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An Advisory Opinion adopted by the Alaska Board of Nursing (AKBON) is designed to help guide emerging changes in nursing practice. While an advisory opinion is not law, it is the AKBON's official opinion on whether certain nursing procedures, policies, and other practices comply with the standards of nursing practice in Alaska. Facility policies may restrict practice further in their setting and/or require additional expectations related to competency, validation, training and supervision to assure the safety of their patient population and/or decrease risk. National evidence based standard references are included. The Alaska Board of Nursing publishes Advisory Opinions regarding safe nursing practice, in accordance with AS 08.68.100(a)(9).

OPINION: LOW-DOSE KETAMINE INFUSIONS IN NON-ACUTE CARE SETTINGS

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Within the Scope of Practice/Role of APRN RN LPN CNA

ADVISORY OPINION

The Board of Nursing has received several inquiries requesting information on the novel uses of low-dose ketamine infusions in non-acute settings in Alaska. Considering these requests, the complexity of patient assessments, interdisciplinary treatment decision-making, potential adverse reactions, advanced monitoring requirements, potential for abuse, and limited literature in respect to guidelines for practice and long-term outcomes^{6-10,35}, it is the Boards position that an advisory opinion is warranted at this time.

Conclusion Statement

This intravenous low-dose ketamine infusion advisory opinion addresses Advanced Practice Registered Nurse (APRN) prescription, administration, and oversite of administration aspects in non-acute care settings as well as Registered Nurse (RN) administration and facility recommendations.

Introduction:

Ketamine is approved by the Federal Drug Administration (FDA) as an intravenous anesthetic agent to be administered by anesthesia providers and has been used for this purpose since the 1960s.¹ However, due to its potential adverse psychomimetic reactions (dizziness, floating “out of body” experiences, dissociation, agitation, visual hallucinations, delusions, and delirium), Ketamine’s use as an anesthetic has had limitations.²⁻⁴ These central nervous system adverse reactions have also made Ketamine an attractive drug of abuse.^{3,5} Ketamine is a schedule III controlled substance regulated by the Drug Enforcement Agency (DEA), requiring a DEA registration for prescribing.

As such, APRNs prescribing low-dose ketamine infusions in the state of Alaska are required to have Prescriptive Authority in addition to their APRN license, a DEA registration number, and to be registered with the Alaska Prescription Drug Monitoring Program (PDMP).

- Federal Register: July 13, 1999 (Volume 64, Number 133) Rules & Regulations p. 37673-37675
- 08.68.705 Maximum Dosage for Opioid Prescriptions
- 12 AAC 44.445 Controlled Substance Prescriptive and Dispensing Authority

Over the last several decades, “off-label” uses for ketamine related to treatment of chronic/complex pain syndromes and specific psychiatric disorders have emerged. Multiple state boards of nursing have developed opinions/guidelines for this innovative practice, including Wyoming, Arizona, Kentucky, Texas, Minnesota, and New York.¹¹⁻¹⁸ Ketamine is not a first-line therapy for chronic pain or psychiatric management but may be considered by a patient’s interdisciplinary team after failure or limited response to traditional treatment modalities.^{18,22,23}

Low-dose ketamine infusions have found utility as an adjunct analgesic for the treatment of postoperative pain in opioid tolerant patients, neuropathic pain, chronic pain (complex regional pain syndrome, ischemic limb pain, phantom limb pain, fibromyalgia), and palliative/cancer pain. Ketamine has also been shown to assist in the treatment of depression and anxiety associated with chronic pain and other chronic illnesses as well as reducing the incidence and severity of opioid side effects, an important factor in patient compliance.^{2-6,20-23,25,27,35}

In addition to its analgesic properties, these Ketamine infusions are proving useful in the treatment of specific disabling psychiatric disorders (major depressive disorder – MDD, depressive episodes associated with bipolar disorder, treatment-resistant depression, suicidal ideations, mood disorders, and post-traumatic stress disorder – PTSD). A rapid and robust, although temporary, anti-depressive effects and potential improvement in mood and suicidal thinking have been demonstrated^{7-10,19-21,24,26-31,35}.

Ketamine Safety Profile:

Ketamine is a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist. These receptors play an important role in central nervous system sensitization, establishing ketamine’s role as an anesthetic. It also binds at other sites (opioid, monoaminergic, cholinergic, nicotinic and muscarinic receptors) attributing its other positive effects like analgesia and mood elevation as well as adverse effects such as tachycardia and psychomimetic effects.²⁰⁻²¹

Although low (sub-anesthetic) doses administered as infusions have been shown to be safe, the safety profile of prolonged ketamine use has not been established.^{6,8,23,29} Potential long-term effects on memory and cognition with use of ketamine in the treatment of chronic pain require further study and should be reserved only for therapy-resistant pain.²²⁻²³

Ketamine has minimal effect on the central respiratory drive when given slowly, although rapid IV injection may cause transient apnea, presenting a compelling argument for its administration by infusion pump only. Ketamine is associated with very few drug-drug interactions and no contraindications are currently known to exist when combined with antidepressants, benzodiazepines, or other psychotropic medications.²¹ The most common side effects include psychotomimetic, dissociative psychiatric symptoms, confusion, inebriation, dizziness, euphoria, elevated blood pressure and tachycardia.^{6,20,29-31} Ketamine can also have deleterious effects on liver and urinary tract function with repeated exposure. There may be a greater risk of ketamine-induced liver injury when infusions are prolonged or repeated over a short timeframe. Monitoring standards and plans for the management of these potential adverse events should be clearly delineated in facility policies and procedures.^{7,29}

Potential for Ketamine abuse and diversion is a widely recognized problem. There is legitimate concern with widespread use in the outpatient setting for physiological and psychological

dependence on ketamine. Appropriate patient screening should be conducted and caution taken when administering ketamine infusions due to the potential risk of abuse, addiction, or complications of long-term use.^{27,32,35} Proper drug disposal measures are important in the prevention of ketamine from being obtained illicitly.^{19,32,35}

Scope of Practice:

Advanced Practice Registered Nurse (APRN)

- The comprehensive scope of practice for all APRNs is determined by their respective national associations and not by the Board of Nursing (12 AAC 44.430). The prescribing and administration of low-dose ketamine infusions is clearly within the respective scopes of practice for the Psychiatric Mental Health APRN (PMHNP), Certified Registered Nurse Anesthetist (CRNA), and Advanced Certified Hospice & Palliative Nurse (ACHPN-APRN).
- Prescribing of low-dose Ketamine infusions should include an interdisciplinary team as appropriate and be patient-centered. The following areas should be considered when developing these teams.
 - Close collaboration regarding assessment, diagnosis, referral, and treatment plans between psychiatric clinicians/pain specialist and ketamine infusion providers is highly recommended³⁵
 - Informed consent should be obtained before treatment and include a clear description of the potential risks, benefits and alternative treatments in accordance with AS 09.55.556 (Informed Consent).
 - Coordination/Communication regarding screening, management, monitoring, management of adverse reactions, and follow-up throughout the treatment course
 - Patients should be engaged as part of the care team in shared decision making.
 - Efforts should be made to minimize the potential for adverse events through consideration of premedication, individualized patient therapy, and appropriate monitoring during the peri-infusion period
 - Consider basing infusion rates on ideal body weight when body mass index exceeds 30. Infusion rates can also differ based on other individual factors such as concurrent prescribed medications and drug history. Frequency and length of treatment should be individualized for each patient as determined by the interdisciplinary team³⁶
- Psychiatric Mental Health APRNs (PMHNP)³³⁻³⁴
 - Manage treatment of individuals who may benefit from low-dose ketamine infusion therapy through diagnosis, identifying areas of focus for care and treatment, and determining level of risk by incorporating knowledge of pharmacological, biological, and complementary interventions with applied clinical skills
 - Refer patients for ketamine infusions to LIPs (e.g., CRNAs) with education and training in the administration of low-dose ketamine infusion
- Certified Registered Nurse Anesthetist (CRNA)³⁴⁻³⁵
 - Educated/Trained in administration of ketamine for anesthesia and the management of complex pain patients and adjuvants to psychotherapy
 - CRNAs involved in this practice must demonstrate interdisciplinary relationships with psychiatric and pain specialists (as applicable) before incorporating administration of low-dose ketamine infusions for chronic pain and psychiatric disorders into their practice
 - When administering ketamine for the treatment of psychiatric patients, CRNAs should collaborate with providers who focus on diagnosing and

- treating psychiatric disorders (e.g., PMHNPs), receiving referrals to provide ketamine infusions to referred patients
- When administering ketamine for the treatment of chronic pain patients, CRNAs should practice within their identified scope of practice, demonstrating additional education and training as necessary.
 - Treatment may include independent practice (i.e., CRNA owns/operates a pain clinic) or in collaboration with other providers (NP, GP, PA, etc...) who may refer patients to a CRNA for the ketamine infusion in the treatment plan for a patient
- CRNAs role in the infusion therapy may include and is not limited to: reviewing health records, pre-infusion assessment, history and physical, ordering/evaluating diagnostic tests as needed, ordering/prescribing adjunct medications, initiating the infusion, monitoring the patient, post-infusion assessment, and managing infusion-related adverse events or complications
- Advanced Certified Hospice & Palliative Nurse (ACHPN-APRN).³⁷
 - Educated/Trained in use of ketamine infusions for refractory and complex pain syndromes and end of life care. ACHPN-APRN should practice within their identified scope of practice, demonstrating additional education and training as necessary.
 - ACHPN-APRN involved in this practice must demonstrate interdisciplinary relationships with pain specialists (as applicable) before incorporating the administration of low-dose ketamine infusions into their practice.
 - ACHPN-APRN role in the infusion therapy would include, but is not limited to: reviewing health records, pre-infusion assessment, history and physical, ordering/evaluating diagnostic tests as needed, and ordering/prescribing ketamine infusions, and adjunct medications. Administration of the ketamine infusions including the monitoring the patient, post-infusion assessment, and managing infusion-related adverse events or complications may also be included in their role with the appropriate education/training.
 - The requirement for LIP to be “readily available” in General Recommendations 3(d) can be waived for palliative and end of life care due to the nature of the administration of higher doses.

Registered Nurse (RN)

- An RN must acquire and demonstrate the knowledge and skills essential to safely administer ketamine in sub-anesthetic doses (low-dose intravenous infusion).
- If a patient’s condition requires doses greater than 0.5-1.0mg/kg over \geq 40minutes, it would be prudent to consider administration or close supervision (“immediately available”) by an appropriately educated/trained LIP. Again, this requirement can be waived in palliative and end of life care.
- It is within the RN Scope of Practice to administer low-dose ketamine infusion for the following purposes when the General Requirements below are met:
 - Analgesia for postoperative, neuropathic, chronic and palliative/cancer pain
 - Anti-depressive and specific treatment outcomes for currently accepted psychiatric diagnosis (MDD, depressive episodes associated with bipolar disorder, treatment resistant depression, suicidal ideations, mood disorders, and PTSD). The BON recognizes that this is an evolving practice in the field of mental health and that the

list of accepted diagnosis that may benefit from low-dose ketamine infusions may enlarge as new applications emerge.

- Psychiatric Mental Health Registered Nurse (PMH RN)³¹
 - Educated/Specializes in promoting mental health through nursing assessment, diagnosis, and treatment of behavioral problems, mental disorders and comorbid conditions across the lifespan

General Recommendations for the Safe Administration of Low-Dose Ketamine Infusions:

1. Organizations providing low-dose ketamine infusions must maintain written policies and procedures
 - a. Policies and procedures should specifically address how to deal with emergency situations requiring an advanced level of care (e.g., ACLS and psychiatric emergencies)
 - b. A specific policy should be established by the organization addressing the procedures for obtaining, storing, wasting, and disposing of ketamine (abuse/diversion protection) – This policy should adhere to all applicable state and federal laws
 - c. A specific policy should be established to support continuous quality improvement efforts to improve processes and patient outcomes
 - d. The involvement of skilled psychiatric mental health nurses in the treatment monitoring and management of patients receiving ketamine infusions can be very beneficial considering the potential for psychiatric adverse effects such as dissociation, agitation, and out-of-body experiences that can be distressing to patients. These potentially “adverse effects” are at times expected in these patients related to medications and disease processes. Infusionist should consider training with PMHNP or mental health experts regarding these effects and the appropriate management techniques.
 - e. Discharge criteria should also be clearly delineated in policy (i.e., how long patients should be monitored after infusions before releasing them from care).
2. Licensed Independent Practitioner (LIP) prescribing the low-dose ketamine infusion – those specializing in complex pain management or psychiatric disorders
 - a. Evaluate, diagnose, and develop treatment plan for the patient
 - b. Place the order for low-dose ketamine infusion (currently recommended in the literature not to exceed 0.5-1.0 mg/kg infusion over $\geq 40\text{min}$) as defined by the organizations policy
 - i. The board recognizes providers may use clinical judgement and experience to make dose adjustments outside of this current recommendation based on patient disease processes, concurrent medications, and tolerance issues. If doses outside of this range are required, the organization should have specific policies delineating safety mechanisms in place to ensure the continued safety of the patient (e.g., LIP must be present for the entire treatment).
 - c. Must be readily available for consultation with administering LIP for adverse events specifically related to patients underlying disorder (e.g., psychotic or manic thoughts during the course of treatment, emergence or worsening of suicidal thoughts, or emotional distress) and other potential adverse outcomes related to the infusion
 - i. Collaborative relationship with psychiatric experts in management of these events during infusions and follow-up strategies are highly recommended. This can be the referring LIP or a qualified representative (partner in practice or other qualified LIP covering call for the prescribing LIP)
3. LIP managing administration of the low-dose ketamine infusion:

- a. To be administered by continuous infusion pump only (NO BOLUS doses)
 - b. Evaluate patient pre and post infusion
 - c. Supervise staff administrating the infusion as applicable (i.e., RN administration)
 - d. Must be readily available in the facility from the time the medication is initiated until the completion of the infusion and the patient is considered returned to baseline health and ready for discharge
 - e. Manage any adverse outcomes while patient is receiving the infusion, including advanced level of care or consulting with psychiatric and pain specialists as applicable
4. Documentation of annual RN competency training should include but is not limited to:
- a. Ketamine – classification, preparation, onset, duration, desired effect, indications, contraindications, medication interactions, side effects, and adverse reactions
 - b. Nursing responsibilities of assessment, monitoring, and documentation
 - c. Anatomy/Physiology, basic airway management (oral airways, bag-valve-mask apparatus, oxygen delivery), and emergency equipment and procedures
 - d. Use of specialized monitoring equipment, sedation scale, pain scale, and infusion pumps
 - e. Level of sedation (minimal, moderate, deep, general anesthesia) with an emphasis on *minimal only* with low-dose ketamine infusions
 - f. Recognition of potential clinical complications and appropriate nursing interventions
5. Level of sedation is monitored and documented with a validated sedation scale (e.g., Richmond Agitation Sedation Scale)
6. Compounded infusions (those mixed by the LIP or RN for administration) must be for “immediate use” and must be started within one hour (USP 797 standards). Infusions prepared by a pharmacist will be subject to applicable organization pharmacy policies and procedures
7. Infusion is administered by an IV infusion pump in a dedicated line to prevent inadvertent boluses of ketamine
8. Ketamine is a schedule III drug and as such state and federal regulations require organizations to have systems in place to guard against theft and diversion (Controlled Substance Act, DEA regulations – CSA Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970; US Department of Justice DEA Diversion Control Division). Joint Commission reference –
<https://www.jointcommission.org/resources/news-and-multimedia/newsletters/newsletters/quick-safety/quick-safety-48-drug-diversion-and-impaired-health-care-workers/>
9. An ACLS certified provider is available in the facility throughout the infusion and until discharge – all staff will have current BLS certification
10. Continuous monitoring includes electrocardiogram (for patients at increased risk of cardiovascular events or with higher dosing), oxygen saturation, blood pressure (may be intermittent according to facility policy), respiratory rate, temperature (when appropriate) and level of sedation immediately prior to, during and following the infusion until the patient returns to pre-infusion baseline and meets discharge criteria
11. RNs have the right and obligation to refuse to administer Ketamine in doses that may induce moderate or deep sedation or general anesthesia
12. Emergency equipment necessary to provide ACLS level of care (e.g., advanced airway, cardiac monitor with defibrillator/AED, oxygen source, emergency medications, etc...) must be operational and immediately available

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