KETAMINE (Ketalar) Fact Sheet [G]

Note: See esketamine fact sheet in this chapter for information on FDA-approved esketamine.

Bottom Line:
Ketamine is an intravenous (IV) agent that appears uniquely effective for patients who need an ultra-rapid antidepressant, such as patients who are acutely suicidal. Its disadvantages are that it is not FDA approved for depression, and that it requires close medical monitoring during administration.

FDA Indications:
Anesthesia.

Off-Label Uses:
Major depression, chronic pain, severe agitation (eg, in the ICU).

Dosage Forms:
Vials for injection (G): 10 mg/mL, 50 mg/mL, 100 mg/mL.

Dosage Guidance:
- Most commonly used dose in depression trials: 0.5 mg/kg given IV over 40 minutes, which is lower than the typical anesthetic dose (2 mg/kg).
- Administration may be repeated periodically, though there is no clear guidance regarding how often it should be given, nor how many total infusions should be given. Currently available data and clinical practice suggest dosing two to three times weekly over two to four weeks.

Monitoring: ECG, blood pressure, and oxygen blood saturation are typically monitored during infusion because of concerns regarding spikes in blood pressure and heart rate.

Cost: $$$$$

Side Effects:
- Most common: Confusion, blurred vision, poor coordination, feeling weird or spaced out, cardiac issues (30% of patients in three clinical trials experienced a spike in blood pressure over 180/100 mmHg and heart rates over 110 beats per minute, but vital signs normalize quickly).
- Serious but rare: Serious reactions (dream-like states, delirium, respiratory depression) are typically associated with higher (anesthetic) doses.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- N-methyl-D-aspartate (NMDA) receptor antagonist.
- In one recent study, co-administration of ketamine with naltrexone (an opiate blocker) prevented its antidepressant effect, implying that ketamine may work in part via opioid receptors (Williams NR et al, *Am J Psych* 2018;175(12):1205–1215. Epub 2018 Aug 29).
- Non-CYP450 metabolism; t ½: 2.5 hours.

Clinical Pearls:
- Efficacy: Meta-analyses of placebo-controlled trials have reported that IV ketamine has an ultra-rapid antidepressant response (at 40 minutes) but that the response attenuates over the course of about one week (Kishimoto T et al, *Psychol Med* 2016;46(7):1459–1472. Epub 2016 Feb 12). Relapse rates are up to 90% four weeks following the ketamine treatment.
- May be as effective as ECT according to a recent open-label randomized trial (Anand A et al, *N Engl J Med* 2023;388(25):2315–2325).
- Continuation therapy appears to be effective, with one study showing robust improvement over placebo after 15 days when ketamine was administered two or three times per week.
- The most common patient experience seems to be a sense of dissociation or disconnection from their bodies, lives, and problems. The therapeutic effect may relate to being able to more objectively examine the sources of their psychic pain.
- Can be prescribed in an intranasal formulation, available from compounding pharmacies (but we recommend using esketamine product formulated for nasal administration).

Fun Fact:
Ketamine was developed in the 1960s and gained a reputation as an unusually safe anesthetic, because it did not slow down breathing or lower blood pressure. For that reason, it was implemented as a "buddy drug" in the Vietnam War, when each soldier carried a vial of ketamine for use in case another soldier required it while awaiting transport to a field hospital.