- Black box warning for neuropsychiatric symptoms including depression, suicidal ideation, suicide, psychosis, and hostility
- May increase risk of cardiovascular events
- Seizures have been reported with use, generally occurring within the first month of therapy
  - Consider risks versus benefits

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Alternative Agents

MARSHALL
SCHOOL OF PHARMACY

Clonidine (Catapres®)

- MOA: alpha$_2$-adrenergic agonist
- Labeled indication for hypertension
- Forms: solution, transdermal weekly patch, and tablet
- Should be considered for use on a case-by-case basis after first-line treatments have been used or considered
- Duration of treatment in trials for smoking cessation ranged from 3 weeks to 12 months

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Clonidine Monitoring/Safety

- Adverse effects: dry mouth, drowsiness, dizziness, constipation, and sedation
- Monitor blood pressure
- Therapy should not be discontinued abruptly due to the risk of withdrawal symptoms (e.g., rebound hypertension)
  - Taper gradually over 6 to 10 days

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Nortriptyline (Pamelor®)

- MOA: believed to increase serotonin and/or norepinephrine in the central nervous system
- Traditionally utilized for major depressive disorder
- Should be considered for use on a case-by-case basis after first-line treatments have been used or considered
- Duration of treatment in trials for smoking cessation was approximately 12 weeks

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Nortriptyline Safety/Monitoring

- Adverse effects: sedation, dry mouth, blurred vision, urinary retention, light-headedness, and tremor
- Has boxed warning for suicidal thinking/behavior
- Should be used with caution in patients with history of cardiovascular disease

DiPiro, JT, et al. 2017. *Pharmacotherapy.* New York, USA: McGraw-Hill Professional Publishing.

Resource

- To become a certified tobacco treatment specialist, visit flcertificationboard.org/certifications/certified-tobacco-treatment-specialist

QUESTIONS?

fitzpatrick5@marshall.edu

MARSHALL

SCHOOL OF PHARMACY