

**Protocol for New Prescribers**  
**Low-dose Sublingual Ketamine for Chronic Pain or Depression**

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*The following protocol is a recommendation for new prescribers. You may choose to adjust the plan, being more or less cautious, depending on patient circumstances and your own preference. Only provide this treatment to a patient who can manage dosing reliably according to instructions, or who has a caregiver who can. See accompanying "Information for Prescribers" for more details and references. Please share feedback with me at: [cgrande1234@hotmail.com](mailto:cgrande1234@hotmail.com)*

**A. Initial Dose.** Add up the total number of points in categories 1 through 6:

- 1) Age:
  - 0= 18-64
  - 1= 65-74
  - 2= 75 or older
- 2) Medical frailty:
  - 0= good health or stable chronic condition
  - 2= very ill (e.g., advanced cancer, significant renal or hepatic dysfunction)
- 3) Opioid history:
  - 0=current or history of moderate to high dose use (30+ mg morphine equivalents daily, for a few months or more)
  - 1=low dose opioids or no significant opioid history
- 4) History of drug sensitivities
  - 0=none or occasional
  - 2=frequent or severe
- 5) Anxiety about the treatment:
  - 0=none or mild
  - 2=severe
- 6) Severity of pain or depression
  - 0= moderate to severe pain or suicidal depression
  - 1= mild pain or depression

<u>Total</u>	<u>Starting Dose</u>	<u>Syrup Concentration</u>	<u>Starting Volume</u>
0:	16 mg	32 mg/ml	0.5 ml
1:	8 mg	16 mg/ml	0.5 ml
2 or more:	4 mg	16 mg/ml	0.25 ml
For greater caution try this:			
	2 mg	8 mg/ml	0.25 ml

**B. Dosing Frequency:**

1. Suicidal ideation: Every 2 hours, maximum 96 mg/day
2. Severe, intractable pain: every 2 hours, maximum 96 mg/day
3. All others: once or twice daily, maximum 96 mg/day

**C. Upward Titration:**

- If inadequate symptom relief and no adverse effects, double the dose every day (every 2 days if moderate-severe kidney disease, for age 75 or older, or for greater caution for anyone else) until symptom relief, uncomfortable side effects or maximum specified dose. Above 64 mg, increment by 32 mg.
- If uncomfortable side effects occur, advise patient to reduce dose to the previous level.
- After phone call or visit (preferably within 1 week), if insufficient relief but no uncomfortable side effects, continue increasing the dose. Doses above 96 mg/day may be helpful, especially in those with high dose opioid use, but use caution – cognitive effects or increased pain may occur above an optimum dose.
- After stabilizing at an effective dose, consider a reduction in dose and/or dosing frequency to achieve the lowest beneficial total amount per day. Tolerance can develop when too high a dose is used for long – and the ketamine would ultimately lose its usefulness.

Note: patients currently using opioids may experience drowsiness or sedation when starting ketamine. This often resolves with a reduction of the opioid dose – which I would consider a favorable outcome – rather than a reduction of the ketamine dose. Develop a plan with the patient for how to do this.

**Followup Plans:**

*NOTE: Schedule a followup visit or at least a phone call within the first week after starting ketamine, and a visit within the first two weeks. Adjustment (change in dose or frequency) can be made during the phone call or visit.*

*Advise the patient not to drive a car or operate heavy machinery until becoming familiar with the effect at each dose level. Provide the patient some background information about the treatment in written form. You are welcome to use my Ketamine Information Handout. The emphasis is on chronic pain but applies to depression as well.*

## EXAMPLES

### **Chronic Pain**

Example 1: 45 years old, moderate chronic pain, daily opioids at 60 mg morphine equivalent. (Total: 0 points)

*Instructions: Ketamine syrup 32 mg/ml, take 0.5 ml twice daily, increase dose daily as directed, max 96 mg/day or as directed*

Example 2: 85 years old with stable chronic disease, no significant opioid history (Total 3 points)

*Instructions: Ketamine syrup 16 mg/ml, take 0.25 ml twice daily, increase dose every 2 days as directed, max 96 mg/day or as directed*

### **Treatment-resistant Depression**

Example 1: 45 years old, moderate depression without suicidality (Total 1 point)

*Instructions: Ketamine syrup 16 mg/ml, take 0.5 ml BID, increase dose daily as directed, max 96 mg/day or as directed*

Example 2: 45 years old, depression with suicidal ideation. (Total: 0 points)

*Instructions: Ketamine syrup 32 mg/ml, take 0.5 ml every 2 hours, max 3 ml daily or as directed*

Example 3: 45 years old, depression with suicidal ideation, extremely anxious about the treatment (Total 2 points)

*Instructions: Ketamine syrup 16 mg/ml, take 0.25 ml every 2 hours, max 2 ml in first 24 hours, double the dose as needed every day to max 6 ml daily or as directed*