Alabama State Board of Medical Examiners

Position Statement on the Off-Label Use of Ketamine for the Treatment of Treatment-Resistant Depression in Outpatient Settings

The Alabama State Board of Medical Examiners ("the Board"), the licensing and regulatory agency for physicians and osteopaths, is charged with protecting the health and safety of Alabama patients. In furtherance of this duty, the Board attempts to ensure that only those physicians who hold a valid medical license practice medicine in the state. The practice of medicine means "[t]o diagnose, treat, correct, advise, or prescribe for any human disease, ailment, injury, infirmity, deformity, pain, or other condition, physical or mental, real or imaginary, by any means or instrumentality." Ala. Code § 34-24-50.

Recent national trends in the off-label use of ketamine have created situations in which non-physician healthcare providers are prescribing and administering ketamine in outpatient settings for the treatment of treatment-resistant depression ("TRD"). Ketamine is a Schedule III controlled substance approved by the United States Food and Drug Administration ("FDA") for the induction and maintenance of general anesthesia. Though research is showing efficacy, ketamine, with the exception of intranasal esketamine (SPRAVATO®), is not currently FDA approved for the treatment of any mental health condition, including TRD, post-traumatic stress disorder or severe suicidal ideation.

It is the position of the Board that the off-label use of ketamine in Alabama for TRD constitutes the practice of medicine. Prior to the administration of ketamine one must obtain written informed consent, conduct a comprehensive history and physical, determine whether a patient is an appropriate candidate for the drug, advise patients how to utilize the drug in treatment of TRD, prescribe and administer the drug, and monitor the patient for adverse reactions.

Only a licensed physician may prescribe ketamine due to the complexity and risks associated with use of the anesthetic agent. When a physician prescribes ketamine for TRD, other licensed professionals may assist in its administration as long as the prescribing physician remains onsite and the licensed professional is under the physician's supervision. The safety requirements governing the use of moderate sedation described in Ala. Admin. Code r. 540-X-10-.06 must be followed when administering ketamine outside of a hospital setting.

There is a substantial risk of harm to the patient whenever ketamine is used. Administration of the drug can lead to life-threatening consequences including respiratory failure, cardiac events and seizures. Physicians using the anesthetic agent for the treatment of TRD in outpatient settings should take all necessary precautions to avoid any untoward event and should consult the guidelines issued by the Board.

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Guidelines for the Off-Label Use of Ketamine for the Treatment of Treatment-Resistant Depression[1] in Outpatient Settings[2]

Who Can Prescribe?

Ketamine must be prescribed by a physician who holds an active license to practice medicine in Alabama. The physician must be trained in the use of ketamine and the diagnosis and treatment of treatment-resistant depression ("TRD"). If the administering physician is not a psychiatrist, a diagnosis of TRD must be confirmed by a psychiatrist prior to initiating treatment.

Patient Selection[3]

Patients must have a current diagnosis of major depressive disorder as defined by The Diagnostic and Statistical Manual of Mental Illnesses (DSM-5-TR) OR have major depressive disorder with suicidal ideation for which a rapid treatment onset is important.

Ketamine should not be used as a first-line treatment for depression. Ketamine should only be considered after a failed response to an adequate trial of at least two antidepressants from at least two different antidepressant classes of adequate dose and duration. Whether ketamine is an appropriate treatment for a particular patient shall be determined by clinical interview or use of a standardized depression scale.

Exclusion Criteria

Ketamine should not be administered to patients with a current diagnosis or history of schizophrenia, schizoaffective disorder, patients with current uncontrolled hypertension, patients who are pregnant, or patients who have had previous serious adverse effects to ketamine. Ketamine

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[1] These guidelines apply only to the off-label use of racemic ketamine for treatment-resistant depression and not the administration of intranasal esketamine (SPRAVATO®) when used in accordance with FDA guidelines.

[2] These guidelines do not apply to anesthesiologists administering ketamine for the induction and maintenance of anesthesia in a hospital setting or to physicians administering ketamine for palliative care.

[3] The Board developed these guidelines after review and consideration of *Ketamine Infusion for Treatment Resistant Depression and Severe Suicidal Ideation*, the National Protocol Guidance published by the Department of Veterans Affairs in February 2022.

should not be used in individuals with previous or current ketamine use disorder. Physicians must use extreme caution when using ketamine in individuals with a history of or active substance use disorder. Physicians should not administer ketamine to patients who are acutely intoxicated.

Required Medical Screening

Physicians must obtain written informed consent, a complete history and physical, including a history of previous antidepressant use, conduct a physical examination, obtain a urine toxicology screen, and obtain informed consent prior to the administration of ketamine. Physicians should prescribe the minimum dose necessary to achieve the desired clinical effect.

Requirements for Location of Administration, Monitoring and Recovery

Ketamine should be administered in a space large enough to accommodate the patient and required personnel.

Ketamine should be administered in a facility which has the means to monitor a patient's heart rate, blood pressure, respiratory rate and oxygen saturation level. Oxygen and medications must be available in the event of sustained alterations in cardiovascular function or potentially dangerous behavioral symptoms by the patient during treatment.

A crash/code cart must be readily accessible.

The prescribing physician must be ACLS certified and trained to establish an airway if necessary.

When a physician prescribes ketamine for TRD, other licensed professionals may assist in the administration of ketamine and psychotherapy as long as the prescribing physician remains onsite and the licensed professional is under the physician's supervision. Licensed professionals who assist in the administration of ketamine must also be ACLS certified.

The prescribing physician or ACLS certified licensed professional must be present during the administration of ketamine. The patient should remain at the outpatient setting for monitoring. The physician must monitor the patient for at least two hours after the administration of ketamine. The physician must monitor the patient's blood oxygen saturation level, blood pressure and heart rate every five to fifteen minutes, and monitor the patient's level of consciousness / mental status by watching for signs of dissociation or distress. The monitoring of the patient can be delegated to other licensed professionals as long as the physician remains onsite.

The physician should have patients complete a questionnaire such as the Patient Health Questionnarie-9 in order to evaluate whether ketamine is providing the desired response. The physician should discontinue use of the anesthetic agent if the patient shows no improvement after a reasonable trial of four to six infusions.

Treatment by psychotherapy should be considered in tandem with ketamine administration.

Dosing and Titration

The physician must determine the appropriate dose for each patient. The most common dose is 0.5 mg/kg of body weight administered by IV infusion over 40 minutes. Higher doses may be more likely to result in adverse cardiovascular effects.

Ketamine infusions should not be given more than twice a week.

Safety Precautions

A physician should never allow the patient to administer ketamine for psychiatric reasons at home and should never allow a family member to monitor the patient.

The infusion should be discontinued if there is a significant increase in blood pressure or heart rate, the patient develops respiratory symptoms such as shortness of breath or wheezing, or if there is evidence of cardiac involvement.

After an infusion of ketamine, the patient should not drive or operate machinery for the remainder of the day.

The patient must be driven home by a caregiver.