OBJECTIVES

- To direct health care professionals working in Addiction & Mental Health (AMH) on the use of intravenous (IV) ketamine for the treatment of depression in adult patients and in alignment with the Alberta Health Services (AHS) Provincial Drug Formulary.

APPLICABILITY

Compliance with this document is required by all Alberta Health Services employees, members of the medical and midwifery staffs, students, volunteers, and other persons acting on behalf of Alberta Health Services (including contracted service providers as necessary).

ELEMENTS

1. Points of Emphasis

1.1 This protocol applies to the use of IV ketamine for the treatment of depression in adult patients. It is not intended to provide direction on the use of ketamine for other indications, age groups or routes of administration.

1.2 AMH programs are required to follow established processes and seek approval from senior AMH Zone Leadership (i.e., Executive Director or Medical Director):

   a) prior to initiating IV ketamine for the treatment of depression in adult patients; and

   b) for the use of ketamine within AMH that may fall outside the parameters set in this protocol, such as in a research environment, which also requires ethics approval.
1.3 IV ketamine is an emerging treatment for major depressive disorder (MDD) and bipolar disorder (BP).

1.4 Ketamine is a high-alert medication. The AHS Management of High-Alert Medications Policy Suite shall be followed in AMH.

1.5 Ketamine has potential for addiction thus close monitoring is advised for patients with a history of substance use disorder who are receiving IV ketamine treatment.

1.6 Ketamine infusions are known to cause transient dissociation and increased blood pressure during infusion.

2. Inclusion Criteria

2.1 IV ketamine treatment shall only be administered to adult patients who undergo a psychiatric consultation and meet the following criteria:

a) a major depressive episode, with an emphasis on acute or potential suicidality or significant functional deficit; and

b) failure to respond to pharmacological treatment, with at least two (2) adequate trials of appropriate psychotropic medications.

3. Exclusion Criteria

3.1 Absolute exclusion criteria for IV ketamine treatment includes:

a) a primary psychotic disorder;

b) dementia/delirium;

c) uncontrolled severe hypertension;

d) pregnancy; or

e) an allergy to ketamine.

3.2 Relative exclusion criteria for IV ketamine treatment includes:

a) an unstable medical condition(s); or

b) a history of adverse reaction to ketamine.

4. Patient Consent and Education

4.1 The most responsible health practitioner or designate shall obtain informed consent from the patient before beginning IV ketamine treatment as per the AHS Consent to Treatment/Procedure(s) Policy Suite.
4.2 Patient and, as appropriate, family education shall be completed regarding the procedure, including written patient information.

4.3 The patient shall be informed that driving is prohibited for 14.5 hours after an infusion session and advised to make transportation arrangements to and from the appointment. The health care professional shall document the education and instruction provided in the health record.

5. **Pre-Infusion Session Preparation**

5.1 A Physician (or designate) shall perform an initial assessment of the patient prior to IV ketamine treatment, including but not limited to the following:

   a) physical examination;
   b) urinalysis;
   c) urine drug screen (as clinically indicated);
   d) blood work (i.e., AST, ALT, CBC, creatinine electrolytes, GGT, hCG);
   e) electrocardiogram (ECG);
   f) vital signs; and
   g) weight (within seven [7] calendar days of first treatment as dose is weight dependent).

5.2 A health care professional shall complete a mental health assessment of the patient one (1) week prior to the start of each course (i.e., six [6] to eight [8] infusion sessions) of IV ketamine treatment, including but not limited to the following:

   a) Quick Inventory of Depressive Symptomatology (QIDS);
   b) World Health Organization Disability Assessment Schedule (WHODAS 2.0); and
   c) Perceived Deficits Questionnaire (PDQ).

6. **Ketamine Infusion Session**

6.1 The health care professional shall:

   a) confirm the following was obtained and documented in the health record:
      
      (i) patient has provided informed consent in accordance with the AHS Consent to Treatment/Procedure(s) Policy Suite;
      
      (ii) initial assessment (as per Section 5.1 above);
(iii) mental health assessment (as per Section 5.2 above);
(iv) written order to provide IV ketamine treatment; and
(v) patient’s history of allergies and previous adverse reactions to sedatives;

b) obtain the following information from the patient and document in the health record:
   (i) all medications including prescribed, over-the-counter, herbal, vitamin, homeopathic, health remedies and substances for recreational use consumed within the preceding 24 hours of the infusion session;
   (ii) any benzodiazepines, sedatives and hypnotics consumed within the preceding 72 hours as they may affect treatment response to ketamine; and
   (iii) changes in perceived health status;

c) report any abnormalities or changes to the Physician; and
d) ensure appropriate monitoring equipment is readily available, set up and operational.

6.2 The Physician (or designate) shall:
   a) review the results of initial assessment;
   b) complete the Preprinted Order Set (PPO) for IV ketamine; and
   c) be available for consultation during each infusion session to address concerns as needed.

6.3 The Physician (or designate) shall take the following into consideration:
   a) ketamine is usually infused intravenously at a dose of 0.5 milligrams (mg) per kilogram (kg). Doses up to and including one (1) mg/kg of ketamine have been validated as safe and effective in research;
   b) ketamine infusions usually occur over 40 minutes. More rapid administration may result in respiratory depression and enhanced pressor response; and
   c) for each IV ketamine treatment, the patient usually receives two (2) to three (3) infusion sessions within seven (7) calendar days and an acute course would be six (6) to eight (8) infusion sessions. Frequency of the infusion session is determined by the treating Physician and on a case-by-case basis.
6.4 An independent double-check shall be completed prior to the administration of ketamine as per the AHS Management of High-alert Medications Procedure and AHS Independent Double-check Guideline.

6.5 The health care professional shall:
   a) establish a line for ketamine that will not be used for other medications;
   b) prime the IV line with sodium chloride 0.9% (i.e., normal saline);
   c) infuse IV ketamine as a secondary IV; and
   d) once the IV ketamine is finished, follow with at least 30 millilitres (mL) of sodium chloride 0.9%.

7. Monitoring

7.1 Monitoring of the patient’s response in comparison to their initial and mental health assessments (as per Sections 5.1 and 5.2 above) is required while receiving IV ketamine treatment.

7.2 During an infusion session, the health care professional shall monitor, assess and document the patient’s adverse effects (see Appendix A: Patient Reaction to Ketamine of this document), level of consciousness, oxygen saturation, respiration rate, blood pressure and pulse at:
   a) initiation;
   b) 20 minutes;
   c) 40 minutes; and
   d) one (1) hour post infusion session.

7.3 A health care professional shall complete a mental health assessment of the patient once a week during each course (i.e., six [6] to eight [8] infusion sessions) of IV ketamine treatment, including but not limited to the following:
   a) Quick Inventory of Depressive Symptomatology (QIDS); and
   b) Perceived Deficits Questionnaire (PDQ).

7.4 A health care professional shall complete the World Health Organization Disability Assessment Schedule (WHODAS 2.0) with the patient at the end of each course (i.e., six [6] to eight [8] infusion sessions) of IV ketamine treatment.

7.5 A Physician (or designate) shall complete the following assessments of the patient one (1) month after the first infusion session and every three (3) months ongoing:
   a) blood work (i.e., AST, ALT, CBC, creatinine electrolytes, GGT, hCG);
b) urinalysis;

c) urine drug screen (as clinically indicated); and

d) weight.

7.6 A Physician (or designate) shall complete the following every six (6) months after the first infusion session:

a) update of the patient’s history;

b) review and reconfirm consent documents; and

c) an electrocardiogram (ECG) for the patient.

7.7 A Physician (or designate) shall complete a physical examination annually after the first infusion session.

8. Documentation

8.1 Documentation shall be completed in accordance with the AHS Clinical Documentation Directive and AHS Clinical Documentation Process Directive.

DEFINITIONS

Adult means a person aged 18 years and older.

Family(-ies) means one or more individuals identified by the patient as an important support, and who the patient wishes to be included in any encounters with the health care system, including, but not limited to, family members, legal guardians, friends and informal caregivers.

Health care professional means an individual who is a member of a regulated health discipline, as defined by the Health Disciplines Act (Alberta) or the Health Professions Act (Alberta), and who practices within scope and role.

Health record means the collection of all records documenting individually identifying health information in relation to a single person.

High-alert medications means medications that bear a heightened risk of causing significant patient harm when used in error. (Institute for Safe Medication Practices [ISMP], 2012)

Independent double-check means a verification process whereby a second health care professional conducts a verification of another health care professional’s completed task. The most critical aspect is to maximize the independence of the double-check by ensuring that the first health care professional does not communicate what they expect the second health care professional to see, which would create bias and reduce the visibility of an error.

Informed consent means the patient’s agreement (or alternate decision-maker) to undergo a treatment/procedure after being provided, in a manner the patient can understand, with the
relevant information about the nature of the treatment/procedure(s), its benefits, potential risks and alternatives, and the potential consequences of refusal.

**Most responsible health practitioner** means the health practitioner who has responsibility and accountability for the specific treatment/procedure(s) provided to a patient and who is authorized by AHs to perform the duties required to fulfill the delivery of such a treatment/procedure(s) within the scope of their practice.

**Patient** means all persons, inclusive of residents and clients, who receive or have requested health care or services from Alberta Health Services and its health care providers. Patient also means, where applicable:

a) a co-decision-maker with the person; or
b) an alternate decision-maker on behalf of the person.

**REFERENCES**

- Appendix A: *Patient Reaction to Ketamine*
- Alberta Health Services Governance Documents:
  - Clinical Documentation Directive (#1173)
  - Clinical Documentation Process Directive (#1173-01)
  - Consent to Treatment/Procedure(s) Policy Suite (#PRR-01)
  - Independent Double-check Guideline (#PS-60-01)
  - Management of High-alert Medications Policy Suite (#PS-46)
- Non-Alberta Health Services Documents:
  - Clinical Protocol for Dose IV Ketamine (Covenant Health)
  - Nursing Guidelines for IV Ketamine (Covenant Health)

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APPENDIX A

Patient Reaction to Ketamine

The following is a list of potential transient side effects, reactions and adverse effects that a patient may experience during IV ketamine infusion sessions:

- **With rapid administration**
  - Respiratory depression and/or apnea, and hypertension, especially if dose is infused less than 60 seconds.

- **Common (more frequent)**
  - Abnormal body sensations (feeling strange or unreal)
  - Blurred vision
  - Dizziness
  - Dream-like state
  - Drowsiness
  - Drowsy or sleepy
  - Dry mouth
  - Headache
  - Hypertension
  - Increased pulse
  - Restlessness
  - Sensitivity to light and sound (i.e., changes in perception of stimuli)

- **Less common (less frequent)**
  - Bradycardia
  - Double vision
  - Hypotension
  - Nausea
  - Nystagmus
  - Rash or reddened skin
  - Vomiting

- **Rare**
  - Auditory and visual hallucinations (i.e., changes in perception of stimuli)
  - Cardiac arrhythmia
  - Confusion
  - Delirium
  - Excitement
  - Increased intracranial pressure
  - Irrational behaviour
  - Laryngospasm
  - Pain at injection site
  - Tremors