

Ketamine Parenteral and Oral Dose Recommendations

- Pharmacology
 - Inhibits glutamate binding to NMDA-R receptor; activity at norepinephrine, serotonin, and muscarinic cholinergic, kappa opioid, and voltage-sensitive calcium channel receptors
- Pharmacokinetics
 - Lipophilic; Crosses blood brain barrier
 - **Protein binding:** 47%
 - **Onset of action:** 1-5 min IV/IM, 15-30 min SC; 30 min
 - **Plasma half-life:** 1-3 hrs (ketamine); 12 hrs (norketamine)
 - **Duration of action:** 4-12 hrs (oral); 10-15 min IV
 - **Metabolism:** N-demethylation via CYP2B6, CYP 2C8/9, CYP 3A4 substrates to norketamine (primary metabolite); norketamine metabolized via hydroxylation and conjugation
 - **Elimination:** Primarily hydroxylated or conjugated norketamine metabolites in urine; 4% unchanged ketamine or norketamine; <5% elimination in feces
- Drug Interactions
 - Increased ketamine levels with concurrent use of CYP2B6 or CYP2C8/9 inhibitors
- Adverse effects
 - **Central nervous system:** Alterations in body image/mood, floating sensations, vivid dreams, hallucinations, delirium, purposeless movement, drowsiness, increased intraocular pressure, increased intracranial pressure, increased muscle tone, memory impairment (long-term use)
 - **Gastrointestinal:** Nausea and vomiting, hepatic damage (long-term oral use)
 - **Cardiovascular:** HTN, tachyarrhythmias
 - **Misc:** lacrimation, salivation, ulcerative cystitis (long term oral use)

Route of Administration	Available Product	How product is stocked	Usual Doses
Oral	Compounded capsules	30mg, 60mg capsules	1mg PO Ketamine = 1mg IV Ketamine <ul style="list-style-type: none"> ● Reported Range: 0.3mg– 1.15mg PO Ketamine = 1mg IV Ketamine Administer in divided doses Q8h <ul style="list-style-type: none"> ● Reported Range: Q4h to Q12h If converting patients from Ketamine infusion to oral, administer first oral dose 4 to 8 hrs after infusion stopped <ul style="list-style-type: none"> ● May titrate every 48-72 hrs ● Typical starting dose in ketamine naïve patient: 10mg-30mg PO Q8h <ul style="list-style-type: none"> ○ Maximum Reported Oral Dose: 800mg/day

Route of Administration	Available Product	How product is stocked	Usual Doses
Intravenous or Subcutaneous	Compounded Infusion	Concentration: 2mg/ml Volume: 500mg/250ml in dextrose 5%	Bolus: 0.1mg/kg-0.4mg/kg Slow IV push Maintenance Infusion: 0.1 mg/kg/hr – 1mg/kg/hr <ul style="list-style-type: none"> Once pain stabilized, may titrate maintenance infusion by 0.05-0.1mg/kg/hr every 24 hrs Due to lack of concrete data, recommend conservative initial doses and dose titrations Maximum Reported Parenteral Dose: 3600mg/day

Example of an IV to Oral Ketamine Conversion

70kg patient on a ketamine infusion at 0.2mg/kg-hr

$70\text{kg (ketamine IV } 0.1\text{mg/kg-hr)}(24 \text{ hrs/day}) = 336\text{mg IV ketamine/day}$

$336 \text{ mg IV ketamine/day (1 mg PO ketamine/1 mg IV ketamine)} = 336 \text{ mg PO ketamine/day}$ 336 mg PO

ketamine/day (3 doses/day) = 112mg [Round to available capsule size 60mg] Final oral regimen: Ketamine 120mg PO Q8h

References

1. Okon T. Ketamine: an introduction for the pain and palliative medicine physician. *Pain Physician*. 2007;10:493-500.
2. Fitzgibbon EJ, Hall P, Schroder C, Seely J, Viola R. Low dose ketamine as an analgesic adjuvant in difficult pain syndromes: a strategy for conversion from parenteral to oral ketamine. *J Pain Symptom Manage*. 2002;23(2):165-170.
3. Benitez-Rosario MA, Feria M, Salinas-Martin A, et al. A retrospective comparison of the dose ratio between subcutaneous and oral ketamine. *J Pain Symptom Manage*. 2003;25(5):400-401.
4. Broadley KE, Kurowska A, Tookman A. Ketamine injection used orally. *Palliat Med*. 1996; 10:247-250.
5. Blonk MI, Koder BG, Bemt PM, Huygen FJ. Use of oral ketamine in chronic pain management: a review. *Eur J Pain*. 2010;14(5):466-72.
6. Benitez-Rosario MA, Salinas-Martin A, Gonzalez-Guillermo T, Feria M. A strategy for conversion from subcutaneous to oral ketamine in cancer pain patients: effect of a 1:1 ratio. *J Pain Symptom Manage*. 2011;41(6):1098-1105.
7. Quibell R, Prommer EE, Mihalyo M, Twycross R, Wilcock A. Therapeutic reviews: ketamine. *J Pain Symptom Manage*. 2011;41(3):640-649.

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