Institut national d'excellence en santé et en services sociaux
Québec

QUÉBEC'S NATIONAL MEDICAL PROTOCOL No. 888021

Administration of benzodiazepines or gabapentin prescribed via an individual prescription for alcohol withdrawal

Developed in collaboration with an advisory committee consisting of Québec clinicians and experts.

CLINICAL SITUATION OR TARGET POPULATION

A person 18 years of age or older who has just stopped consuming alcohol and who has a valid prescription for benzodiazepines or gabapentin for alcohol withdrawal in an outpatient or inpatient setting[1] (with a fixed-schedule dosing regimen).

A person 18 years of age or older who has just stopped or significantly reduced his/her alcohol consumption, who has a valid prescription for benzodiazepines for alcohol withdrawal (with a symptom-triggered dosing regimen) and who presents with:

- at least one of the following symptoms during withdrawal managed in an outpatient setting: nausea, vomiting, anxiety, tremors, sweating, irritability, strong alcohol cravings, or night-time insomnia;

  OR

- signs and symptoms of moderate to severe withdrawal in an inpatient setting[1], based on the CIWA-Ar score[2] (see Appendix I).

CONTRAINDICATIONS TO THE APPLICATION OF THIS PROTOCOL

- Pregnancy or breastfeeding
- Hospitalization in an intensive care unit
- The presence of seizures or signs and symptoms suggestive of delirium tremens (confusion or perceptual disturbances together with tachycardia, hypertension, or fever)
- For withdrawal managed in an outpatient setting, the active use of other central nervous system depressants (e.g., benzodiazepines, GHB or opioids)

INSTRUCTIONS

1. HEALTH STATUS ASSESSMENT

1.1 Inquire about recent alcohol consumption

- Record the amount, date and time of the last alcohol use.
  - It is important that the person stops using alcohol as soon as he/she starts the withdrawal pharmacotherapy.

1.2 Ask about the use of other substances

- Ask the person if he/she is actively using other psychoactive substances (e.g., benzodiazepines, GHB, opioids or psychotropic medications).

[1] For example, in a hospital, addiction rehabilitation centre or prison setting.
[2] If the clinical care setting impedes the use of the CIWA-Ar scale, the Modified CIWA-Ar (see Appendix II) can be used.

1.3 Signs and symptoms

- Check for signs and symptoms suggestive of alcohol withdrawal syndrome:
  - Nausea
  - Vomiting
  - Tremor
  - Sweating
  - Headache
  - Anxiety
  - Agitation
  - Insomnia
  - Perceptual disturbances
  - Disorientation
- If in-person visit, take the person's vital signs and assess the severity of the withdrawal syndrome using the CIWA-Ar scale[1] (see Appendix I).
- Check for the following warning signs and symptoms:
  - Seizures
  - The presence of signs and symptoms suggestive of delirium tremens (confusion or perceptual disturbances together with tachycardia, hypertension, or fever)

1.4 Social situation

- Inquire about the person's social situation:
  - Housing insecurity or instability
  - Isolation
  - Vulnerability
- Check if arrangements have been made with members of the interprofessional team to optimize the person's psychosocial management and support.

2. TREATMENT APPROACH

2.1 Treatment objective

Pharmacotherapy is aimed at:

- Preventing or treating the signs and symptoms of alcohol withdrawal syndrome (e.g., reducing or maintaining their severity at a mild level);
- Avoiding their worsening and the associated health risks; and
- Creating an opportunity to facilitate a transition to supportive relapse prevention therapy, when indicated.

2.2 General information on pharmacotherapy

An individual prescription for active or anticipated alcohol withdrawal syndrome usually includes a benzodiazepine or gabapentin, plus thiamine supplements.

[1] If the clinical care setting impedes the use of the CIWA-Ar scale, the Modified CIWA-Ar (see Appendix II) can be used.

General information on the main drugs used					
	Drug	**Oral onset of action**	**Duration of action**	**Active metabolites**	**Most common drug adverse effects**
Benzodiazepines	Diazepam[1]	Rapid (30 minutes)	Long	Yes	Ataxia, confusion, dizziness, drowsiness, fatigue, muscle weakness, psychomotor slowing, apnea, respiratory depression, mental depression, irritability. Risk of falling for persons 65 years of age or older.
	Lorazepam[2]	Intermediate (30 to 60 minutes)	Intermediate	No	
Anticonvulsants	Gabapentin	Slow (1 to 3 hours)	Intermediate	No	Central nervous system depression, drowsiness, ataxia, fatigue, dizziness, nystagmus, peripheral edema, tremors, diarrhea.

1 IV, IM or IR administration possible.
2 IV, IM or SL administration possible.

2.3 Administering drugs

Regardless of the withdrawal setting, drug administration should, whenever possible, be supervised.

Administration		
	Outpatient withdrawal	**Inpatient withdrawal**
Benzodiazepines	**Symptom-triggered therapy**: One dose is taken at the time intervals indicated on the individual prescription if the person has at least one withdrawal symptom (nausea, vomiting, tremor, sweating, anxiety, agitation, irritability, headache, difficulty sleeping, or strong alcohol cravings); OR **Fixed-schedule therapy:** One dose is taken at the time intervals specified on the individual prescription.	**Symptom-triggered therapy:** Administer one dose at the time intervals indicated on the individual prescription if the withdrawal syndrome is considered moderate or severe, based on the CIWA-Ar score[1] (see Appendix I) or if the heart rate is higher than 100 bpm[2]; OR **Fixed-schedule therapy:** Administer one dose at the time intervals specified on the individual prescription. If the dosing regimen includes additional PRN doses, follow the symptom-triggered dosing instructions for those doses.
Gabapentin	**Fixed-schedule therapy with additional PRN doses:** Regular dosing is done at the time intervals indicated on the individual prescription. An additional dose is taken at the indicated time intervals if the person has at least one sign or symptom: • anxiety, tremor, irritability, strong alcohol cravings, or night-time insomnia.	

1 If the clinical care setting impedes the use of the CIWA-Ar scale, the Modified CIWA-Ar (see Appendix II) can be used.
2 Take the person's level of discomfort and his/her tolerance into account when administering the doses.

Tapering Off the Therapy	
Benzodiazepines	Reduce the dose or frequency gradually in the manner indicated on the individual prescription so as to limit the duration of treatment to 10 days.
Gabapentin	If gabapentin is not continued as relapse prevention therapy[1], reduce the dose or frequency gradually in the manner indicated on the individual prescription.

[1] A new prescription must be written in order to continue gabapentin as pharmacotherapy for relapse prevention (if need be, refer to the NMP on relapse prevention for the dose adjustments).

3. INFORMATION TO BE PROVIDED

Discuss the following items with the person and, if appropriate, with his/her family member or caregiver:

General Considerations
– Explain the importance of ceasing alcohol use as soon as pharmacotherapy has begun because of the risk of overdose. – Check with the person to see whether he/she needs assistance finding a family member, caregiver or healthcare professional able to provide support during withdrawal. – Review the main symptoms of alcohol withdrawal syndrome that can occur during treatment (see Section 2.4). – Inform the person about the potential adverse drug effects (see Section 2.2). – Explain the importance of adhering to the treatment and especially the dosing intervals. – Underscore the importance of regular and adequate hydration, especially to compensate for withdrawal-related vomiting, sweating or diarrhea.
Precautions
– Inform the person of the risks associated with driving and other activities that require alertness (e.g., operating machinery, working at heights, swimming, hunting and boating) during at least the entire duration of the prescription because of the sedative effect of the medication or possible seizures due to withdrawal. – Give the person the telephone number of a member of the healthcare team who can be contacted in case he/she has any questions or needs. – Remind him/her to contact the healthcare team if the withdrawal symptoms worsen despite the medication, if any significant adverse drug effects occur, or if he/she uses alcohol during the treatment. – Tell him/her to contact emergency services in the event of seizures, hallucinations, confusion, or fever.

4. FOLLOW-UP

4.1 For outpatients

* *An in-person follow-up is preferable, but an occasional follow-up by telephone or videoconference is also an option, depending on how the person's status evolves, and when feasible.*

** *A person in a situation of instability, vulnerability, or isolation, or a person with special needs may necessitate adapting the proposed follow-up procedures, including closer medical monitoring and more frequent contact. Optimize the person's support with the interprofessional team.*

- At least twice during the first week of treatment (including once during the first 24 to 72 hours), then again according to how the person's status evolves:
  - Inquire about and record the following:
    - The last benzodiazepine or gabapentin dose (quantity and time), adherence to the dosing interval, and adherence to the treatment in general;
    - The person's comfort regarding the symptoms and signs of alcohol withdrawal (nausea, vomiting, tremor, paroxysmal sweats, anxiety, agitation, irritability, headaches, difficulty sleeping, intense thirst, strong alcohol cravings) to identify any need to optimize the medication;
    - The occurrence of seizures or signs or symptoms of delirium tremens (confusion or perceptual disturbances together with tachycardia, hypertension, or fever);
    - The occurrence of adverse effects due to the treatment, including the level of awareness or alertness (see Section 2.2);
    - Fluid intake (amount and frequency);
    - The use of alcohol or other psychoactive substances (e.g., benzodiazepines, GHB, opioids or psychotropic medications); and
    - The person's emotional state, including suicidal thoughts.
  - If in-person visit, take the person's vital signs and assess the severity of the withdrawal syndrome using the CIWA-Ar scale[1] (see Appendix I).
- At the end of treatment:
  - Have a member of the interprofessional team provide a follow-up to support relapse prevention (if need be, refer to NMP No. 888027 - Relapse Prevention).

4.2 For inpatients

- Do a follow-up (as described below) 1 to 2 hours after medication is administered for at least the first 2 or 3 doses and at the following minimum frequencies, which are to be adjusted according to how the person's signs and symptoms evolve:
  - Mild withdrawal syndrome (CIWA-Ar[1] score <8) AND heart rate ≤ 100 bpm: every 8 hours;
  - Moderate or severe withdrawal syndrome (CIWA-Ar[1] score ≥ 8) OR heart rate> 100 bpm: according to the frequency of dose administration until the signs and symptoms are controlled.

[1] If the clinical care setting impedes the use of the CIWA-Ar scale, the Modified CIWA-Ar (see Appendix II) can be used.

- At each follow-up:
  - Measure the person's heart rate, blood pressure, temperature, respiratory rate and oxygen saturation.
  - Assess the change in the severity of the signs and symptoms of alcohol withdrawal using the CIWA-Ar scale[1] (see Appendix I).
  - Ask the person about his/her discomfort.
  - Check for the occurrence or presence of:
    - Seizures;
    - Signs and symptoms of delirium tremens (confusion or perceptual disturbances together with tachycardia, hypertension, or fever);
    - A high level of sedation, as indicated by a score <-2 on the Richmond Agitation-Sedation Scale (see Appendix III).
  - Check hydration.
- Frequently during treatment:
  - Inquire about the person's emotional state, including suicidal thoughts.
- At the end of treatment:
  - Have a member of the interprofessional team provide a follow-up to support relapse prevention (if need be, refer to NMP No. 888027 - Relapse Prevention).

[1] If the clinical care setting impedes the use of the CIWA-Ar scale, the Modified CIWA-Ar (see Appendix II) can be used.

5. SITUATIONS REQUIRING SPECIAL ATTENTION, REASSESSMENT OR FURTHER INVESTIGATION

- A history of complications associated with alcohol withdrawal (seizures, delirium tremens);
- The use of other psychoactive substances (e.g., benzodiazepines, GHB, opioids or psychotropic medications) during treatment;
- An intolerable level of discomfort despite mild withdrawal symptoms (e.g., a CIWA-Ar[1] score <8);
- Signs and symptoms of alcohol withdrawal poorly controlled despite the prescribed doses of medication (e.g., in an inpatient setting, no decrease in the CIWA-Ar[1] score after 2 or 3 administrations of medication or, in an outpatient setting, persistence of significant withdrawal symptoms after 24 to 48 hours of treatment);
- The administration of more than 12 mg of lorazepam or more than 60 mg of diazepam during the past 12 hours;
- The development of more severe signs or symptoms (e.g., seizures, pronounced agitation, confusion, disorientation or hallucinations);
- The occurrence of fever;
- Persistent vomiting that is preventing rehydration and oral dosing;
- A worsening of existing medical or psychiatric conditions;
- The appearance or worsening of depressive symptoms or suicidal thoughts;
- Signs of over-sedation (e.g., a score <-2 on the Richmond Agitation-Sedation Scale), impaired equilibrium, or persistent drowsiness despite a dose reduction;
- An ambient air pulse oximetry value ≤ 92%;
- A respiratory rate of 10 or less;
- Unstable vital signs or syncope;
- Moderate to severe dehydration;
- Signs of benzodiazepine or gabapentin abuse or misuse;
- Any alcohol use during withdrawal;
- In the case of outpatient withdrawal, irregularity in picking up the doses at the pharmacy.

REFERENCES

This protocol is based on the latest scientific data and best practice recommendations, which were enhanced with contextual information and the perspectives of Québec clinicians and experts. For details on the process used to develop this national medical protocol and to consult the references, see the report in support of this protocol.

[1] If the care context limits the use of the CIWA-Ar scale, the Modified CIWA (see Appendix II) can be used.

APPENDIX I CLINICAL INSTITUTE WITHDRAWAL ASSESSMENT ALCOHOL REVISED SCALE — CIWA-Ar

Heart rate: _____/ min Blood pressure: _____ / _____

Nausea and vomiting: Ask "Do you feel sick to your stomach? Have you vomited?" Observe.

0 No nausea and no vomiting
1 Mild nausea with no vomiting
2
3
4 Intermittent nausea with dry heaves
5
6
7 Constant nausea, frequent dry heaves, and vomiting

Tactile disturbances: Ask "Have you any itching, any pins and needles, any burning or any numbness, or do you feel bugs crawling on or under your skin?"

0 No disturbances of this type
1 Very mild itching, pins and needles, burning, or numbness
2 A mild degree of the above-mentioned disturbances
3 A moderate degree of the above-mentioned disturbances
4 Moderately severe hallucinations
5 Severe hallucinations
6 Extremely severe hallucinations
7 Continuous hallucinations

Tremors: Evaluate with arms extended and fingers in front of the examiner. Observe.

0 No tremor
1 Not visible, but can be felt at the fingertips
2
3
4 Moderate, with the patient's arms extended
5
6
7 Severe, even with arms not extended

Auditory disturbances: Ask "Are you more aware of the sounds around you? Are they harsher? Do they frighten you? Are you hearing any sound that is disturbing to you? Are you hearing things you know are not there?"

0 No disturbing sounds
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

Paroxysmal sweats: Observe.

0 No sweat visible
1 Sweat barely perceptible, palms moist
2
3
4 Beads of sweat on forehead
5
6
7 Drenching sweats

Visual disturbances: Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?"

0 No disturbances of this type
1 Very mild sensitivity
2 Mild sensitivity
3 Moderate sensitivity
4 Moderately severe hallucinations
5 Severe hallucinations
6 Extremely severe hallucinations
7 Continuous hallucinations

Anxiety: Ask "Do you feel nervous?" Observe.

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

Headaches: 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. Focus instead on severity.

0 No headache
1 Very mild
2 Mild
3 Moderate
4 Moderately severe
5 Severe
6 Very severe
7 Extremely severe

Agitation: Observe.

0 Normal activity
1 Somewhat more than normal activity
2
3
4 Moderately fidgety and restless
5
6
7 Paces back and forth during the evaluation or thrashes about

Orientation disturbances: 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 Gets date wrong by no more than 2 days
3 Gets date wrong by more than 2 days
4 Disoriented for place and/or person

Total score: _____ (maximum score = 67)

When interpreting the score, one must take into account the data from the clinical evaluation and any confounding factors (e.g., the effect of medications, medical conditions, communication difficulties).

Severity of alcohol withdrawal syndrome as assessed by the CIWA-Ar			
Severity	**Mild**	**Moderate**	**Severe**
Score	<8	8 to 18	≥ 19

APPENDIX II MODIFIED CLINICAL INSTITUTE WITHDRAWAL ASSESSMENT ALCOHOL REVISED SCALE —MODIFIED CIWA-Ar

Modified version of the Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA-Modified)

Source: Wojtecki CA, Marron J, Allison EJ Jr, Kaul P, Tyndall G. Systematic ED assessment and treatment of alcohol withdrawal syndromes: a pilot project at a Veterans Affairs Medical Center. J Emerg Nurs. 2004 Apr; 30(2):134-40.

MODIFIED CIWA-Ar SCALE	
Heart rate	
<80	0
80 to 90	1
> 90	2
Blood pressure	
<150/90	0
150/90 to 180/95	2
> 180/95	3
Nausea or vomiting	
No nausea or vomiting	0
Mild nausea with dry heaves	1
Constant nausea with vomiting	2
Tremors	
No tremors	0
Palpable at fingertips only	1
Moderate and grossly visible	2
Severe, even with arms at side	3
Anxiety	
No anxiety or agitation	0
Mildly anxious with increased activity	1
Moderately anxious with associated restlessness	2
Severely anxious with near-panic reaction	3
Disorientation/confusion	
Oriented	0
Mild — uncertain about date or place	1
Moderate — disoriented as to time, place and person and surrounding events	2
Severe — completely disoriented as to time, place and person or has auditory, tactile or visual disturbances	3
Perspiration	
None	0
Mild – barely perceptible with moist palms	1
Severe — drenching sweats	2
Total score (maximum score =18)	

Severity of alcohol withdrawal syndrome as assessed by the Modified CIWA-Ar			
Severity	**Mild**	**Moderate**	**Severe**
Score	0 to 6	7 to 12	≥ 13

APPENDIX III RICHMOND AGITATION-SEDATION SCALE (RASS)

Source: CMQ, 2015. La sédation-analgésie Lignes directrices.

Instruction	Description/Definition	Level
Observe the patient quietly		
If he/she shows spontaneous motor activity, assess the level of agitation:	Combative: immediate danger to staff	+ 4
	Very agitated: pulls or removes tubes or catheters and/or is aggressive toward staff	+ 3
	Agitated: frequent non-purposeful movements and/or fights ventilator	+ 2
	Restless: anxious or apprehensive, but movements oriented, and not vigorous or aggressive	+ 1
If he/she is calm and responds or not to simple commands:	Alert and calm: eyes open spontaneously Conscious: RASS 0 + responds to simple commands	0
If he/she is calm and eyes are open: assess the level of hypoalertness (or drowsiness), state the patient's name, but without touching him/her, in an increasingly louder voice and in an especially loud voice if he/she might be hearing-impaired (elderly, prolonged stay in resuscitation: a plug of earwax, antibiotic or furosemide toxicity):	Drowsy: not fully alert but has sustained awakening, with eye contact to voice (> 10 s)	– 1
	Slight sedation: briefly awakens, with eye contact to voice (<10 s)	– 2
	Moderate sedation: movement or eye opening to voice, but no eye contact	– 3
If the patient makes no movement, including when his/her name is called loudly: rub the shoulder and then the sternum in a non-nociceptive manner:	Deep sedation: no response to voice, but movement or eye opening to physical stimulation (non-nociceptive rubbing of the shoulder or sternum)	– 4
	Unarousable: no response to voice or physical stimulation (non-nociceptive rubbing of shoulder and sternum).	– 5