WorkSafe
Travail sécuritaire NB

Summary of Ketamine/Esketamine Information

What is it?

Ketamine is a dissociative drug producing a sense of mind-from-body separation (dissociation). It works by stopping the brain from getting nerve messages about pain. It also alters how you experience sight and sound. Esketamine, a stereoisomer of ketamine, has been explored for its potential therapeutic properties in treating depression.

Two main types of ketamine are used to treat major depression that hasn't responded to two or more antidepressant medications of adequate dose and duration (treatment-resistant depression):

- Racemic Ketamine: Most often given as an infusion into the bloodstream, this is sometimes called intravenous or IV ketamine. It is a mixture of two mirror-image molecules: "R" and "S" ketamine. Ketamine is legal when prescribed by a medical doctor. While it was approved decades ago as an anesthetic by Health Canada, it is used off-label to treat depression.
- Esketamine (Spravato): Approved by Health Canada in 2020, it's given as a nasal spray. It uses only the "S" molecule. To date, most research has been on IV ketamine infusions.

Literature Review

Recent published evidence relating to the use of ketamine/esketamine for major depression, sometimes seen accompanying traumatic psychological injury (TPI), shows some potential as an initial treatment, though long-term outcomes are unclear.

Recommendation

Ketamine/esketamine is generally not recommended for routine treatment. The use of ketamine and esketamine should be carefully considered, and all treatments must be pre-approved by WorkSafeNB. Certain diagnostic and monitoring criteria must be provided when requested by WorkSafeNB. Ketamine/esketamine may be considered (subject to pre-approval and initial sign-off by WorkSafeNB) to treat major depression related to a compensable injury that hasn't responded to two or more antidepressant medications of adequate dose and duration (treatment-resistant depression).

NOT RECOMMENDED

WorkSafeNB does not recommend ketamine and esketamine treatments:

- If there is evidence of psychotic disorder (MDD with psychotic symptoms), bipolar disorder, obsessive-compulsive disorder, and/or cluster B personality; or
- In clients with ongoing substance use disorder, unless a statement of safety is submitted from the treating physician; or
- If the treatment is for a non-compensable condition.

How to Get Authorization:

TREATMENT AUTHORIZATION IS CONTINGENT UPON:

Provision of diagnostic and monitoring information provided to WorkSafeNB (in the form of WorkSafeNB Ketamine/Esketamine Treatment Monitoring Program documentation), which must be completed by two independent professionals specializing in mental health agreeing and showing:

- The patient has met the eligibility criteria as a candidate for the treatment; and
- A comprehensive monitoring program has been established.

REVIEW BOOKLET CRITERIA FOR APPROVAL

Essential criteria to establish that the patient is a candidate for the treatment are:

- For clients diagnosed with TPI and ongoing Major Depressive Disorder as defined by DSM-5-TR criteria.
- When the obtained score on the Patient Health Questionnaire for Depression (PHQ-9) is indicative of moderately severe or severe depression (iscore > 15).
- When at least two 4-week trials of first-line psychotropics have been ineffective, as evidenced by a failure to achieve a greater than 5-point reduction from the baseline severity score on the PHQ-9.
- There should be documentation of medication adherence to the previous antidepressant trials. OR
- If the patient has a compensable diagnosis and is demonstrating active suicidality and is under the care of a psychiatrist, in which case an assessment for suicidality must be completed and confirmed in writing by an independent mental health professional on a three-month basis.

Safety and Monitoring During Administration

The WorkSafeNB Ketamine/Esketamine Treatment Monitoring Program allows for systematic documentation and review of the ketamine/esketamine treatment process. The physical and psychological monitoring and safety during each session are tracked in real-time, while ongoing monitoring and quarterly reviews ensure that the treatment is continuously evaluated for safety and efficacy.

The monitoring program documentation must include evidence of:

- A 4-week Induction Trial: Evidence of therapeutic benefit should be evaluated after the 4-week induction period to determine the need for continued treatment.
- Psychometric Monitoring of Depression: Standardized psychometric assessment of depression severity using the Patient Health Questionnaire for Depression (PHQ-9) should be conducted before initiating a trial of (es)ketamine with repeated assessments to monitor treatment response.
- Quarterly Progress Reports: Detailed reports every three months evaluating the client's progress, potential side effects, and overall well-being as demonstrated on repeat psychometric testing. Reports are to be formatted as specified in the WorkSafeNB Ketamine/Esketamine Review Booklet.
- Ongoing Approval: Continuation of (es) ketamine treatment is contingent upon clear benefits being demonstrated, reported, and maintained in the quarterly assessments. Maintenance therapy will require review by a WorkSafeNB medical consultant (relating to medication-related measures) and psychology consultant (relating to mental health-related issues and progress).

ADDITIONALLY:

- Ideally, the patient should be maintained on an oral antidepressant during treatment with (es)ketamine.
- While WorkSafeNB has set recommended standards relating to initial and continued authorization of (es)ketamine therapy, WorkSafeNB is not responsible for the credentials or accreditation of the provider or for review and assessment of adherence to clinical standards or for the provider's decision to administer the treatment.

Ketamine as a Treatment for Chronic Pain

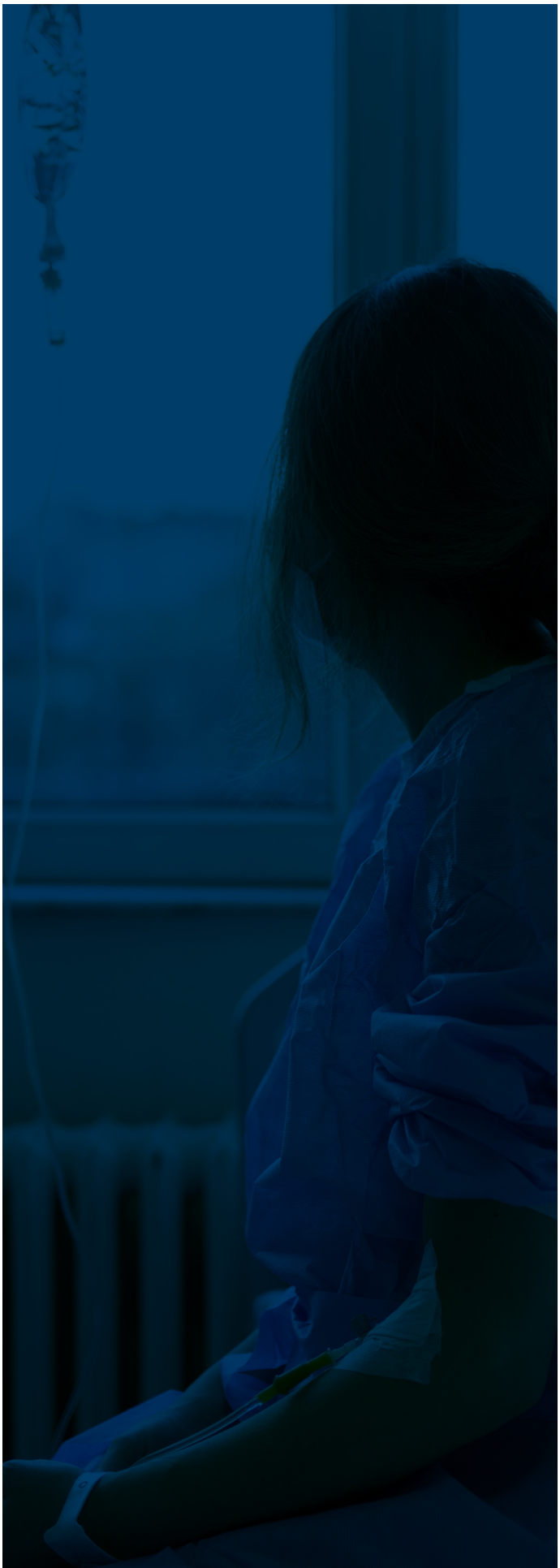
Ketamine hydrochloride (HCl) is also used to manage chronic pain conditions. It functions as an NMDA receptor antagonist and has shown efficacy in treating conditions such as Complex Regional Pain Syndrome (CRPS) and refractory neuropathic pain.

Chronic Pain Policy Ketamine for chronic pain is generally not recommended for routine treatment. Its use must be carefully reviewed and approved, with clear monitoring of functional outcomes as outlined in the chronic pain policy. Patients considered for ketamine treatment must meet specific criteria and demonstrate inadequate response to conventional treatments.

Exception: **Use as Anesthetic Agent**
An exception to the generally not recommended provision is the use of ketamine as an anesthetic agent within a hospital setting. In these cases, ketamine is used for its potent anesthetic effects, either as a sole anesthetic or as an induction agent before other general anesthetics.

RECOMMENDATION HIGHLIGHTS

- Ketamine is used for anesthesia and various pain-related indications.
- It interacts with opioid, monoaminergic, and muscarinic receptors, as well as voltage-sensitive calcium ion channels.
- Evidence supports its use for short-term analgesia in chronic pain refractory to conventional treatments.



Resources:

- The Canadian Network for Mood and Anxiety Treatments' 2016 Guidelines for Management of Adults with Major Depressive Disorders concluded that IV ketamine is a fast-acting and effective antidepressant but reserved its use as a third-line agent for severe symptoms, significant suicidal ideation or for treatment-resistant depression. (canmat.org/sdm_downloads/2016-depression-guidelines)

Canadian Agency for Drugs and Technologies in Health (CADTH) published their review of esketamine in April 2021. They recommended it not be reimbursed for the treatment of major depressive disorder, primarily due to a lack of high-quality evidence and uncertain balance between benefits and harms, but did not specifically make a recommendation for Treatment-Resistant Depression. (cadth.ca/esketamine-hydrochloride)

References

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