

TITLE

MANAGEMENT OF LOW-DOSE KETAMINE CONTINUOUS INTRAVENOUS INFUSIONS FOR ANALGESIA - ADULT

SCOPE

Provincial: Acute Care

DOCUMENT

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NOTE: The first appearance of terms in bold in the body of this document (except titles) are defined terms – please refer to the Definitions section.

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OBJECTIVES

- To standardize the administration of low-dose ketamine continuous intravenous (IV) infusions for acute **pain** management in adult **patients** being cared for in a hospital setting.
- To outline safe care and monitoring requirements of patients following the administration of low-dose ketamine continuous IV infusions for analgesia.

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 Procedure does not direct clinical practice in care areas where requirements for monitoring ketamine infusions may differ based on speciality and acuity (e.g., Intensive Palliative Care Units [IPCU], Emergency Departments, Intensive Care Units [ICU], Coronary Intensive Care Units [CICU], Cardiovascular Intensive Care Units [CVICU], Post Anesthetic Care Units [PACU], and Operating Rooms).
 - a) These clinical areas may determine the applicability of this Procedure, or parts of this Procedure, for patients receiving low-dose ketamine IV infusions for analgesia.

- 1.2 Refer to the AHS *Low Dose Ketamine Infusion for Analgesia – Adult, Acute Care Clinical Knowledge Topic* and the AHS *Provincial Parenteral Manual* for more information.
- 1.3 An **order** from an **authorized prescriber** with the **Acute Pain Service (APS)** or Anesthesia is required for:
- low-dose ketamine continuous IV infusion initiation, dose, parameters for dose adjustments, and discontinuation of infusion; and
 - all analgesics, antiemetics, antipruritics, and sedatives while the patient is receiving the low-dose ketamine continuous IV infusion.
- 1.4 Ketamine is a **high-alert medication** (refer to the AHS *Management of High-Alert Medications Policy Suite* and supporting resources for education on Insite).
- 1.5 An **independent double-check** (refer to the AHS *Independent Double-Check Guideline* and the AHS *Management of High-Alert Medications Policy Suite*) shall be performed when:
- preparing the medication (where applicable);
 - initiating the programming of the infusion;
 - changing the dose of the infusion (where applicable); and
 - changing the ketamine solution bag.
- 1.6 Independent double-checks may be performed for any change in **pump settings** (i.e., dose adjustments), or as determined by site processes or the **health care professional** (this is called a “second check” in Connect Care).
- The health care professional shall request a co-sign to document in Connect Care from another health care professional who is competent to administer low-dose ketamine continuous IV infusions.
- 1.7 Refer to the AHS *Vascular Access Device Infusion Therapy: Adult & Pediatric Clinical Care Topic*.
- 2. Health Care Professional Requirements**
- 2.1 Health care professionals performing activities related to the administration of low-dose ketamine continuous IV infusions shall follow regulatory and AHS organizational requirements for education and training. Zone requirements and/or educational resources are available on Insite.

3. Infusion Management Considerations

- 3.1 Prior to proceeding with low-dose ketamine continuous IV infusion therapy, the health care professional shall discuss with the patient:
- a) the expected effects of the treatment; and
 - b) the potential side effects including **psychotomimetic effects** with the patient (refer to Appendix A: *Potential Side Effects of Low-dose Ketamine Continuous Intravenous Infusion*). Explain that the patient may have dream-like sensations. Psychotomimetic effects may be reduced with low lighting and a quiet environment.
- 3.2 When managing low-dose ketamine continuous IV infusions, the health care professional shall:
- a) establish a maintenance line infusing concurrently to maintain patency of the venous access device;
 - b) assess each patient for pain using a valid **pain assessment tool** (refer to Appendix B: *Valid Pain Assessment Tools [Self Report – Unidimensional]*). A pain management plan and/or functional pain goal(s) should be established with the patient;
 - c) increase monitoring in patients receiving low-dose ketamine continuous IV infusion plus opioids as there is a greater risk for the patient to become over-sedated;
 - (i) Naloxone does not reverse ketamine but does reverse the effects of opioid-induced respiratory depression.
 - (ii) Ketamine can produce an opioid dose-sparing effect that may necessitate an opioid dose reduction.
 - (iii) Patients may need to be monitored for **withdrawal symptoms** with any opioid dose reduction.
 - d) deliver low-dose ketamine continuous IV infusion via the drug library of a SMART (Safer Medication Administration through Technology) infusion pump; and
 - e) verify low-dose ketamine continuous IV infusion pump settings and medication against the medication orders when assuming care of the patient at the beginning of the shift and with all transitions in care as per the AHS *Invasive Infusion Line and Tubing Verification Policy*.
- 3.3 If a patient experiences a clinical adverse event that could be attributed to the low-dose ketamine continuous IV infusion (including respiratory depression), the pump shall be sent to Clinical Engineering for investigation.

4. Infusion Preparation, Equipment, and Set-Up

- 4.1 Premixed ketamine solution for infusion may be provided by Pharmacy (refer to the AHS *Provincial Parenteral Manual*). Communication with Pharmacy is required to ensure a sufficient supply of the infusion solution or ketamine vials (if mixing) are available.
- 4.2 If mixing ketamine, the health care professional shall:
- a) store the vials in designated controlled substances storage and sign for them on the controlled substances record;
 - (i) The standard concentration is one milligram per millilitre (1 mg/mL).
 - b) prepare and clearly label a ketamine infusion bag.
- 4.3 The recommended dose is 0.1 – 0.3 milligrams per kilogram per hour (mg/kg/h). Select populations may require a higher dose as determined by the authorized prescriber.
- 4.4 Prior to programming the infusion pump, the health care professional shall obtain the patient's current weight (within 24 hours).
- a) Weight is required for the calculation of dosing. Use the actual body weight up to a maximum weight of 100 kilograms (kg).
 - b) For weights greater than 100 kg, use 100 kg to calculate the dose (i.e., if the patient weighs 175 kg, use 100 kg to calculate the infusion rate).
- 4.5 Equipment:
- a) ketamine solution bag labelled with the correct medication and concentration (concentration of 1 mg/mL for IV administration);
 - b) two (2) SMART infusion pumps, or one (1) SMART infusion pump with at least two (2) channels;
 - (i) One (1) pump/channel (with drug library) is dedicated to the low-dose ketamine continuous IV infusion and the other pump/channel is dedicated to the maintenance line.
 - c) two (2) port-less IV administration sets;
 - d) IV infusion bag of maintenance solution (dextrose 5% in water [D5W], or normal saline);
 - e) double lumen saline lock;
 - f) normal saline flush; and

g) lockbox (if applicable).

4.6 For set-up, the health care professional shall:

- a) prime one (1) port-less IV administration set with the ketamine solution and prime the other port-less IV administration set with a maintenance solution (D5W, or normal saline). Prime a double lumen saline lock / Y-connector;
- b) select the SMART pump/channel that will be dedicated to the low-dose ketamine continuous IV infusion and select ketamine from the drug library and program:
 - (i) drug amount (how many mg in IV bag) if applicable on SMART pump;
 - (ii) diluent volume (how many millilitres [mL] in IV bag);
 - (iii) patient's weight (to a maximum of 100 kg);
 - (iv) dose (in mg/kg/h according to orders); and then
 - (v) insert the tubing containing the ketamine solution into this pump.
- c) load and program the second pump/channel for the maintenance solution;
 - (i) The maintenance solution shall infuse to maintain patency of the venous access device.
- d) ensure a patent IV site is dedicated for low-dose ketamine continuous IV infusion;
- e) connect each of the two (2) administration sets (the ketamine tubing and the maintenance line tubing) to the primed double lumen saline lock that will attach to the patient's dedicated venous access device site;
- f) label each set of tubing with its respective contents in accordance with the AHS *Invasive Infusion Line and Tubing Verification* Policy; and
- g) close and lock the door to the ketamine lockbox (if applicable). Do not start ketamine infusion until Section 5 is completed.
- h) Refer to the following:
 - (i) *AHS Analgesic Intravenous Infusions Module*; and
 - (ii) *AHS Vascular Access Device Infusion Therapy: Adult & Pediatric Clinical Care Topic*.
 - (iii)

5. Infusion Initiation

- 5.1 The health care professional shall confirm the presence of complete medication orders from an authorized prescriber with APS or Anesthesia on the patient's **health record** (refer to the AHS *Medication Orders Policy Suite* and the AHS *Low Dose Ketamine Analgesia Infusion for Analgesia Adult Orders Form*).
- 5.2 The authorized prescriber with APS or Anesthesia shall include the following in the medication orders:
- a) medication;
 - b) concentration;
 - c) route;
 - d) mode of delivery (continuous infusion);
 - e) continuous rate dose (recommended dose is 0.1 – 0.3 mg/kg/h);
 - f) monitoring requirements;
 - g) naloxone, if the patient is on concurrent opioids; and
 - h) other medication(s) to manage potential side effects such as psychotomimetic effects.
- 5.3 In accordance with the AHS *Medication Administration Policy*, the health care professional shall confirm that **informed consent** (express or implied) for the treatment/procedure (including medications to be administered) was obtained from the patient, unless a valid exception to informed consent applies, as per the AHS *Consent to Treatment/Procedure(s) Policy Suite*.
- a) If it is determined that the patient lacks capacity to consent, the authority of an **alternate decision-maker** shall be recognized in accordance with the AHS *Consent to Treatment/Procedure(s): Adults with Impaired Capacity and Adults who Lack Capacity Procedure*.
- 5.4 Prior to initiation, the health care professional shall:
- a) complete the baseline assessment including but not limited to:
 - (i) pain score (refer to Appendix B: *Valid Pain Assessment Tools [Self Report – Unidimensional]*);
 - (ii) sedation level (refer to Appendix C: *Examples of Sedation Level Assessment Tools*);
 - (iii) respiratory rate;

- (iv) blood pressure;
 - (v) pulse; and
 - (vi) oxygen saturation level.
 - b) assess the patient to determine:
 - (i) their understanding of the education provided regarding the low-dose ketamine continuous IV infusion;
 - (ii) their ability to ask for analgesia; and
 - (iii) other actual or potential problems.
 - c) confirm patient identity and perform an independent double-check prior to starting the low-dose ketamine and maintenance infusions (refer to the *AHS Patient Identification Policy*).
- 5.5 Once Section 5 has been completed, the health care professional may start both infusions (ketamine solution and maintenance solution).

6. Assessment, Monitoring, and Maintenance

- 6.1 Ongoing monitoring sequence and assessment shall include pain score, sedation level, respiratory rate, pulse, blood pressure, and oxygen saturation level. The monitoring sequence should be ordered by the authorized prescriber as follows (refer to the *AHS Low Dose Ketamine Analgesia Infusion for Analgesia Adult Orders Form*):
- a) every 15 minutes for one (1) hour; then
 - b) every two (2) hours for four (4) hours; then
 - c) every four (4) hours for the duration of the infusion and 12 hours post-discontinuation of infusion.
- 6.2 The health care professional shall:
- a) follow the authorized prescriber's monitoring orders (refer to the *AHS Low Dose Ketamine Analgesia Infusion for Analgesia Adult Orders Form*);
 - b) repeat the monitoring sequence after increasing the infusion rate of ketamine, or after stopping for more than one (1) hour and then restarting the infusion; and
 - c) revise the pain management plan and goals according to patient response.

- 6.3 Patients receiving low-dose ketamine continuous IV infusions in addition to opioid medications may require monitoring and assessment that exceed the parameters identified in this Procedure. More frequent monitoring for sedation and/or apnea may be required for patients at risk.

7. Ketamine Continuous IV Infusion Discontinuation

- 7.1 The health care professional shall:
- a) confirm the presence of an order from an authorized prescriber with APS or Anesthesia for discontinuation of the infusion therapy is in the patient's health record; and
 - b) turn off the low-dose ketamine continuous IV infusion and disconnect the ketamine administration tubing set from the patient.
- 7.2 After discontinuation of the low-dose ketamine continuous IV infusion, the health care professional should:
- a) maintain IV access for eight (8) or 12 hours as ordered, after discontinuing the infusion;
 - b) assess pain frequently, according to patient response; and
 - c) continue monitoring every four (4) hours for 12 hours post-discontinuation, or as ordered and as warranted by the patient's condition and status.

8. Documentation

- 8.1 Health care professionals shall document all assessments, interventions, and responses to interventions in the patient's health record.
- 8.2 Initial documentation shall include the following:
- a) date and time of therapy initiation;
 - b) pain score and functional goal;
 - c) indication of the patient's level of understanding of the treatment, including awareness of the need to notify the health care professional of any psychotomimetic effects;
 - d) baseline assessment and vital signs; and
 - e) ketamine dose, infusion pump settings, and pump identification number.
- 8.3 Ongoing documentation shall include all of the following:
- a) assessments;

- b) changes to low-dose ketamine infusion dose;
 - c) patient teaching;
 - d) patient's response to therapy;
 - e) any unexpected/adverse findings, including interventions taken; and
 - f) communication with members of the health care team, including the **most responsible health practitioner (MRHP)**.
- 8.4 Record any rate changes to the low-dose ketamine continuous IV infusion as per documentation standards.
- 8.5 All independent double-checks shall be documented in the health record.
- 8.6 Record the pump identification number in the patient's health record and with any pump exchange.

DEFINITIONS

Acute Pain Service (APS) means all acute care physicians practicing within Acute Pain Service roles, and will include on-call anesthesiologists responsible for providing pain management options for patients, or other designated clinicians (e.g., Nurse Practitioner, Surgeon).

Alternate decision-maker means a person who is authorized to make decisions with or on behalf of the patient. These may include, specific decision-maker, a minor's legal representative, a guardian, a 'nearest relative' in accordance with the *Mental Health Act* (Alberta), or an agent in accordance with a Personal Directive, or a person designated in accordance with the *Human Tissue and Organ Donation Act* (Alberta). This also includes what was previously known as the substitute decision-maker.

Authorized prescriber means a health care professional who is permitted by federal and provincial legislation, their regulatory college, Alberta Health Services, and practice setting (where applicable) to prescribe medications.

Health care professional means an individual who is a member of a regulated health discipline, as defined by the *Health Professions Act* (Alberta), and who practises 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 (MRHP) means the health practitioner who has responsibility and accountability for the specific treatment/procedure(s) provided to a patient and who is authorized by Alberta Health Services to perform the duties required to fulfill the delivery of such a treatment/procedure(s), within the scope of their practice.

Order means a direction given by a regulated health care professional to carry out specific activity(-ies) as part of the diagnostic and/or therapeutic care and treatment to the benefit of a patient. An order may be written (including handwritten and/or electronic), verbal, by telephone or facsimile.

Pain means a subjective experience encompassing both noxious sensation and suffering. Pain is best understood from the patient's perspective and description of that experience. The patient's experience of pain is expressed within the context of the illness, family, social network, community, culture, and spiritual orientation. The patient's pain affects this matrix of relationships and is in turn altered by them.

Pain assessment tool means a reliable and valid measurement tool used to assess pain intensity.

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.

Psychotomimetic effects means a psychological reaction that may occur during the administration of medications, such as vivid dreams, hallucinations, delirium, confusion, irrational behaviour and dysphoria.

Pump settings means the mode of delivery that is programmed into the SMART pump that may include but is not limited to the following: continuous rate, continuous plus bolus, intermittent bolus, clinician bolus, bolus dose, bolus lockout interval, and hourly limit.

Withdrawal symptoms means unpleasant physical and mental symptoms that occur when a person stops taking a substance their body is dependent on. Symptoms may include: irritability, diaphoresis, tremors, abdominal cramps, vomiting, diarrhea, rhinorrhea, gooseflesh.

REFERENCES

- Appendix A: *Potential Side Effects of Low-dose Ketamine Continuous Intravenous Infusion*
- Appendix B: *Valid Pain Assessment Tools (Self Report - Unidimensional)*
- Appendix C: *Examples of Sedation Level Assessment Tools*
- Alberta Health Services Governance Documents:
 - *Consent to Treatment/Procedure(s): Adults with Impaired Capacity and Adults who Lack Capacity Procedure (#PRR-01-02)*
 - *Consent to Treatment/Procedure(s) Policy Suite (#PRR-01)*
 - *Independent Double-Check Guideline (#PS-60-01)*
 - *Invasive Infusion Line and Tubing Verification Policy (#PS-15)*
 - *Management of High-Alert Medications Policy Suite (#PS-46)*
 - *Medication Administration Policy (#HCS-244)*
 - *Medication Orders Policy Suite (#PS-93)*
 - *Patient Identification Policy (#PS-06)*
- Alberta Health Services Forms:
 - *Low Dose Ketamine Analgesia Infusion for Analgesia Adult Orders Form (#20993)*
- Alberta Health Services Resources:
 - *Analgesic Intravenous Infusions Module*
 - *Low-Dose Ketamine Continuous Intravenous Infusion (Resource Manual)*
 - *Low Dose Ketamine Infusion for Analgesia - Adult, Acute Care Clinical Knowledge Topic*
 - *Provincial Parenteral Manual*
 - *Vascular Access Device Infusion Therapy: Adult & Pediatric Clinical Care Topic*

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APPENDIX A**Potential Side Effects of Low-dose Ketamine Continuous Intravenous Infusion**

<u>Central Nervous System:</u>	<ul style="list-style-type: none"> • Psychotomimetic effects • Impaired physical and mental abilities • Increased cerebral spinal fluid volume • Increased intracranial pressure • Nystagmus • CNS depression • Neuromuscular tonic-clonic movements • Tremors • Increased muscle tone • Diplopia • Pupil dilation • Sedation
<u>Cardiovascular:</u>	<ul style="list-style-type: none"> • Hypertension and tachycardia are common • Arrhythmia, hypotension, and bradycardia are less common
<u>Respiratory:</u>	<ul style="list-style-type: none"> • Rapid administration may cause respiratory depression or apnea. • Increase in bronchial secretions • Bronchodilation • Laryngospasm
<u>Ear, Nose, Throat:</u>	<ul style="list-style-type: none"> • Hypersalivation • Increased secretions
<u>Gastrointestinal:</u>	<ul style="list-style-type: none"> • Nausea • Vomiting
<u>Local:</u>	<ul style="list-style-type: none"> • Pain • Erythema • Irritation (tissue irritant)

Note: Most major complications related to low-dose ketamine infusion are a consequence of rapid administration or the use of concurrent opioids and may lead to respiratory depression.

APPENDIX B**Valid Pain Assessment Tools (Self Report - Unidimensional)**

Measure	Indicator	Considerations
Numeric Rating Scale (NRS)	<ul style="list-style-type: none"> • Asks patients to rate their pain from 0 to 10 • Scored 0-10 with the anchors of 0 being no pain and 10 being pain as bad as it can be 	<ul style="list-style-type: none"> • Used in adults, older adults • Well established evidence of reliability, validity and ability to detect change • Quick and easy to use
Modified Verbal Descriptor Scale (VDS)	<ul style="list-style-type: none"> • A list of adjectives used to describe different levels of pain intensity • 4 point (or more) VDS descriptors (e.g., no pain, mild, moderate and severe) 	<ul style="list-style-type: none"> • Used with adults to explain pain intensity (no pain is 0, mild is 1 to 3, moderate 4 to 6, severe 7 to 10) • Established validity and reliability
Faces Pain Scale - Revised (FS-R)	<ul style="list-style-type: none"> • Revised to be compatible with scoring with other self-rating scales • 6 gender neutral faces range from no pain to as much pain is possible • Scored 0 to 10 	<ul style="list-style-type: none"> • Intended for use in children and the elderly • Well established evidence of reliability, validity and ability to detect change • Quick and easy to use

Note: Other valid self-report unidimensional and multidimensional pain assessment tools are available. In addition, valid behavioural pain assessment tools are available for adults and elders unable to self-report pain.

APPENDIX C**Examples of Sedation Level Assessment Tools**

Measure	Indicator	Reference
Pasero Opioid-Induced Sedation Scale (POSS)	1 = Awake and alert 2 = Slightly drowsy, easily aroused 3 = Frequently drowsy, arousable, drifts off to sleep during conversation 4 = Somnolent, minimal or no response to verbal and physical stimulation S = Normal sleep, easy to arouse	Pasero C. Assessment of sedation during opioid administration for pain management. J PeriAnesthesia Nurs. 2009 Jun;24(3):186-90.
Richmond Agitation Sedation Scale (RASS)	+4 = Combative +3 = Very agitated +2 = Agitated +1 = Restless 0 = Alert and calm -1 = Light sedation -2 = Moderate sedation -3 = Deep sedation -4 = Unarousable	Ely EW, Truman B, Shintani A, Thomason JWW, Wheeler AP, Gordon S, et al. Monitoring sedation status over time in ICU patients: the reliability and validity of the Richmond Agitation Sedation Scale (RASS). JAMA 2003; 289:2983-2991.
Ramsay Scale (RS)	1 = Awake, patient anxious and agitated or restless or both 2 = Awake, patient cooperative, orientated and tranquil 3 = Awake, patient responds to commands only 4 = Asleep, a brisk response to a light glabellar tap or louder than usual conversation level 5 = Asleep a sluggish response to a light glabellar tap or loud verbal commands or strong glabellar tap 6 = Asleep, no response to a light glabellar tap or loud noise	Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxolone-alphadalone. BMJ. 1974; 2:656-659.

Note: Other tools are available to assess sedation level. These are examples of tools that are used in AHS settings. Refer to your program resources for instructions on assessment and documentation when using these or other sedation level assessment tool.