**REMINDER: Summer Hours - Monday - Friday 8:30am - 5:30pm and Saturday 8:30am - 1pm**

## News from Good Life

Thank you for entrusting in the compounding services at Good Life Pharmacies to help meet the unique medication needs of your patients. We are excited to share our monthly newsletter with you and look forward to continuing to be your medication problem solvers.

Be sure to visit our new website at **www.goodliferx.com.** You or your patients can contact us via our HIPAA-compliant forms and learn how compounding can provide solutions for your medication challenges.

Please don't hesitate to let us know how we can be of further assistance to you and your practice.

Sincerely,
Jim Andreesen, R.Ph.
Angie Svoboda, Pharm.D. FIACP
Ray Scott, R.Ph.

# Updates Regarding an Urgently Needed Therapy Available from Compounding Pharmacists: Intranasal Ketamine for Treatment-Resistant Depressionn

There is an urgent need for more rapidly effective pharmacotherapies for major depressive disorder and bipolar disorder that are efficacious and tolerable for depressed patients who respond poorly to conventional treatments. Since our June 2018 newsletter, multiple controlled trials have been posted to PubMed. In a new article published in June 2018, Rakofsky and Rapaport of Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia, discuss new therapies that are available as treatment options for major depressive disorder and bipolar disorder, such as intranasal ketamine.
Continuum (Minneap Minn). 2018 Jun;24(3, BEHAVIORAL NEUROLOGY AND PSYCHIATRY):804-827.

Research has now demonstrated a rapid, non-sustained antidepressive response to a single infusion of ketamine, with controlled studies of intranasal therapy that appear promising.
Depress Anxiety. 2016 Aug;33(8):698-710.

The N-methyl-D-aspartate glutamate receptor antagonist ketamine, delivered via an intravenous route, has shown rapid antidepressant effects in patients with treatment-resistant depression. Intravenous ketamine infusion has been found to attenuate suicidal symptoms. The benefits, however, are transient and seldom persist beyond 1-2 weeks.

Some data suggest that repeated infusions, such as on alternate days, prolong the duration of response. However, frequently repeated intravenous ketamine infusion is not a practical treatment strategy for maintenance therapy. And, the oral bioavailability of ketamine is only 8%-17% because of extensive first-pass metabolism so oral therapy is not a viable option. Therefore, the intranasal route has been investigated.
Gen Hosp Psychiatry. 2015;37(2):178-184.

Intranasal drug delivery (INDD) systems offer a route to the brain that bypasses problems related to gastrointestinal absorption, first-pass metabolism, and the blood-brain barrier; onset of therapeutic action is rapid, and the inconvenience and discomfort of parenteral administration are avoided. INDD has found several applications in neuropsychiatry, such as to treat migraine, acute and chronic pain, Parkinson disease, disorders of cognition, autism, schizophrenia, social phobia, and depression.
J Clin Psychiatry. 2015 May;76(5):e628-31.

In a randomized, double-blind, placebo-controlled, crossover trial conducted in 20 patients with major depression, Lapidus et al. of the Icahn School of Medicine at Mount Sinai, New York, tested the safety, tolerability, and efficacy of intranasal ketamine in patients with depression who had failed at least one prior antidepressant trial. Eighteen patients completed 2 treatment days with intranasal ketamine hydrochloride or saline solution. The researchers found that a single intranasal dose of ketamine (50 mg) outperformed saline by 7.6 points on the Montgomery-Asberg Depression Rating Scale as assessed 24 hours after dosing; the response rate was 44% vs 6%, respectively. Anxiety ratings also decreased significantly more with ketamine. Patients showed significant improvement in depressive symptoms at 24 hours after ketamine compared to placebo. Intranasal ketamine was well tolerated with minimal psychotomimetic or dissociative effects and was not associated with clinically significant changes in hemodynamic parameters.
Biol Psychiatry. 2014 Dec 15;76(12):970-6.

Growing evidence of the rapid antidepressant effects of intranasal ketamine represents a promising advance in treatment-resistant depression (TRD) therapeutics. Most studies report a duration of response up to 7 days and remission up to 3-5 days after a single dose. Investigators enrolled more than 200 patients aged 18 to 64 years at 39 sites in the United States, Germany, Poland, Spain, and the Czech Republic. All of the participants had not responded to at least two previous antidepressants. Between August 2015 and June 2017, patients were randomly assigned to receive daily for 4 weeks a newly initiated open-label antidepressant plus intranasal esketamine or placebo. The mean age for each treatment group was 44.9 and 46.4 years, respectively; women constituted 65.8% and 57.8% of the groups, respectively. All of the participants had moderate to severe TRD, with mean baseline MADRS scores of 37.0 and 37.3, respectively.

The primary efficacy endpoint (change from baseline to day 28 on the MADRS total score) was significantly greater for the treatment group compared with the placebo group (adjusted mean difference, -4.0; 95% confidence interval [CI], -7.31 to -0.64; 1-sided P = .01). "Response was rapid in onset and increased over time during repeated dosing," per the investigators.

More of the patients who received esketamine achieved remission, defined as a MADRS total score of 12 or less at day 28, than those who received placebo (52.5% vs 31.0%, respectively; P = .001). Response rate, defined as achieving at least a 50% improvement over baseline on the MADRS, was achieved by 69.3% vs 52.0% of the groups, respectively.

"Most adverse events ... subsided spontaneously by 60 to 90 minutes post dose," said presenting author Vanina Popova, MD. In addition, "there was no pushback" in regards to the nasal delivery system. "The route of administration was well received, and it was certainly more convenient than intravenous administration," she said.
American Psychiatric Association (APA) 2018. Abstracts P7-065 and P8-054, presented May 8, 2018.
Psychiatry Clin Neurosci. 2018 May 10.

***While the above study used an isomer of ketamine (eskatamine), intranasal ketamine has been shown to***

***be effective with minimal side effects. Ask our compounding pharmacist for more information.***

Ketamine is a racemic mixture of the enantiomers R-ketamine and S-ketamine (esketamine). S-ketamine has greater analgesic and anesthetic effects than R-ketamine. Animal data suggest potential advantages for R-ketamineover S-ketamine. Case reports, case series, and some small randomized controlled trials suggest that single or repeated intravenous infusions (0.2-0.4 mg/kg) or intranasal administrations (28-84 mg) of S-ketamine have antidepressant action in patients with medication-refractory depression and that the observed benefits are similar in magnitude to the antidepressant benefits reported with racemic ketamine. However, there are no direct comparisons between S-ketamine and either R-ketamine or racemic ketamine in depressed patients.

J Clin Psychiatry. 2017 Jun;78(6):e674-e677.

Ketamine and esketamine are not currently approved treatments for depression, but the clinical use of ketamine is increasing in a variety of practice settings internationally.

CNS Drugs. 2018 May 7. [Epub ahead of print]

A study by Galves et al. concluded that the drug formulation, the delivery device, the technique and individual patient factors play an important role in tolerability and efficacy when using intranasal ketamine for Treatment Resistant Depression.

J Psychopharmacol. 2018 Apr;32(4):397-407.

## Good Life Pharmacist Honored for Outstanding Community Service

Angela K. Svoboda, PharmD, RP, is the recipient of the 2018 Bowl of Hygeia Award for outstanding community service. Svoboda was presented with the award at the NPA Annual Convention on June 8, 2018. The Bowl of Hygeia is sponsored by the American Pharmacists Association Foundation, the National Alliance of State Pharmacy Associations, and the American Pharmacists Association with support from Boehringer Ingelheim. **READ MORE ON OUR BLOG**


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