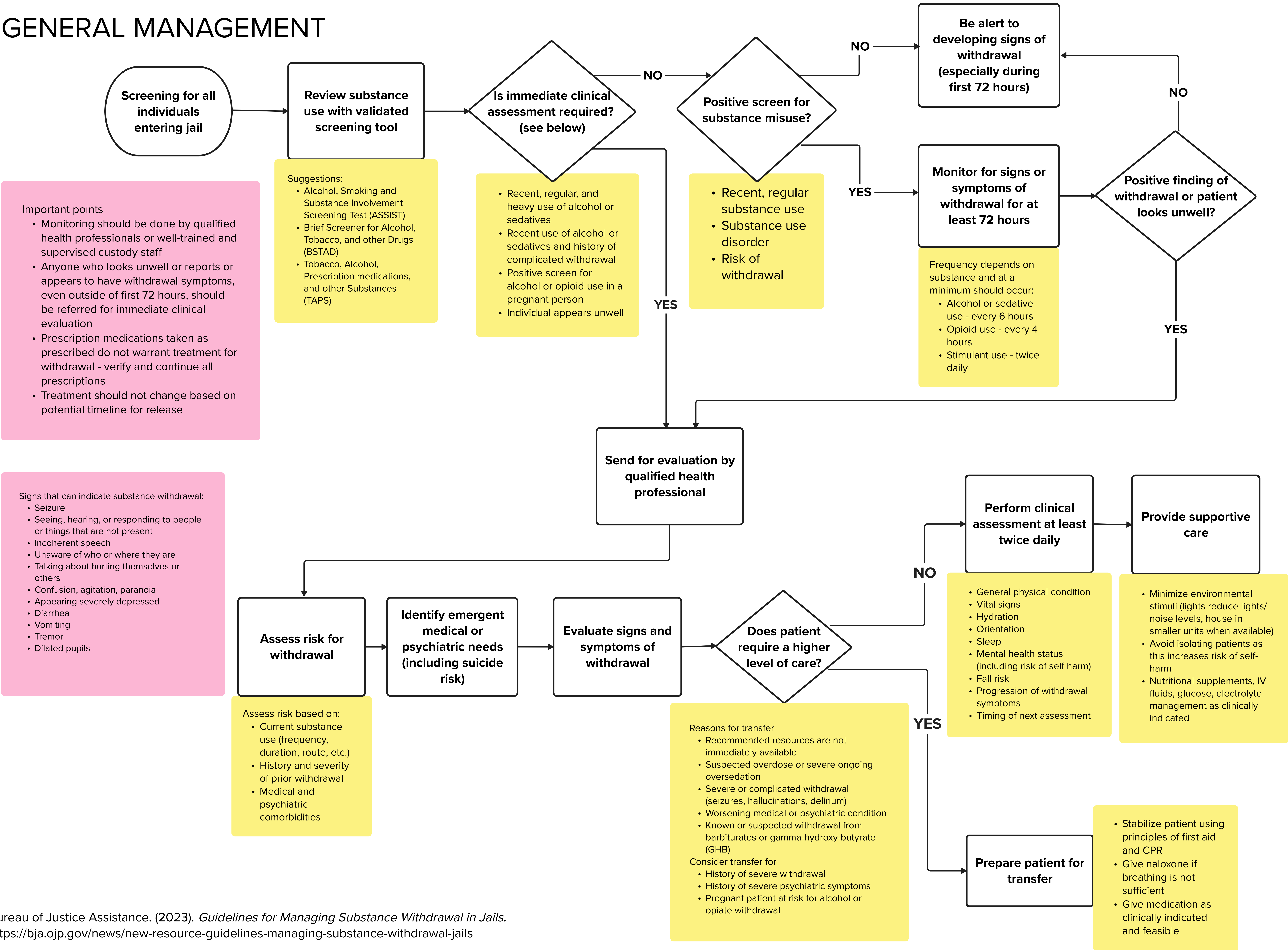
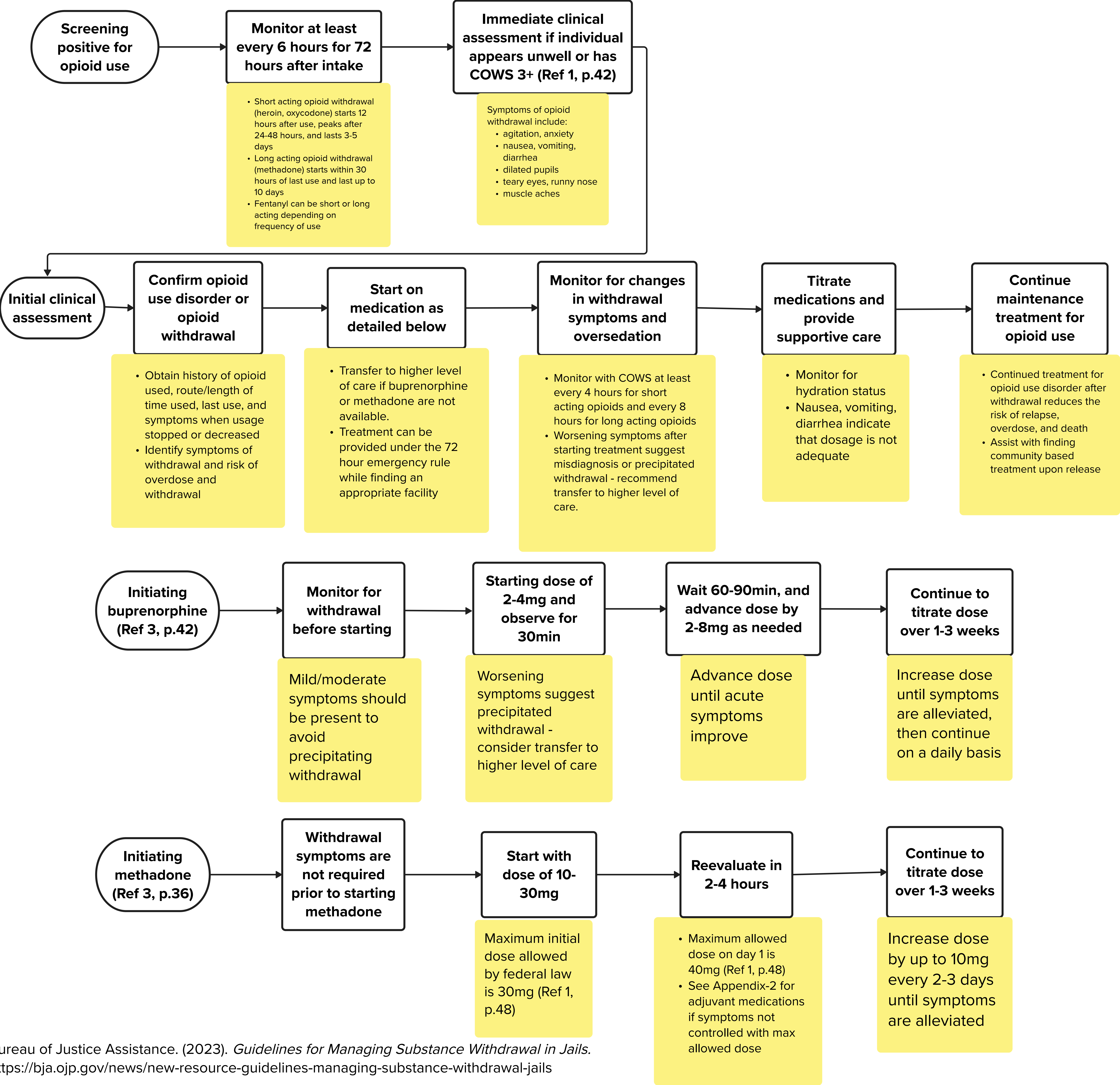


GENERAL MANAGEMENT



OPIOID WITHDRAWAL MANAGEMENT

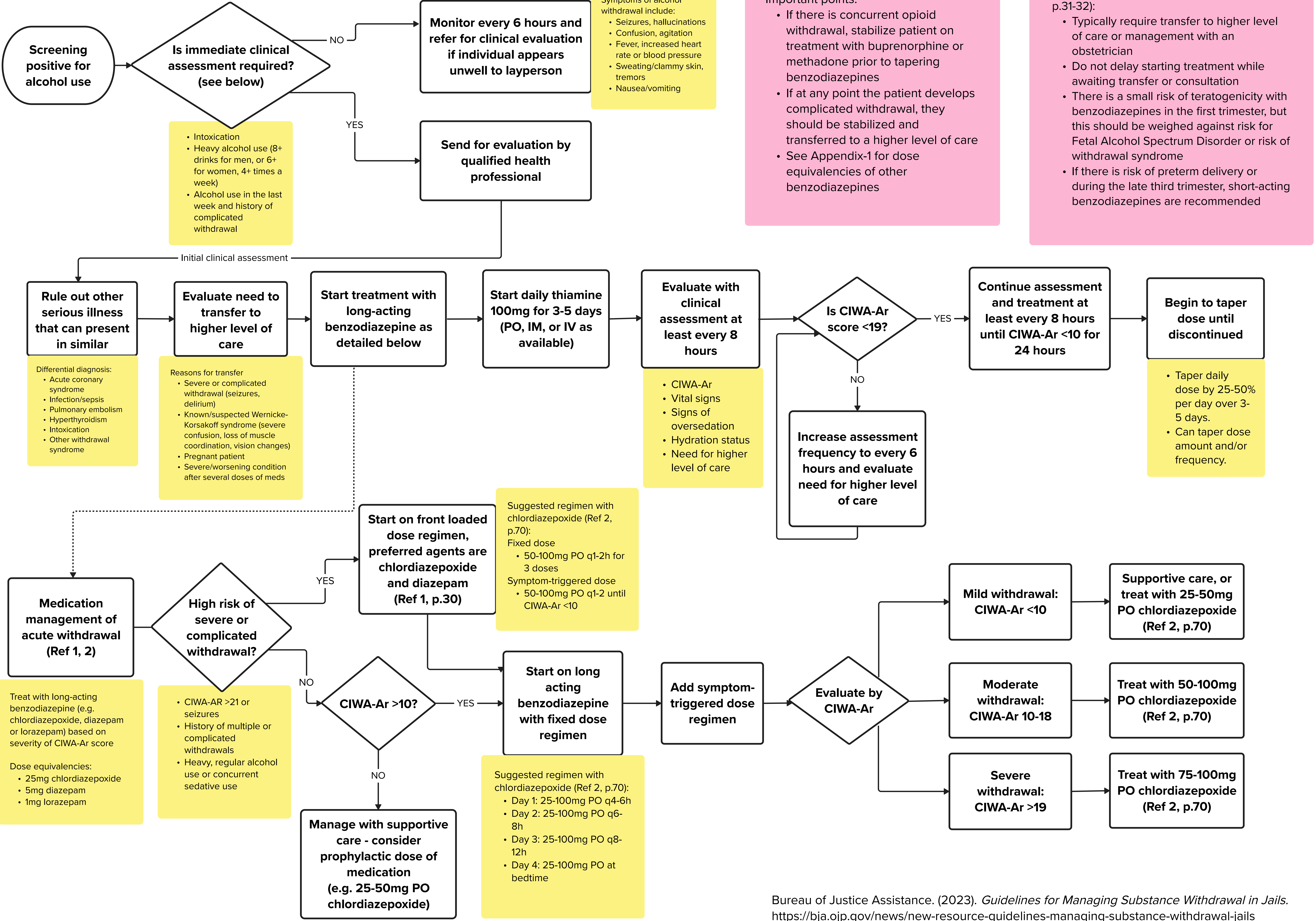


- Important points
- Individuals may not be aware they used drugs contaminated with opioids, and they are at risk for withdrawal
 - Polysubstance use or withdrawal from other substances does not preclude treatment for opioid withdrawal
 - See Appendix-3 for low dose buprenorphine initiation that can avoid precipitating withdrawal

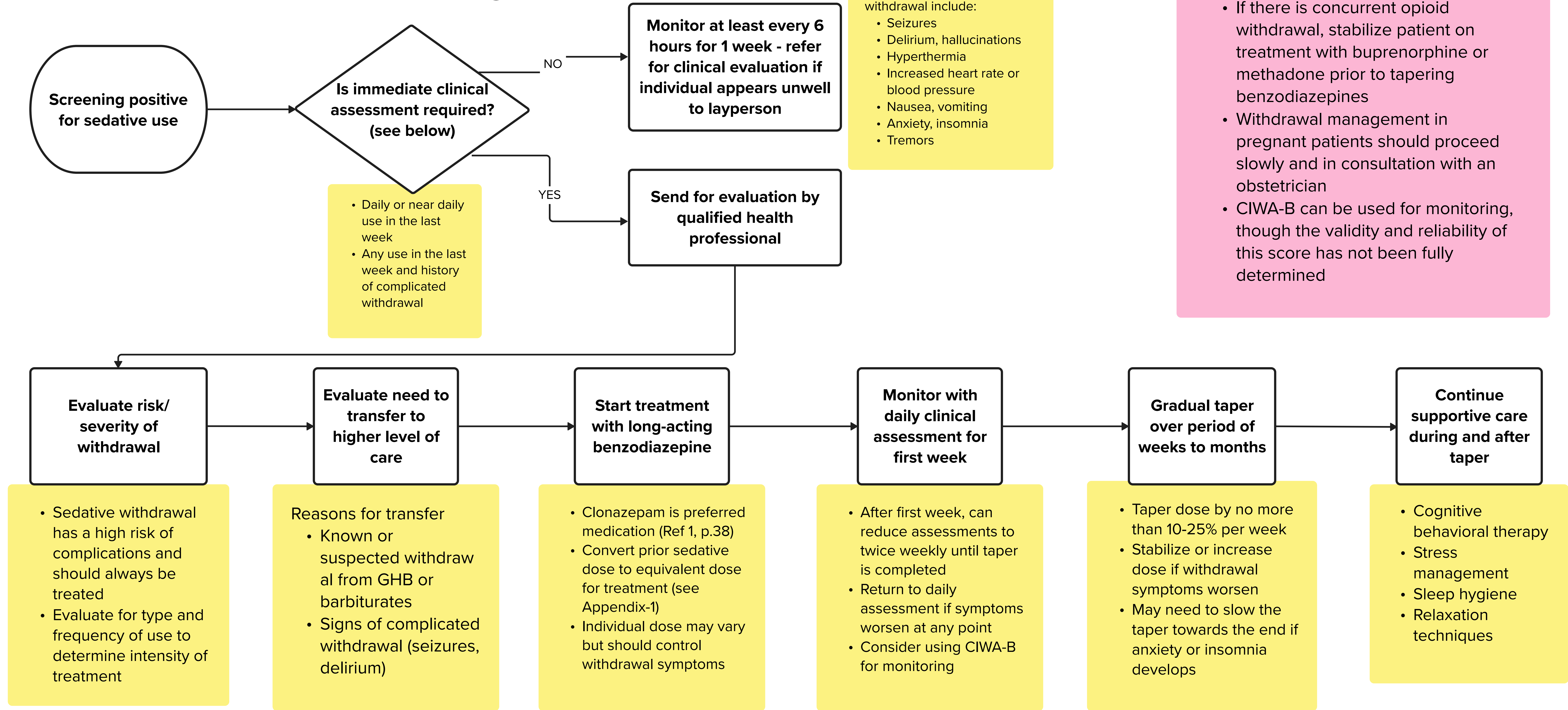
- Considerations for pregnant patients (Ref 1, p.51):
- Methadone and buprenorphine are safe for use during pregnancy and reduce the risk of miscarriage and preterm delivery
 - Provider should have obstetric experience and care may require transfer to the hospital
 - Pregnancy increases medication clearance - regularly evaluate need for increased and/or split dose starting in 2nd trimester
 - After delivery, continue maintenance treatment but reduce dose if there is oversedation

- Adjuvant medications:
- Can be used while titrating dose of first-line medications, but should not be required once buprenorphine/methadone is at adequate dose
 - See Appendix-2 for full list
 - Alpha-2-adrenergic antagonists (e.g. lofexidine or clonidine) can be used in people declining buprenorphine/methadone, but are contraindicated if low blood pressure
 - Naltrexone is not approved for treatment of acute withdrawal

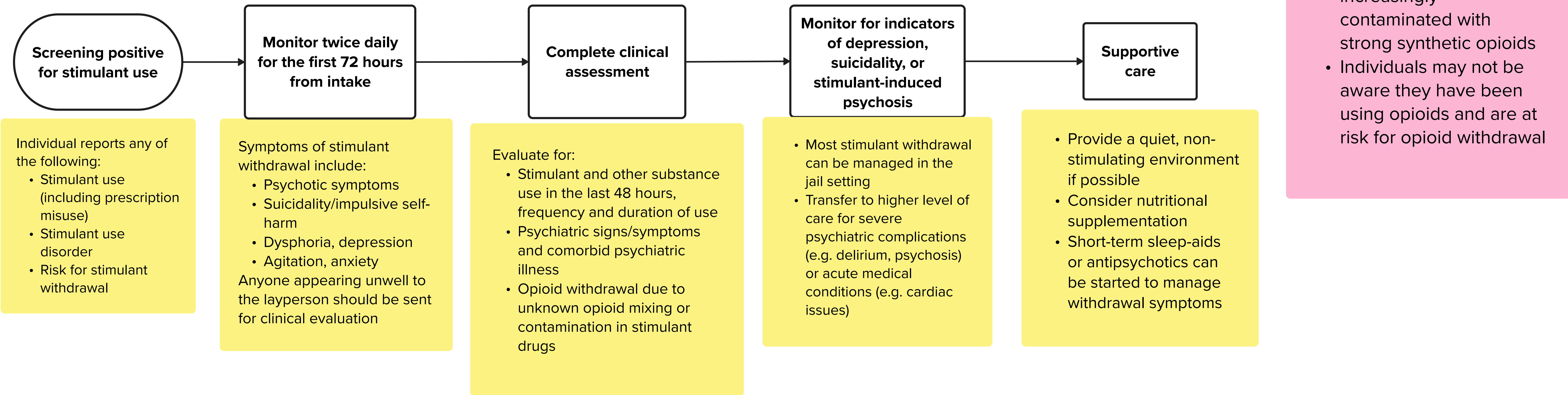
ALCOHOL WITHDRAWAL MANAGEMENT



SEDATIVE WITHDRAWAL MANAGEMENT



STIMULANT WITHDRAWAL MANAGEMENT



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2. American Society of Addiction Medicine. *The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management*. 2020 Jan. Available at: <https://www.asam.org/quality-care/clinical-guidelines/alcohol-withdrawal-management-guideline>
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4. Park TW. Benzodiazepine use disorder. *UpToDate*. Retrieved December 17, 2023, from <https://www.uptodate.com/contents/benzodiazepine-use-disorder>
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Wolters Kluwer

Pharmacology of benzodiazepines used to treat anxiety symptoms/disorders

Drug	Adult oral total daily dose (mg)*	Comparative potency (mg) [¶]	Onset after oral dose (hours)	Metabolism	Elimination half-life (hours) ^Δ
Alprazolam	0.5 to 6	0.5	1	CYP3A4 to minimally active metabolites.	11 to 15
Alprazolam extended release	0.5 to 6 once daily	0.5	1		16 (older adults) 20 (hepatic impairment) 22 (obesity)
Bromazepam ^{◇ §}	6 to 30	7.5	1	CYP1A2. No active metabolite.	8 to 20
Chlordiazepoxide [§]	5 to 100	10	1	CYP3A4 to active metabolites.	30 to 100 Prolonged in older adults and hepatic impairment
Clonazepam	0.5 to 4	0.25 to 0.5	0.5 to 1	CYP3A4. No active metabolite.	18 to 50
Clorazepate	15 to 60	7.5	0.5 to 1	CYP3A4 to active metabolite.	36 to 200
Diazepam	4 to 40	5	0.25 to 0.5	CYP2C19 and 3A4 to active metabolites.	50 to 100 Prolonged in older adults and renal or hepatic impairment

Lorazepam immediate release	0.5 to 6 0.5 to 4 (hypnotic)	1	0.5 to 1	Non-CYP glucuronidation in liver. No active metabolite.	10 to 14
Lorazepam extended release	1 to 6 mg [¥]	1	0.5 to 1	Non-CYP glucuronidation in liver. No active metabolite.	13 to 27
Oxazepam	30 to 120 15 to 30 (hypnotic)	15 to 30	1 to 2	Non-CYP glucuronidation in liver. No active metabolite.	5 to 15
Prazepam ^{◇ §}	15 to 60	15	2 to 3	CYP3A4 to active metabolites.	30 to 200 Prolonged in older adults

Data on drug metabolism and activity of metabolite(s) are for assessment of potential for CYP drug interactions and risk of accumulation. Risk of accumulation is greater, and dose reduction necessary, for older or debilitated adults and for patients with renal or hepatic insufficiency.

* Range of usual **total** daily dose for treatment of adults with anxiety or panic disorder typically given in divided doses two to four times daily.

¶ Important: Data shown are approximate equal potencies relative to lorazepam 1 mg orally and are NOT recommendations for initiation of therapy or for conversion between agents.

Δ Half-life of parent drug and pharmacologically active metabolite, if any.

◇ Not available in the United States.

§ Use only when other preferred agents are unavailable or not tolerated.

¥ To be used only when converting from immediate release lorazepam. Total daily dose is equal to the current total daily dose of immediate release lorazepam. Dose is given once daily in the morning after discontinuing immediate dose lorazepam tablets the night before.

Graphic 65653 Version 13.0

Adjunctive treatments for opioid withdrawal symptoms

Symptoms	Medication	Usual effective dose range (adult)	Notes
Anxiety			
Anxiety, irritability, restlessness	Diphenhydramine*	50 to 100 mg orally every 4 to 6 hours as needed (maximum 300 mg daily)	<ul style="list-style-type: none"> May also treat nausea Use reduced dose in hepatic impairment IV and IM administration available
	Hydroxyzine	25 to 100 mg orally every 6 to 8 hours as needed (maximum 400 mg daily)	<ul style="list-style-type: none"> May also treat lacrimation and rhinorrhea Use reduced dose (50%) in renal or hepatic impairment IM administration available
	Clonazepam [¶]	0.5 to 1.5 mg orally every 6 to 8 hours as needed (maximum 6 mg daily)	<ul style="list-style-type: none"> Use with caution and reduce dose in mild hepatic or renal impairment; active metabolites can accumulate Avoid in moderate to severe hepatic impairment or hepatic encephalopathy
	Lorazepam [¶]	1 mg orally every 4 to 6 hours as needed (maximum 6 mg daily)	<ul style="list-style-type: none"> Relatively safe in mild to moderate hepatic impairment; use of reduced dose may be needed Avoid in severe hepatic impairment or hepatic encephalopathy IV and IM administration available; use caution in renal impairment due to propylene glycol diluent
	Oxazepam [¶]	15 to 30 mg orally every 6 to 8 hours as needed (maximum 120 mg daily)	<ul style="list-style-type: none"> Relatively safe in mild to moderate hepatic or renal impairment Use with caution in severe renal impairment Avoid in severe hepatic impairment or hepatic encephalopathy
Gastrointestinal			

Abdominal cramping	Dicyclomine*	10 to 20 mg orally every 6 to 8 hours as needed (maximum 160 mg daily)	<ul style="list-style-type: none"> IM administration available (lower doses are used) Use with caution and reduce dose in renal or hepatic impairment
Diarrhea	Bismuth*	~524 mg orally every 30 to 60 minutes as needed (up to 4200 mg daily)	<ul style="list-style-type: none"> Monitor for dehydration and maintain fluid levels with oral and/or IV hydration
	Loperamide	4 mg orally followed by 2 mg after each loose stool (maximum 16 mg daily)	
Nausea/vomiting	Ondansetron* ^Δ	4 to 8 mg orally or IV every 12 hours as needed (maximum 16 mg/day)	<ul style="list-style-type: none"> Monitor for dehydration and maintain fluid levels with oral and/or IV hydration Dose-dependent QT interval prolongation; risk of rare, potentially fatal, ventricular arrhythmia; use with caution (eg, monitor baseline and post-dose ECG) or avoid in patients with features of elevated risk^Δ Use caution and reduced dose (50%) in severe hepatic impairment
	Prochlorperazine	5 to 10 mg orally three times daily before meals or every six hours as needed (maximum 40 mg/day)	<ul style="list-style-type: none"> Monitor for dehydration and maintain fluid levels with oral and/or IV hydration Use with caution in mild to moderate hepatic impairment; avoid in severe hepatic impairment IV and rectal administration available
	Promethazine	25 mg orally every 4 to 6 hours as needed (maximum 50 mg/day)	<ul style="list-style-type: none"> Monitor for dehydration and maintain fluid levels with oral and/or IV hydration Use with caution in mild to moderate hepatic impairment; avoid in severe hepatic impairment IM and rectal administration available (IV use not recommended)
Insomnia, pain, muscle spasm, and restless legs			
Insomnia	Trazodone*	25 to 100 mg orally at bedtime	<ul style="list-style-type: none"> May titrate nightly up to 300 mg at bedtime if needed Use with caution in severe hepatic or renal impairment

	Doxepin	6 to 50 mg orally at bedtime	<ul style="list-style-type: none"> Use with caution and reduce dose in severe hepatic impairment
	Mirtazapine	7.5 to 15 mg orally at bedtime	<ul style="list-style-type: none"> May need to use lower dose in moderate to severe hepatic or renal impairment
	Quetiapine	50 to 100 mg orally at bedtime	<ul style="list-style-type: none"> Use lower initial dose (25 mg) in hepatic impairment and adjust based on response
	Zolpidem [¶]	5 to 10 mg orally at bedtime	<ul style="list-style-type: none"> A dose of 5 mg is usually appropriate for female patients, and those with mild or moderate hepatic impairment Avoid in severe hepatic impairment or hepatic encephalopathy
Muscle aches [◇] , joint pain, headache	Ibuprofen* [§]	400 mg orally every 4 to 6 hours as needed (maximum 2400 mg daily)	<ul style="list-style-type: none"> Patient should be well hydrated and without significant kidney disease Use with caution in mild to moderate hepatic or renal impairment Avoid all NSAIDs in severe renal or hepatic impairment or cirrhosis
	Acetaminophen	650 to 1000 mg orally every 4 to 6 hours as needed (maximum 4000 mg daily)	<ul style="list-style-type: none"> Appropriate analgesic for most patients Use reduced dose (ie, 2000 mg daily) or avoid in hepatic impairment or if malnourished
	Ketorolac [§]	15 to 30 mg IV or IM every 6 hours as needed (maximum 120 mg daily)	<ul style="list-style-type: none"> Patient should be well hydrated and without significant kidney disease Limit use to 5 days or less Use with caution and reduce dose (50%) in older adults and patients with mild to moderate renal impairment Use with caution in mild to moderate hepatic impairment Contraindicated in severe renal or hepatic impairment or volume depletion
	Naproxen [§]	500 mg orally twice daily with meals	<ul style="list-style-type: none"> Patient should be well hydrated and without significant kidney disease Use with caution in mild to moderate hepatic or renal impairment Avoid all NSAIDs in severe renal or hepatic impairment or cirrhosis
Muscle spasm [◇] , restless legs	Cyclobenzaprine*	5 to 10 mg orally every 8 hours as needed (maximum 30	<ul style="list-style-type: none"> Use reduced dose in mild hepatic impairment Avoid in moderate to severe hepatic impairment

		mg daily)	
	Baclofen	5 to 10 mg orally every 8 hours as needed (maximum 60 mg daily)	<ul style="list-style-type: none"> Use reduced dose in renal impairment
	Diazepam ¶	5 to 10 mg orally every 6 to 12 hours as needed (maximum 40 mg daily)	<ul style="list-style-type: none"> Use with caution in hepatic or renal impairment Avoid in severe hepatic impairment or hepatic encephalopathy IM and IV administration available
	Methocarbamol	750 to 1500 mg orally every 8 hours as needed (maximum 6 g daily)	<ul style="list-style-type: none"> Use with caution in hepatic or renal impairment IM and IV administration available (lower doses are used); avoid parenteral formulation in renal impairment (propylene glycol additive)

- A calm quiet environment with supportive and reassuring staff can be instrumental for helping patients overcome most symptoms of acute opioid withdrawal and decreases the need for pharmacologic interventions.
- Patients who have diarrhea, vomiting, or sweating should be monitored for dehydration and fluid levels maintained with oral and/or intravenous fluids.
- The role of opioid replacement therapies and alpha-2 agonists (eg, clonidine) in management of acute opioid withdrawal and maintenance pharmacotherapy in opioid use disorder is discussed separately; refer to accompanying text.
- This is not a complete list of cautionary information or dose adjustments in organ impairment. For additional information refer to the Lexicomp drug monographs included within UpToDate.

IV: intravenous; IM: intramuscular; NSAID: nonsteroidal anti-inflammatory drug.

* Author's first choice.

¶ Use of benzodiazepines and benzodiazepine agonists (eg, zolpidem) is NOT recommended in patients receiving methadone or buprenorphine therapy unless under close medical supervision. Patients who resume heroin (diamorphine) use after a period of abstinence are at high risk of fatally overdosing, particularly if heroin use is resumed in combination with benzodiazepines, alcohol, or other drugs with sedative characteristics (eg, quetiapine). The use of benzodiazepines should be limited to 5 to 10 days in total and tapered. They are not recommended for use in supervised outpatient withdrawal and should be reserved for inpatient settings where frequent clinical monitoring is provided.

Δ Risk of QTc prolongation or torsades de pointes is also elevated with advanced age, female sex, heart disease, congenital long QT syndrome, hypokalemia or hypomagnesemia, overly rapid IV administration, and combination of drugs with QTc prolonging effects (eg, methadone). Refer to topic on acquired long QT syndrome.

◇ Warm baths, rehydration, and gentle stretching are also helpful for relieving muscle aches and cramps.

§ Safety concerns of NSAID use in older adults and patients with, or at elevated risk for, cardiovascular disease, gastrointestinal bleeding, organ dysfunction, or thrombotic events are addressed separately in UpToDate.

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Graphic 106793 Version 6.0

Patient Guidelines for Buprenorphine “Micro-Dosing” Induction

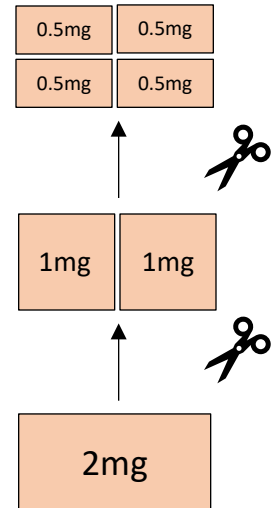
To reduce the risk of precipitated withdrawal when starting buprenorphine/naloxone, we would like you to start at very low doses and increase slowly. Please follow the schedule below and call us at _____ if there are any problems.

PREPARING YOUR DOSES:

On Days 1-5, we will use **2mg buprenorphine/naloxone films**:

- **Days 1-2:** Cut ONE 2mg film into four equal pieces to achieve the lowest dose needed (0.5mg or 1/4th of a 2mg film).
- **Day 3:** Cut ONE 2mg film into two equal pieces to achieve the lowest dose needed (1mg or 1/2 of a 2mg film).
- **Days 4-5:** Use full 2mg films. You do NOT need to further prepare the films.

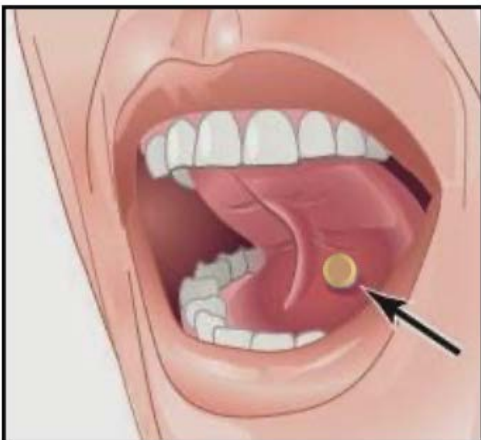
On Days 6-7, we will use **8mg buprenorphine/naloxone films**. You do NOT need to cut or further prepare these films.



DAILY DOSING INSTRUCTIONS:

On each day, take your 1st dose of buprenorphine/naloxone about 10-15 minutes **BEFORE** using any other opioid-based substances (i.e. heroin, fentanyl, methadone, prescription pills, etc.)

Place the film **under your tongue** and let it melt completely.



Day 1:	Take ¼ of a 2mg film (0.5 mg) ONCE
Day 2:	Take ¼ of a 2mg film (0.5 mg) TWICE daily
Day 3:	Take ½ of a 2mg film (1 mg) TWICE daily
Day 4:	Take one full 2mg film (2mg) TWICE daily
Day 5:	Take two full 2mg films (4mg) TWICE daily
Day 6:	Take one full 8mg film (8mg) TWICE daily
Day 7:	STOP using any non-buprenorphine opioid-based substances. Continue taking buprenorphine/naloxone 8mg films TWICE or THREE TIMES daily (as advised by your medical provider).

PLEASE RETURN TO CLINIC ON:

Starting Buprenorphine

Symptom Management Guide

Clinic Name: _____

Clinic Phone Number: _____



The following medications have been prescribed to help you manage the symptoms of opioid withdrawal while you wait to take the first dose of buprenorphine. You can keep using these medications after you take your first dose if you keep on having withdrawal symptoms.

If you feel much worse after starting medications within 1-2 hours after starting buprenorphine, please call us at _____ during business hours or seek care in a local Urgent Care or Emergency Department.

Prescribed?

☐

If You Feel This, Then...

Cold sweats, Chills, Feeling "Jittery"



Take This...

Clonidine
0.1 mg tablet

In This Way...

Take 1 tablet by mouth every 6 hours as needed. Stop taking if you feel dizzy.

Do not use more than 4 tablets in one day.

Prescribed?

☐

Anxiety, Problems Sleeping



Hydroxyzine
50 mg tablet

Take 1 tablet by mouth every 6 hours as needed. Stop taking if you feel too sleepy.

Do not use more than 4 tablets in one day.

Prescribed?

☐

Nausea or Vomiting



Ondansetron
4 mg tablet

Take 1 tablet by mouth every 6 hours as needed.

Do not use more than 4 tablets in one day.

Prescribed?

☐

Diarrhea



Loperamide
2 mg tablet

Take 2 tablets as your first dose. Take 1 additional tablet after each episode of diarrhea.

Do not use more than 6 tablets in one day.

Clinical Opiate Withdrawal Scale

Introduction

The Clinical Opiate Withdrawal Scale (COWS) is an 11-item scale designed to be administered by a clinician. This tool can be used in both inpatient and outpatient settings to reproducibly rate common signs and symptoms of opiate withdrawal and monitor these symptoms over time. The summed score for the complete scale can be used to help clinicians determine the stage or severity of opiate withdrawal and assess the level of physical dependence on opioids. Practitioners sometimes express concern about the objectivity of the items in the COWS; however, the symptoms of opioid withdrawal have been likened to a severe influenza infection (e.g., nausea, vomiting, sweating, joint aches, agitation, tremor), and patients should not exceed the lowest score in most categories without exhibiting some observable sign or symptom of withdrawal.

APPENDIX 1

Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name: _____ Date and Time ____/____/____:____	
Reason for this assessment: _____	
Resting Pulse Rate: _____ beats/minute <i>Measured after patient is sitting or lying for one minute</i> 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate <u>greater</u> than 120	GI Upset: over last 1/2 hour 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 <u>multiple episodes</u> of diarrhea or vomiting
Sweating: over past 1/2 hour not accounted for by room temperature or patient activity. 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat <u>streaming</u> off face	Tremor observation of outstretched hands 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness Observation during assessment 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	Yawning Observation during assessment 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 <u>yawning</u> several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	Anxiety or Irritability 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches <i>If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored</i> 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh skin 0 skin is smooth 3 piloerection of skin can be felt or hairs standing up on arms 5 prominent piloerection
Runny nose or tearing <i>Not accounted for by cold symptoms or allergies</i> 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	<div style="text-align: right;">Total Score _____</div> <div style="text-align: center;">The total score is the sum of all 11 items</div> Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.