Appendices for Substance Use Disorders

Adapted from APA Guidelines of Treatment of Patients with Substance Use Disorder
http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/substanceuse.pdf

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Appendix A
Medical Detoxification Protocols for Alcohol, Benzodiazepines, Barbiturates, Opioids

Diazepam loading protocol for alcohol withdrawal*:
** For CIWA score of =>10. Loading protocol will not prevent seizures in patients taking large doses of benzodiazepines or barbiturates in addition to alcohol.*

Basic protocol:	▪ Diazepam 20 mg PO q 1-2 H until symptoms abate (CIWA well below 10) *(Some inpatients require several hundred milligrams)* ▪ Observe for 1-2 hours after last dose ▪ Take-home medication is generally not required; if take-home diazepam is necessary, give no more than 2-3 10 mg tablets ▪ Thiamine 100 mg IM then 100 mg PO for 3 days
If history of withdrawal seizures:	▪ Diazepam 20 mg q1H for a **minimum** of three doses
If can't tolerate oral diazepam:	▪ Diazepam 2.5 mg IV/min - maximum 10-20 mg q1H; or lorazepam SL
If severe liver disease, severe asthma, respiratory failure, elderly, debilitated, low serum albumin:	▪ Lorazepam SL, PO 1-2 mg q2-4H PRN
If hallucinations:	▪ Haloperidol 2-5 mg IM/PO q1-4 H - max. 5/day ** Haldol lowers seizure threshold. Use with caution in 1st 3 days; give 3 doses of diazepam 20 mg as seizure prophylaxis.*
Admit to hospital if:	▪ Still in withdrawal after 80 mg or more of diazepam ▪ Delirium tremens, recurrent arrhythmias or multiple seizures ▪ Medically ill

Diazepam tapering for benzodiazepine withdrawal*+:

**Patients using benzodiazepines in a dose equivalent to diazepam => 50 mg/day risk seizures, psychosis, or delirium if their dose is stopped abruptly. The risk is greater with use of benzodiazepines with a short half life.*

+ Benzodiazepines with a long half-life (such as diazepam) can have a substantially prolonged duration of action in patients who are elderly or debilitated, or who have severe liver disease or low serum albumin. Use substantially lower initial doses or use shorter-acting agents such as lorazepam. Caution is also required when using benzodiazepines in patients who have severe asthma, COPD or respiratory failure.

Outpatient protocol: *For patients taking <50 mg/day diazepam equivalent* *Inpatient preferable for patients taking 50-100 mg/day but outpatient possible if:* *Not physically dependent on other drugs* *Medically, psychiatrically stable* *Unlikely to access benzodiazepines from other sources*	Convert to equivalent dose of diazepam (maximum 80-100 mg/day) in divided doses Taper by 5 mg per week (or 5 mg per 3-4 days at doses above 50 mg) Adjust initial dose and rate of taper according to symptoms May need to slow taper at doses below 20 mg Dispense daily, bi-weekly or weekly depending on dose and patient reliability
If <u>typical</u> daily use over past 2 months is equivalent to diazepam 100 mg or more:	Consider hospitalization & addiction medicine consult Start taper at one-half to two-thirds the equivalent diazepam dose Administer tid-qid If significant withdrawal on this dose, increase next day's total dose by 10-30 mg May give PRN diazepam 10-15 mg 1-3 times per day for acute withdrawal* Hold diazepam & decrease daily dose if drowsiness or sedation Taper by 5-15 mg per day as inpatient (taper by no more than 10% of daily dose; slow taper as dose decreases) May switch to outpatient protocol at doses less than 50 mg Adjust initial dose and rate of taper according to symptoms *cute withdrawal consists of severe anxiety & insomnia, and signs of autonomic hyperactivity (tremor, sweating, tachycardia, and hypertension).*
For patients on alprazolam or triazolam	Taper with alprazolam and triazolam, or equivalent dose of clonazepam. *(Diazepam may not be effective for alprazolam or triazolam withdrawal; equivalent diazepam dose is uncertain).*

Benzodiazepine equivalence table *Note: Equivalences are approximate. Careful monitoring required to avoid oversedation, especially in the elderly.*

Drug	**Equivalence to 5 mg diazepam (mg)**
Alprazolam (Xanax)*	0.5
Bromazepam (lectopam)	3
Chlordiazepoxide (Librium)	10-25
Clonazepam (Rivotril)	0.5
Clorazepate (Tranxene)	7.5
Flurazepam (Dalmane)	15
Lorazepam (Ativan)	0.5 - 1
Nitrazepam (Mogadon)	5-10
Oxazepam (Serax)	15
Temazepam (Restoril)	10-15
Triazolam (Halcion)*	0.25

* *Equivalency uncertain.*

Adapted from: Kalvik A., Isaac P., Janecek E. Benzodiazepines: Treatment of anxiety, insomnia and alcohol withdrawal. Pharmacy connection Sept/ Oct 1995 20-32.

Phenobarbital loading protocol for barbiturate and sedative-hypnotic withdrawal

Patients using barbiturates or sedative-hypnotics in a dose equivalent to phenobarbital =>150 mg/day risk seizures, psychosis, or delirium if their dose is stopped abruptly.

Phenobarb loading (daily dose equivalent to phenobarb 150 mg or greater for at least one month)	Admit Order stat blood barbiturate level Begin loading when barbiturate level below toxic value or patient in withdrawal (tremor, tachycardia, sweating etc.) Phenobarb 120 mg PO/hour until intoxicated (3 or more of: emotional lability, nystagmus, slurred speech, ataxia, drowsiness) Discharge when no longer drowsy or safe home environment
If patient can't take phenobarbital orally or if medically urgent:	Continuous i.v. method: IV phenobarb 2.4 mg/kg/hour (10 mg/mL Normal saline) If urgent, may initiate with 1.75 mg/kg i.v. push over 5 minutes
Outpatient Tapering (If patient is stable and dose less than 150 mg phenobarb equivalent)	Convert to equivalent phenobarbital dose Taper by 30 mg phenobarb q1-3 days Adjust initial dose and rate of taper as needed

Barbiturate & sedative-hypnotic equivalence table

Adapted from: Smith D., Wesson D. Pharmacologic therapies for sedative-hypnotic addiction. American Society of Addiction Medicine, 1994.

Note: Equivalences are approximate. Careful monitoring is required to avoid oversedation, especially in the elderly.

Drug	**Equivalence to 30 mg phenobarbital (mg)**
Amobarbital	100
Butabarbital	100
Butalbital	100
Pentobarbital	100
Secobarbital	100
Chloral hydrate	500
Ethchlorvynol (Placidyl)	500
Meprobamate (Equagesic)	1200

Clonidine Protocol for Opioid Withdrawal

Outpatient:
Clonidine 0.1 mg PO qid; warn about symptoms of postural hypotension and drowsiness
May increase to 0.2 mg qid after first day (but risk of hypotension increases)
Continue qid for 3-5 days then PRN for 3-5 more days
Additional treatment options: naproxyn or other NSAID; acetaminophen; loperamide; dimenhydrinate; diazepam 10 mg HS

Inpatient:
Check BP prior to each dose
Hold if BP < 90/60 or marked postural drop
May increase to 0.3 mg qid

Appendix B
Addiction Research Foundation
Clinical Institute Withdrawal Assessment for Alcohol (CIWA-A)

NAUSEA AND VOMITING - Ask 'Do you feel sick to your stomach? Have you vomited?' Observation. 0 no nausea and no vomiting 1 2 3 4 intermittent nausea with dry heaves 5 6 7 constant nausea, frequent dry heaves and vomiting	AGITATION - Observation. 0 normal activity 1 somewhat more than normal activity 2 3 4 moderately fidgety and restless 5 6 7 paces back and forth during most of the interview, or constantly thrashes about
TREMOR - Arms extended and fingers spread apart. Observation. 0 no tremor 1 not visible, but can be felt fingertip to fingertip 2 3 4 moderate, with patient's arms extended 5 6 7 severe, even with arms not extended	TACTILE DISTURBANCES - Ask 'Have you any itching, pins and needles sensations, any burning, any numbness or do you feel bugs crawling on your skin?' Observation. 0 none 1 very mild itching, pins and needles, burning or numbness 2 mild itching, pins and needles, burning or numbness 3 moderate itching, pins and needles, burning or numbness 4 moderately severe hallucinations 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations
PAROXYSMAL SWEATS - Observation. 0 no sweat visible 1 barely perceptible sweating, palms moist 2 3 4 beads of sweat obvious on forehead 5 6 7 drenching sweats	AUDITORY DISTURBANCES - Ask 'Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?' Observation. 0 not present 1 very mild harshness or ability to frighten 2 mild harshness or ability to frighten 3 moderate harshness or ability to frighten 4 moderately severe hallucinations 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations
ANXIETY - Ask 'Do you feel nervous?' Observation.	VISUAL DISTURBANCES - Ask 'Does the light appear to be too bright? Is its color different? Does it hurt your

0 no anxiety, at ease 1 mildly anxious 2 3 4 moderately anxious, or guarded, so anxiety is inferred 5 6 7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions	eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?' Observation. 0 not present 1 very mild sensitivity 2 mild sensitivity 3 moderate sensitivity 4 moderately severe sensitivity 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations
HEADACHE, FULLNESS IN HEAD - Ask 'Does your head feel different? Does it feel like there is a band around your head?' Do not rate for dizziness or light-headedness. Otherwise, rate severity. 0 not present 1 very mild 2 mild 3 moderate 4 moderately severe 5 severe 6 very severe 7 extremely severe	ORIENTATION AND CLOUDING OF SENSORIUM - Ask 'What day is this? Where are you? Who am I? 0 oriented and can do serial additions 1 cannot do serial additions or is uncertain about date 2 disoriented for date by no more than 2 calendar days 3 disoriented for date by more than 2 calendar days 4 disoriented for place and/or person

Total CIWA-A Score _____

Appendix B- Substance Use Disorders:
Resources in Ontario

Addiction Research Foundation Division of the Centre for Addiction and Mental Health - 595-6000; http://www.camh.net/ - variety of assessment and treatment programs.

Drug and Alcohol Registry of Treatment (DART) - 800-565-8603. Clearinghouse providing information for health professionals about treatment options in Ontario.

Addiction Clinical Consultation Service (ACCS) - 800-720-ACCS (2227). Puts physicians and other care-providers in touch with a consultant who will provide telephone advice regarding management of alcohol and other drug problems, including management of medical complications and withdrawal.

Metro Addiction Assessment Referral Service (MAARS) - 416-481-1446 - helps patients from the Greater Toronto Area find the community resources they need to deal with their substance abuse problems; provides information about treatment options, telephone screening, comprehensive assessment and referrals.

Canadian Centre on Substance Abuse: http://www.ccsa.ca/. Clearinghouse for literature and resources on addictions

Physician Health Program 1 800 268- 7215 x 2972. Confidential service provided by the Ontario Medical Association. Offers support, referral and advocacy for physicians with alcohol and drug problems.

Appendix C
Pharmacotherapy for substance dependence

1. Naltrexone (ReVia)

Action:

- Alcohol consumption causes endogenous endorphin release. Naltrexone, a competitive opioid antagonist, blocks the action of endorphins, thus reducing the pleasurable and reinforcing effects of alcohol.
- Controlled trials have shown that naltrexone is moderately effective in reducing craving for alcohol and the frequency and intensity of alcohol binges.

Indication:

- Treatment of alcohol dependence, in conjunction with supportive counseling and a treatment program.

Dose and duration of treatment

- 25 mg for three days, then 50 mg per day (as a single daily dose). If 50 mg is ineffective, the dose may be increased to 100 mg; 150 mg per day is the maximum dose.
- If effective, treatment should be continued for three to six months, or longer if no adverse effects and patient continues to derive benefit.

Precautions and contraindications

- Will trigger severe opioid withdrawal if patient is physically dependent on opioids. Opioids should be discontinued for 10 days before starting naltrexone.
- Discontinue naltrexone 3 days prior to elective surgery.
- If urgent need for anesthesia or analgesia, use non-opioid analgesics and anesthetics, and consult with anesthetist.
- Patient should be treated for alcohol withdrawal during or prior to initiation of naltrexone (patients will find it hard to reduce drinking if they are having ongoing withdrawal symptoms.)

Hepatotoxicity

- High doses (300 mg/day) can cause reversible elevations in transaminases
- Check bilirubin and liver transaminases at baseline and two weeks, then monthly.
- Don't prescribe if high bilirubin or transaminases > 3 X normal.
- Discontinue prescribing if AST, ALT rises three times above baseline.
- Its safety in cirrhosis is not known. Use only if other treatment options have failed; monitor closely.

2. Disulfiram (Antabuse)

Action:

- Covalently binds to acetaldehyde dehydrogenase, causing a toxic buildup of acetaldehyde if alcohol is consumed.

Indications:

- Treatment of alcohol dependence. Probably most effective in older, socially stable individuals who take disulfiram under the daily supervision of a spouse or pharmacist.

Dose:

- 125–250 mg HS

Duration of action:

- 7 days (range 2–10 days).

Duration of treatment:

- If effective, continue for three to six months, or longer if no adverse effects and patient continues to derive benefit.

Warning for patients

- *The patient should be warned that consumption of alcohol within seven days of a dose of disulfiram could cause a potentially fatal reaction.*
- If the patient discontinues disulfiram and relapses to alcohol: Stop drinking and wait at least 48 hours before resuming disulfiram.
- Avoid alcohol-containing cough medicines and food.

Monitoring

- Liver transaminases at baseline, two weeks, then monthly for three months.

Adverse effects with drinking

- Reaction is dependent on dose of alcohol consumed.
    - **Common:** Flushed face, vomiting, headache, chest pain, palpitations.
    - **Serious:** Seizures, hypotension, vagally induced dysrhythmias

Adverse effects without drinking

- Fatigue (often resolves in a few weeks)
- Garlicky taste in mouth
- Acne
- Toxic hepatitis
- Peripheral neuropathy
- Erectile dysfunction

- Depression
- Psychosis

Precautions and contraindications

Cardiovascular:

- Patients with coronary artery disease or congestive heart failure and patients on antihypertensive agents are less able to tolerate disulfiram-induced hypotension.
- Contraindicated in unstable angina, recent myocardial infarction.
- Use with caution in patients with stable coronary artery disease, hypertension and congestive heart failure.

Psychiatric:

- Contraindicated in schizophrenia and other psychotic states; can exacerbate psychosis.
- May exacerbate a primary mood disorder, although alcohol-induced depression often improves with disulfiram-facilitated abstinence.

Reproductive:

- Contraindicated in pregnancy; may cause congenital defects.

GI:

- Contraindicated in severe cirrhosis of the liver; can cause toxic hepatitis.

3. Acamprosate

Chronic alcohol use causes an up-regulation in excitatory neurotransmitters such as glutamate, which in turn causes alcohol withdrawal and craving. Acamprosate (not yet available in Canada) antagonizes glutamate, thus reducing withdrawal symptoms and craving. Controlled trials have found that acamprosate increases abstinence rates in alcohol dependent patients [Sass, 1996 #2].

4. Ondansetron

Ondansetron, a selective 5-HT3 receptor antagonist, was found in one controlled trial to reduce drinking in "early onset" alcoholics (patients who become dependent on alcohol before the age of 25). Ondansetron is presumed to act by attenuating dopamine release in the mesolimbic reward center. The effective dose in this trial was 4 ug/kg BID. Further research is needed on this medication, and it is not yet indicated for use in alcohol dependence.

5. Methadone

Rationale for methadone treatment in opioid dependence:
In the appropriate dose, methadone relieves drug cravings and withdrawal symptoms for 24 hours, without inducing sedation or euphoria. Due to cross-tolerance, patients on methadone experience less euphoria with opioid use, diminishing the reinforcing effects of illicit opioids. Methadone retains patients in treatment; patients must attend the clinic if they are to receive the medication. Methadone programs provide counseling and monitoring of drug use. Treatment is often long-term (months or years).

Effectiveness
A number of controlled trials and large cohort studies have demonstrated that methadone is a highly effective treatment for opioid dependence.

Pre and post results from two cohort studies of methadone treatment for heroin dependence:

	Pre	**Post**
Socially productive	36%	76%
Arrest rate/100 person years	201	1.2
Injection drug use	81%	29%
Mortality rate		Decreased by factor of 11

Pharmacology

Route:
- Oral. Mixed with orange juice to prevent intravenous use.

Half-life:
- Average 24 hours (range 16–55 hours).

Absorption:
- Fully absorbed within 30 minutes.

Peak serum level:
- Two to four hours

Duration of action:
- Up to 24 hours for relief of withdrawal symptoms; 6-8 hours for analgesia.

Side Effects:

- Similar to other opioids. Initial titration carries greater risk of overdose than other oral opioids because its long half-life leads to bioaccumulation.

Indications

- Physical and psychological dependence on high doses of potent opioids (e.g., heroin, hydromorphone)
- Long history of opioid dependence (usually one or more years)
- Failed at other forms of treatment, or unwilling to try, or unlikely to succeed given chronicity of use or other factors

Components of methadone programs

- Daily methadone dispensing supervised by a pharmacist
- Take-home doses ("carries") if doing well (to a maximum of 6 carries/week in Ontario; this varies with jurisdiction).
- Regular supervised urine drug screens
- Individual or group counseling