

## Ketamine for Depression: A Q&A with Psychiatrist Alexander Papp, MD

By Gabrielle Johnston, MPH | December 21, 2017

**E**very year, 15 to 20 million persons are diagnosed and treated for depression, making it the most common type of mental illness in the United States, according to the Centers for Disease Control. For roughly 30 percent of these patients, however, standard treatment options, such as antidepressants and talk therapy, are not effective. But for some, there may be a new option: ketamine, a medication originally developed as an anesthetic drug, but now being used to address treatment-resistant depression. Alexander Papp, MD, psychiatrist at UC San Diego Health, discusses the potential of ketamine as a remedy for depression when other treatments fail.



**Question:** How does ketamine work to reduce depression?

**Answer:** Ketamine works by quickly increasing the activity of the neurotransmitter glutamate in the frontal cortex of the brain, while also allowing new synapses to form in the same area. The speediness of ketamine in producing an antidepressant effect occurs because this drug bypasses the traditional serotonin route and goes directly to activating glutamate. This is very different from traditional antidepressants, which first increase the activity of serotonin in multiple different areas of the brain, and then ultimately affect glutamate. This process usually takes two to four weeks to take effect, while ketamine yields an almost immediate effect.

**Q:** What is treatment-resistant depression?

**A:** Treatment-refractory depression, better known as treatment-resistant depression, is a term used to describe cases of major depressive disorder that do not adequately respond to appropriate courses of at least two antidepressants. In this situation, “responding” to an antidepressant means not only improvement in mood, but experiencing a full disappearance of the majority of the depressive symptoms and a return to normal functioning.

**Q:** What is ketamine and how is it traditionally used in medicine?

**A:** Ketamine was originally developed as an anesthetic and an analgesic or pain reliever. Currently, ketamine is approved and labeled by the U.S. Food & Drug Administration (FDA) for both of these uses in the United States.

**Q:** Are there any adverse effects of ketamine as a treatment? Is this why some consider it to be an “experiential” treatment for depression?

**A:** As a treatment for depression, ketamine has a few mild adverse effects. These can include a dream-like feeling, blurred or double vision, dizziness, nausea or vomiting and short anxiety reactions after receiving a dose. This treatment is not experimental because this is an FDA-approved drug that is being used for “off-label” or a less common use. An “off-label” use means that it is administered as a treatment that the FDA did not originally approve. The FDA approves medications only for a certain number of uses, but most medications eventually develop off-label uses due to the clinical experience that develops over time. As an example, the drug Prazosin was approved for the treatment of high blood pressure in 1976 but it is now mostly used for the treatment of nightmares in patients with post-traumatic stress disorder, a use that was not originally approved.

**Q:** When should a patient ask their doctor about trying ketamine as a treatment for depression?

**A:** You should speak to your doctor when you have tried several antidepressant medications



or combinations of medications, taken at the highest dose levels for at least two months, without

a return to normal functioning. In these cases, it is also important to have other medical reasons for depression, such as a hormonal imbalance, ruled out as well.

**Q:** Apart from ketamine, are there any other treatments for this treatment-resistant depression on the horizon?

**A:** New studies have been published about administering Botox injections into the frown muscles on the forehead to treat depression. Botox is an FDA-approved drug to treat a variety of conditions, ranging from excessive sweating to muscle spasms to cosmetic uses, but its use to treat depression is another example of off-label use.

There are also a variety of other treatments available for this type of depression. Two of the more common options are repetitive transcranial magnetic stimulation and deep brain stimulation. Both of these are FDA-approved and are covered by some insurance plans.

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