



CONCERNS & RECOMMENDATIONS FOR SAFE & EFFECTIVE AT-HOME KETAMINE PRESCRIPTIONS

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Amidst increased public interest and controversy around at-home ketamine, including recent reports that some telehealth companies offer self-administered subcutaneous treatment, the [American Society of Ketamine Physicians, Psychotherapists & Practitioners \(ASKP3\)](#), the largest society and think tank for ketamine practitioners, is releasing a summary of guidelines for at-home use. The aim is to underscore the importance of responsible treatment and emphasize the significance of safety and proper patient selection.

AT-HOME KETAMINE VIA UNSAFE DELIVERY METHODS

When administered correctly and with supervision, ketamine is often one of the only solutions for patients suffering from chronic suicidality, treatment resistant depression, PTSD and chronic pain. ASKP3 maintains its long-standing position that ketamine is most appropriate in medically-supervised settings, though we acknowledge that there are some situations in which it may be appropriate for a clinician to prescribe compounded oral or sublingual ketamine for use at-home between face-to-face appointments.

However, ASKP3 has become aware of at least one telehealth company offering liquid injectable ketamine with syringes intended for subcutaneous delivery in unsupervised, at-home settings on an ongoing basis. For a number of reasons, we do not feel there is adequate evidence or research to support this practice as safe and appropriate as at-home administration. While we do believe subcutaneous delivery shows promise, subcutaneous injection of ketamine can be harmful to patients, and poses substantial risk for misuse, abuse and diversion.

Regarding potential for direct harm, current liquid ketamine formulations have a pH that is more acidic than orange juice, and a high osmolality that is approximately 60% of the salt content of ocean water. Off-label injection into delicate subcutaneous tissues can cause a sterile abscess that is painful and can last for weeks. The lesion can even resemble a burn, with reports in the research community that post-infusion lesions have required surgical intervention. A consistently safe subcutaneous ketamine formulation would need to address these issues, which is arguably one of the reasons ketamine was never FDA approved for this route of administration.

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In addition, for long-term viability, injectable ketamine for use at home should be delivered via a tamper resistant device that is difficult to misuse, abuse, share or divert. Sending syringes and liquid ketamine to patients for home use is substantially outside of community standards and is highly risky at both the individual and community level. This practice will undoubtedly put patients, the community, and this important mental health movement at risk. In addition, it presents substantial medical-legal risk for prescribers and the companies encouraging such treatment recommendations.

ASKP3 RECOMMENDATIONS FOR ORAL AT-HOME KETAMINE PRESCRIPTIONS

Practice [standards and ethics](#) were produced by ASKP3 in 2020 with iterative input from more than 500 members, including some of the world's top doctors, clinicians and therapists administering ketamine for psychiatric and pain indications.

The following is meant to provide additional context and recommendations based on current events and concerns. These include best practices for: dosing, environment, delivery mechanism, contraindications, and patient-physician communication.

TREATMENT GUIDELINES & CONTRAINDICATIONS

Patients who have previously undergone supervised, in-office ketamine treatments and have been observed without any complications may be potential candidates for at-home oral ketamine therapy. However, many factors need to be considered before a provider can make such a determination. Substance use disorders or excessive alcohol use, psychosis, history of mania, uncontrolled hypertension, and history of any intracranial hemorrhage or aneurysm are relative contraindications for at-home ketamine. It is imperative to review concomitant medications, both prescribed and over-the-counter, and counsel patients not to combine ketamine with alcohol or non-authorized medications or substances.

The goals of an at-home oral ketamine protocol should be clearly defined with the patient and determined to be appropriate and medically necessary. For example, a protocol might be initiated to extend the benefits of in-office ketamine treatment. However, prescribers should first explore other methods to extend the effects of in-office ketamine treatment before at-home ketamine is prescribed.

DELIVERY

Oral ketamine in the form of sublingual (SL) lozenges and rapid disintegrating tablets are currently a common route of administration (ROA) prescribed for at-home use. Oral dosing can



also be a viable ROA, especially in pain conditions where frequent doses are often needed. SL is the most common ROA being prescribed by telehealth

companies providing ketamine prescriptions without in-office assessment of patients and ketamine safety and efficacy. Compared to parenteral (i.e., intravenous, intramuscular and subcutaneous) routes of administration, oral preparations are likely the safest and most viable option for at-home ketamine when prescribers are seeking to balance dosing, safety and efficacy.

Even within this relatively safe ROA for treatment, however, outlying protocols that are dangerous to patients and facilitate drug diversion do exist. Some patients are being prescribed very high dose SL formulations – reported in the community to be in excess of 1200 mg/dose – with instructions to spit out the drug after a set time period. Accidentally swallowing a full dose would be very dangerous, even deadly, due to the extreme strengths prescribed. In addition, easy subversion of the “hold and spit” protocol to “hold and swallow” is an obvious way to get a more pronounced effect from each dose, which can directly enable misuse, abuse and diversion to the community. As such, ASKP3 believes this is a highly risky protocol that puts both patients and the community at risk.

PHARMACOKINETICS

Regardless of safety and efficacy, off-label, compounded forms of oral ketamine are less researched than intravenous (IV) ketamine, and are generally accepted as less precise and perhaps less effective for a number of key reasons:

1. **Bioavailability:** Oral and sublingual ketamine has lower bioavailability compared to IV administration. When taken by these routes of administration, ketamine undergoes significant breakdown in the liver, called first-pass metabolism. This reduces the amount of active drug reaching systemic circulation.
2. **Onset and Duration:** Oral and sublingual ketamine are more variable in both onset and duration compared to IV ketamine, which is 100% bioavailable, acts quickly and is highly predictable.
3. **Dosing:** Because of low bioavailability and inter-person variation in liver metabolism, high and varying doses of oral ketamine are often required to achieve similar effects to IV ketamine, which can increase the risk of side effects due to long acting metabolites.

While oral and sublingual ketamine can be effective for some conditions, particularly chronic pain and certain psychiatric disorders, its effects are generally less potent, less durable and less predictable than IV, IM, or intranasal ketamine and esketamine.



ENVIRONMENT

The patients prescribed at-home ketamine should be given clear instructions about the appropriate at-home environment and need for secondary support. Essential

considerations include not being alone, not being responsible for the care of others (e.g. children, elderly, the disabled), and not needing to drive for the remainder of the day. The environment should be safe, familiar, and comfortable, with minimal distractions and obligations. An emergency plan should be discussed with a responsible adult who should be present at the time of treatment.

MITIGATING ADDICTION RISK

Patients with a recent history of substance abuse should not be prescribed an at-home ketamine protocol without a serious risk-benefit analysis. To further mitigate risk of abuse, physicians should start with a low dose and increase slowly only as indicated to achieve a balance of safety and efficacy. Prescriptions should authorize only what is needed between points of contact or other appropriate clinical intervals. Patients should strictly follow the dosing instructions provided by the prescriber and not adjust dosing and frequency without discussing changes with their treatment team.

PATIENT-PHYSICIAN COMMUNICATION

An initial consultation and risk assessment should be performed in person. The patient should be sent home with clear instructions regarding dose and frequency, safety considerations and guidance regarding when treatment is appropriate. Patients should be given instructions on safe storage to minimize diversion and to keep the medication away from children or pets. Clinical follow-up through various means, and the frequency of in-person follow-up assessments, should occur in the context of an established provider-patient relationship and meet community standards-of-care and state guidelines for prescribing controlled substances.

A PLEA FOR INSURANCE COVERAGE

ASKP3 postulates that many patients seek treatment through online companies, which often cost less and provide less medical supervision and patient-physician communication than in-person office settings, due to lack of insurance coverage for IV ketamine infusions. This cost burden on patients creates a notable lack of affordability and restricted access to medically supervised ketamine infusions. Given the body of evidence supporting IV ketamine for appropriate pain and mental health disorders, ASKP3 requests medical insurance companies examine and revise benefit plans and initiate prior authorization processes for this important evidence-based



treatment for patients who: a) are in need of effective treatment; b) have an appropriate psychiatric or pain diagnosis, and; c) will be monitored during treatment by clinicians with reasonable training and education to safely administer and monitor treatment.

“Home use can increase access and act as an adjunct to in-office treatments, but it does not increase equitable access to some of our most vulnerable populations without necessary funds. Even telehealth services are often substantially out of reach for society’s least privileged. Equitable access can only improve with insurance coverage. ASKP3 believes that this is an appropriate next step in the evolution of this essential treatment, which is supported by Phase II clinical evidence confirming a high efficacy and safety profile when used at appropriate intervals in supervised settings,” says Sandhya Prashad, MD, Founding Member & President, ASKP3.

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