1) Summary of Guidelines
2) General Treatment Principles
   a) Somatic treatments are but one component of a comprehensive treatment plan that includes therapeutic modalities such as individual and group therapies that reinforce recovery.
   b) Efficacy is directly related to adherence.
3) Somatic Treatments
   a) Pharmacotherapy for Nicotine Dependence
      i) Nicotine replacement therapies (NRTs) – can start before quit date

| Type | Instructions and dosing | Side effects/concerns | Formulary Considerations | Comments |
|---|---|---|---|---|
| **Patch (OTC)** | **Initiation**<br>• **If ≥ 15 cigarettes/day, start with 21 mg patch**<br>• **If < 15 cigarettes/day, start with 14 mg patch**<br>**Taper schedule**<br>• **Taper over 6-12 weeks**<br>• **Can be longer if individual is heavily nicotine dependent**<br><br>No dosing guidelines for pediatric population<br><br>Teen (16-18 yrs) dosing: ?? | Possible skin irritation at patch site<br>Safe in overdose | Therapy lasting up to **14 weeks** per calendar year. Renewable for another 14 weeks by PA | Do not cut in half |
| **Gum (OTC)** | **Doses**<br>• **2 mg – standard**<br>• **4 mg – for heavy smokers (>25 cigarettes a day)**<br>• **Dose every hour**<br>**Instructions**<br>• **Chew one piece of gum very slowly until a slight tingling or distinctive taste is noted.**<br>• **Then the gum should be placed between the cheek and gum until the taste of tingling is almost gone.**<br>• **Repeat over 30 min for each piece of gum.**<br>• **Avoid beverages other than water immediately before or during. pH changes can blunt nicotine absorption.**<br>Taper<br>• Over 6-12 weeks (can be longer)<br>• Reduce dose of gum or lozenge<br>• Increase time between doses | | Therapy lasting up to **14 weeks** per calendar year. Renewable for another 14 weeks by PA | |

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| | No dosing guidelines for pediatric population | | | |
| **Lozenge (OTC)** | **Doses**<br>• **2 mg – standard**<br>• **4 mg – for heavy smokers (>25 cigarettes a day)**<br>• **Dose every hour**<br>**Instructions**<br>• **Must be sucked (vs bitten or chewed).**<br>• **Avoid beverages other than water immediately before or during. pH changes can blunt nicotine absorption.**<br>Taper<br>• Over 6-12 weeks (can be longer)<br>• Reduce dose of gum or lozenge<br>• Increase time between doses<br><br>No dosing guidelines for pediatric population | | Therapy lasting up to **14 weeks** per calendar year. Renewable for another 14 weeks by PA | Caution – lozenges contain phenylalanine – should not be used in individuals with phenylketonuria |
| **Nasal Spray (Prescription)** | Dose<br>• 100 doses per bottle<br>Instructions<br>• Apply spray to each nostril every 1-2 hours<br><br>No dosing guidelines for pediatric population | (Short term) nasal and throat irritation, rhinitis, sneezing, coughing and watery eyes | Not on formulary | Avoid with individuals with other substance use disorders that involve snorting – reinforces the behavior. |
| **Inhaler (Prescription)** | Cartridges of nicotine placed inside hollow cigarette like plastic rods and produce nicotine vapor.<br><br>Instructions<br>• Start between 6 to 16 cartridges daily<br>• Use is as needed for 12 weeks, can be longer<br><br>No dosing guidelines for pediatric population | Throat irritation or coughing | Not on formulary | Facilitates/reinforces hand to mouth behaviors of smoking. |

(1) General note – NRTs are not as effective for women

ii) Medications

| Medication | Mechanism of Action | Dose and Administration | Adverse Effects | Formulary Considerations | Comments |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| **Buproprion SR (Zyban)** | Antidepressant – dopamine and norepinephrine reuptake inhibitor | • **Target dose – 300 mg/day**<br>• **Start at 150 mg daily and increase to 150 mg twice a day after 7-14 days.**<br>• No dosing guidelines for pediatric population | • Headaches, jitteriness, insomnia, and GI symptoms.<br>• Caution in individuals with history of seizures or eating disorder. | On formulary<br>No PA required | Equally effective in men and women |
| **Varenicline (Chantix)** | Selective partial agonist activity at neuronal nicotinic acetylcholine receptors that competitively blocks exogenous nicotine binding | • **Target is 1 mg twice a day**<br>• **Start 1 week prior to quit date**<br>• **Starter pack titration – 0.5 mg daily for 3 days, 0.5 mg twice a day for 4 days, then increase as tolerated to 1 mg twice a day**<br>• Take with food and a full glass of water<br>• No dosing guidelines for pediatric population | • Nausea – most common and dose dependent<br>• Headache and sleep disturbances<br>• Neuropsychiatric symptoms such as irritability, depression, suicidal thoughts | On formulary<br>PA required<br>Must have tried bupropion and NRT | Cessation rate is highest at 44%, but only while taking varenicline. |
| **Nortriptyline** | Secondary amine tricyclic antidepressant. | • **Dose range 75 mg to 150 mg/day**<br>• **Monitor serum levels for dose > 100 mg** | Arrhythmias, hypotension, HTN, tachycardia, MI, heart block, stroke, confusion, hallucination, insomnia, tremors, ataxia, dry mouth, blurred vision, skin rash | On formulary | Found to be effective in Cochrane review by Hughes et al (2007) |

iii) Combination Strategies

| | |
|---|---|
| Nicotine Patch plus | Gum |
| | Lozenge |
| | Inhaler |
| | Spray |
| Bupropion SR plus | Patch |
| | Gum |
| | Lozenge |
| Varenicline Plus | Gum |

| | |
|---|---|
| | Lozenge |
| | Inhaler |
| | Spray |

b) Pharmacotherapy for Alcohol-Related Disorders

i) Notes

(1) Acamprosate can be used to improve abstinence rates. It should be continued if the person starts drinking, since there is evidence that acamprosate reduces alcohol consumption, at least for a period to assess whether there is overall patient benefit attributable to acamprosate.

(2) Naltrexone can be used to reduce risk of lapse becoming a relapse, but there is less evidence to support its use in maintaining abstinence. Naltrexone may therefore be a better choice if someone is 'sampling' alcohol regularly but wishes to be abstinent.

(3) For acamprosate and naltrexone there is no consistent evidence to suggest which types of patient will respond, and relapse prevention medication should be offered to/considered for everyone who is alcohol dependent wanting to be abstinent

(4) Disulfiram is effective if intake is witnessed. Disulfiram can be offered as a treatment option for patients who intend to maintain abstinence, and for whom there are no contraindications.

(5) SSRIs should be avoided, or used with caution in type 2 alcoholism.

(a) Type 2 alcoholics – early onset, positive family history, impulsive/antisocial personality traits

| Medication | Mechanism of Action | Dose & Administration | Adverse Effects | Formulary Considerations | Comments |
|---|---|---|---|---|---|
| **Naltrexone (ReVia)**<br><br>**Naltrexone long acting injection (Vivitrol)** | μ opioid antagonist which may block the pleasurable effects of alcohol mediated through the release of endogenous opioids. | **Oral: Start at 25mg/day for 7 days to improve tolerability. Target dose 50mg/day.**<br><br>**Injection: 380mg IM monthly**<br><br>Patients must be opioid free for 7-10 days before starting naltrexone.<br><br>No dosing guidelines for pediatric population | Nausea, headache, anxiety, sedation. Warnings of hepatotoxic effects are derived from studies using dosages up to 350mg/day for obesity and dementia. No reports of hepatotoxicity at recommended daily dose of 50mg. Liver enzymes in alcoholic patients tend to improve with naltrexone likely due to reduced alcohol consumption. | Oral formulation:<br>On formulary<br>No PA<br><br>IM formulation:<br>PA required, cost significant | One of the best studied and underutilized treatments for alcohol dependence. Studies favor a reduction in heavy drinking over complete abstinence.<br><br>Contraindicated in patients who are opioid dependent or receiving chronic treatment with opioids for pain or addiction treatment.<br><br>Long acting injection may improve adherence If expect adherence problem from the outset, may start with IM injection.<br><br>Some studies demonstrating efficacy when combined with acamprosate. |

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| **Acamprosate (Campral)** | Synthetic analogue of endogenous amino acid homotaurine. Acts by attenuating the excessive glutamatergic neurotransmission which ensues after chronic alcohol intake. | **Starting and target dose is 666mg TID (2 x 333mg tablets TID)**<br><br>$Cl_{Cr}$ 30-50ml/min initial dose 333mg TID<br><br>$Cl_{Cr}$ <30ml/min contraindicated<br><br>No dosing guidelines for pediatric population | Diarrhea | On formulary<br>Include diagnosis of alcohol abuse or alcohol dependence in prescription | High pill burden with TID dosing.<br><br>Comparative studies show inferiority to naltrexone.<br><br>Primarily renally cleared therefore safe in liver disease but dose needs to be adjusted in renal impairment.<br><br>Some studies demonstrating efficacy when combined with naltrexone. |
| **Topiramate (Topamax)** | Attenuates alcohol induced mesolimbic dopamine release by enhancing GABAergic neurotransmission at GABA-A receptors and antagonizing glutamatergic neurotransmission at non-NMDA receptors | **Start at 25mg QHS and titrate up to 300mg daily in divided doses.**<br><br>No dosing guidelines in pediatric population for alcohol dependence. With dosing for epilepsy, can treat 16+ with adult dosing. | Paresthesias, taste perversion, anorexia, impaired concentration, secondary angle-closure glaucoma, acute myopia, uncommon but serious metabolic acidosis, risk of Steven's Johnson, hepatotoxicity, pancreatitis | On formulary<br>Include diagnosis of alcohol abuse or alcohol dependence in prescription | Limited data and clinical experience in alcohol dependence.<br><br>Side effects common and dose related<br><br>RCTs have shown to improve percentage of heavy drinking days, harmful drinking consequences, physical health, and quality of life. |
| **Gabapentin (Neurontin)** | Binds to alpha-2-delta subunit of voltage sensitive calcium channel closing presynaptic channels | **Start at 300 mg HS, then 300 mg TID on day 2; add 300 mg on days 3, 4, and 5 to reach 600 mg TID.** Can be titrated to a maximum of 1200 mg TID, if needed. Go slower if toleration problems occur. | Sedation, dizziness, ataxia, fatigue, tremor, vomiting, dyspepsia, diarrhea, dry mouth, constipation, weight gain. Renally excreted. | On formulary<br>Include diagnosis of alcohol abuse or alcohol dependence in prescription | Limited, but growing data. |
| **Disulfiram (Antabuse)** | Irreversibly inhibits acetaldehyde dehydrogenase which results in accumulation of acetaldehyde when alcohol is consumed | **250mg/day at least 12hr after last drink. Maximum dose 500mg/day. Should be dosed in the morning when the desire to abstain** | Idiosyncratic dose-independent hepatotoxicity, optic neuritis, neuropathies, metallic aftertaste. Rarely may exacerbate psychosis. | On formulary<br>No PA | An aversive agent intended to dissuade patients from consuming alcohol due to the potential effects of acetaldehyde accumulation.<br><br>Acetaldehyde accumulation produces medical risks, therefore do not be use in patients |

| | | | | | |
|---|---|---|---|---|---|
| | producing flushing, tachycardia, shortness of breadth, headache, and nausea. | **from drinking is greatest.** | | | unable to abstain or understand severity of alcohol-disulfiram reaction.<br><br>Limited effectiveness in clinical trials possibly linked to poor adherence. Supervised administration is best.<br><br>Patients need to avoid all exposure to alcohol including sauces, aftershave lotion, mouthwashes, and cough medicines. Effects can last up to 14 days. |

ii) Treating intoxication
iii) Treating withdrawal
  (1) Benzodiazepines
  (2) Adrenergic agonists and antagonists
  (3) Anticonvulsants
  (4) Antipsychotics

c) Pharmacotherapy for Marijuana-Related Disorders
  i) None current with clear-cut efficacy
  ii) At present there is no clear evidence base for pharmacological treatment of cannabis withdrawal and no pharmacological treatment can be recommended.
  iii) We do not recommend the use of antidepressant drugs for the treatment of cannabis withdrawal.
d) Pharmacotherapy for Cocaine-Related Disorders
  i) None current with clear-cut efficacy
  ii) There is no convincing evidence supporting the use of pharmacological treatment for amphetamine and cocaine abuse and dependence. Psychosocial interventions such as CBT and contingency management remain the mainstay of treatment .
  iii) The use of dopamine agonists, antidepressants or anticonvulsants is not recommended solely for cocaine abuse or dependence.
  iv) Disulfiram is not yet an established treatment for cocaine use, but clinicians should be alert to further studies as the current small evidence base is of interest.
  v) There is no clear evidence to support substitute prescribing of dexamphetamine for treatment of cocaine or amphetamine dependence, but definitive studies are warranted and clinicians should be alert to further studies.
e) Pharmacotherapy for Methamphetamine-Related Disorders
  i) None current with clear-cut efficacy
  ii) There is no convincing evidence supporting the use of pharmacological treatment for amphetamine and cocaine abuse and dependence. Psychosocial interventions such as CBT and contingency management remain the mainstay of treatment .
  iii) The use of dopamine agonists, antidepressants or anticonvulsants is not recommended solely for cocaine abuse or dependence.

iv) Disulfiram is not yet an established treatment for cocaine use, but clinicians should be alert to further studies as the current small evidence base is of interest.

v) There is no clear evidence to support substitute prescribing of dexamphetamine for treatment of cocaine or amphetamine dependence, but definitive studies are warranted and clinicians should be alert to further studies.

f) Pharmacotherapy for Opioid-Related Disorders

i) Treating dependence and abuse

| Medication | Mechanism of Action | Dose & Administration | Adverse Effects | Formulary Considerations | Comments |
|---|---|---|---|---|---|
| **Methadone** | Full μ opioid agonist with a half-life of 24 hours. | No single dose is optimal for all patients.<br>Some require ≤ 40 mg/day<br>Others can require > 100 mg/day<br>Heroin addicts with psychiatric co-morbidities generally require higher doses<br><br>No dosing guidelines for pediatric population | Constipation, increased sweating, sexual difficulties, some cognitive effects.<br>Overdose produces respiratory depression and death.<br>Caution with other medications that affect QTc as methadone can increase QTc. | Special dispensation | Available only through specially licensed opioid treatment programs.<br>Primary goals:<br>• Achieve stable maintenance dose<br>• Facilitate patient engagement in a comprehensive program<br>Can be divert for abuse |
| **Buprenorphine -Naloxone (Suboxone)** | Mixed opiod agonist-antagonist. Partial agonist effect on μ receptor and an antagonist effect on κ receptor.<br>Mixed with naloxone to prevent diversion. | Dosing is sublingual (formulation is a film)<br>Initiation via induction – individual must be in moderate withdrawal from all opioids.<br>Range falls between 8-2 and 32-8 mg/day<br><br>No dosing guidelines for pediatric population | Sedation, headache, insomnia, sweating, constipation, nausea.<br>Overdose does NOT produce significant respiratory depression | PA required<br>-If Medi-Cal – must fill out TAR for state approval<br>-If other insurance – fill out HPSM related PA<br>Special license required | Caution when prescribing with benzodiazepines – fatalities have been reported, mainly when both are taken parenterally.<br>Must have DEA waiver to prescribe for opioid dependence.<br>Combination with naloxone reduces diversion. |
| **Naltrexone (ReVia)** | μ opioid antagonist which may block the pleasurable effects of alcohol mediated through the release of endogenous opioids. | Oral: Start at 25mg/day for 7 days to improve tolerability. Target dose 50mg/day.<br>Can be given three times a week: 100 mg on Mon and Wed, 150 mg on Fri.<br><br>Patients must be opioid free for 7-10 days before | Nausea, headache, anxiety, sedation. Warnings of hepatotoxic effects are derived from studies using dosages up to 350mg/day for obesity and dementia. No reports of hepatotoxicity at recommended daily dose of 50mg. Liver enzymes in alcoholic patients tend to improve with naltrexone likely due to reduced alcohol | Oral formulation:<br>On formulary<br>No PA | Efficacy for opioid dependence is mixed.<br>Positive results in inpatient studies.<br>Higher dropout rates with outpatient srtudies likely related in part to the absence of a psychoactive effect.<br>Most effective in individuals who are motivated. |

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| | | starting naltrexone.<br><br>No dosing guidelines for pediatric population | consumption. | | |

ii) Treating intoxication
iii) Treating withdrawal

4) Behavioral Therapies (Based on NIDA Principles of Drug Addiction Treatment, 2nd Ed)
   a) Cognitive-Behavioral Therapy
      i) Efficacy for Alcohol, Marijuana, Cocaine, Methamphetamine, Nicotine
   b) Contingency Management Interventions/Motivational Incentives
      i) Efficacy for Alcohol, Stimulants, Opioids, Marijuana, Nicotine
   c) Motivational Enhancement Therapy
      i) Efficacy for Alcohol, Marijuana, Nicotine
   d) The Matrix Model
      i) Efficacy for Stimulants
   e) 12-Step Facilitation Therapy
      i) Efficacy for Alcohol, Stimulants, Opiates

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