

The Consumer's Guide to NMDA Receptor Antagonists for Major Depressive Disorder



6 ESSENTIAL FACTS ABOUT NMDA RECEPTOR ANTAGONISTS FOR MDD

1. There are two drugs for depression that contain an NMDA receptor antagonist.

One is a version of an anesthesia medication called ketamine, an NMDA receptor antagonist that is sometimes used as an intravenous (IV), off-label treatment for severe depression and can relieve symptoms quickly. The U.S. Food and Drug Administration (FDA) [approved](#) a nasal spray version called esketamine, or S-ketamine, in 2019, under the brand name Spravato.

A year later, the FDA expanded the approved uses of esketamine to include treating people with MDD who have attempted suicide or thought about it.

In 2022 the FDA approved a second medication, a combination drug with the brand name Auvelity. It's composed of two active ingredients: bupropion (an antidepressant) and dextromethorphan (an NMDA receptor antagonist that's also a common cough suppressant).

2. NMDA receptor antagonists are taken in different ways.

Esketamine nasal spray is a self-administered medication, but you'll have to go to your doctor's office to take it, according to [Mark Niciu, MD, PhD](#), an assistant professor of psychiatry at the University of Iowa Carver College of Medicine in Iowa City.

After you do, you'll need to stay for at least two hours so your doctor can monitor your vital signs — heart rate, blood pressure, temperature,

and respiratory rate — and look out for side effects. Esketamine nasal spray is taken twice a week for the first four weeks and then once a week or every other week thereafter.

You can take the bupropion-dextromethorphan pill at home, but you'll need to follow a specific schedule: once a day for the first three days and twice a day at 8-hour intervals going forward.

3. NMDA receptor antagonists work faster than traditional antidepressants.

Most people won't feel significant relief for at least six to eight weeks after starting a typical antidepressant. NMDA receptor antagonists work more quickly: The effects of esketamine nasal spray often kick in within a week or two, although this can vary.

"Sometimes, patients respond after the second treatment, others after the fourth treatment, and so forth," says [Paul Kim, MD, PhD](#), an assistant professor of psychiatry and behavioral sciences at the Johns Hopkins University School of Medicine in Baltimore.

The bupropion-dextromethorphan pill usually takes a bit longer to take effect, but it still works faster than typical antidepressants. You may start to see results in two to four weeks, says [Dan Iosifescu, MD](#), an associate professor of psychiatry at NYU Grossman School of Medicine and the director of clinical research at the Nathan Kline Institute for Psychiatric Research in New York.

