**METHODS:** Data were pooled from three 6-week trials: KINECT (NCT01688037), KINECT 2 (NCT01733121), KINECT 3 (NCT02274558). Outcome data were analyzed in the safety population by pooled VBZ doses (40 mg, 80 mg) and PBO. Outcomes of interest included: treatment-emergent adverse events (TEAEs) related to depression or suicidality; mean score change from baseline to Week 6 in the Calgary Depression Scale for Schizophrenia (CDSS, for participants with schizophrenia/schizoaffective disorder) or the Montgomery-Åsberg Depression Rating Scale (MADRS, for participants with mood disorder); and, worsening from baseline in Columbia-Suicide Severity Rating Scale (C-SSRS) suicidal ideation scores. All outcomes were analyzed descriptively.

**RESULTS:** There were 400 total participants in the pooled safety population; 286 participants had schizophrenia/schizoaffective disorder (40 mg, n = 82; 80 mg, n = 70; PBO, n = 134) and 114 had a mood disorder (40 mg, n = 28; 80 mg, n = 42; PBO, n = 44). Over one-third of participants had a lifetime history of suicidal ideation or behavior (40 mg, 45%; 80 mg, 39%; PBO, 37%). Few participants had a depression- or suicide-related TEAE, with no apparent differences between VBZ and PBO: suicidal ideation (40 mg, 3.6%; 80 mg, 0.9%; PBO, 2.2%); depression (40 mg, 0%; 80 mg, 1.8%; PBO, 1.1%); depressive symptom (40 mg, 0.9%; 80 mg, 0%; PBO, 0.6%); suicide attempt (40 mg, 0%; 80 mg, 0.9%; PBO, 0%). Mean changes from baseline to Week 6 in depression scale scores were generally small and similar across treatment groups: CDSS total score (40 mg, -0.5; 80 mg, -0.6; PBO, -0.3); MADRS total score (40 mg, -0.2; 80 mg, -1.7; PBO, 0.6). Few participants had a shift from no suicidal ideation at baseline (C-SSRS score = 0) to any suicidal ideation during treatment (C-SSRS score = 1-5): 40 mg, 3.9% (4/103); 80 mg, 0.9% (1/111); PBO, 2.9% (5/174).

**CONCLUSION:** Data from 3 double-blind, placebo-controlled trials indicate that once-daily VBZ treatment was not associated with a worsening in depression-related symptoms or an increased risk of suicidal ideation or behavior.

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## Cognitive Impairment Following Overdose on Lamotrigine

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**ABSTRACT:** Objective: To generate hypotheses, accumulate scientific data about rare presentations, and serve as a major educational tool.

**METHOD:** This is a retrospective case report of a patient in inpatient unit.

**INTRODUCTION:** Lamotrigine is a mood stabilizer with unique mechanisms of action. At therapeutic levels, it has been reported that Lamotrigine is neuroprotective and improves cognition. In this case, we present a patient who suffered significant cognitive slowing following overdose on Lamotrigine.

**CASE:** A 17yo white male with a diagnosis of Autism spectrum disorder and Bipolar disorder type 1 was admitted for bizarre behavior and profound cognitive impairment. His past psychiatric history was significant for two suicide attempts - first by overdose on baby aspirin and second by overdose on Lamotrigine, both of which had occurred about six months prior to his presentation and had each required an inpatient hospitalization. His family reported that since his overdose on Lamotrigine, he had been withdrawn, aloof, and appeared depressed. His school teachers had noticed significant decline in his memory, attention and concentration, and there had been noticeable impairment in his ability to follow commands or complete a task. On assessment, he was noted to have significant psychomotor slowing, latency in speech and thought blocking. At the time of his presentation, he was on Lithium 300mg BID. A careful review of his previous medical records revealed that he had been on a combination of Seroquel, Lamotrigine and Lithium prior to his overdose attempt on Lamotrigine. During this hospitalization, Seroquel was restarted. Patient tolerated the medication well. There were no safety concerns and he was deemed safe to discharge under 24hr supervision of his family. He has since been followed up in clinic. Although he continues to have some cognitive slowing, overall, he has demonstrated slow but steady improvement.

**DISCUSSION:** Lamotrigine acts by blocking voltage sensitive sodium channels. It also reduces release of glutamate, a major excitatory neurotransmitter in the central nervous system. Glutamate modulates synaptic plasticity, a property thought to be vital for memory and learning. While too much glutamate causes over activation of NMDA receptors resulting in increased intracellular oxidative stress and eventually apoptosis, too little glutamate may lead to decreased glutamate mediated postsynaptic excitation of neural cells and thus impacting memory formation, learning and cognition. At

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therapeutic levels (2.5- 15mcg/ml), it has been reported that Lamotrigine is neuroprotective and improves cognition. At the time of overdose, our patient had a Lamotrigine level of 21.5mcg/ml. There is limited literature on cognitive effect of supra-thrapeutic levels of Lamotrigine. As such, a causal relationship cannot be determined from a single care report. Also in differentials to consider are schizophrenia and seizures from lamotrigine withdrawal.

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## Improvements in Clinical Global Impression of Change With Deutetrabenazine Treatment in Tardive Dyskinesia From the ARM-TD and AIM-TD Studies

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**ABSTRACT:** Introduction: Tardive dyskinesia (TD) is an involuntary movement disorder that is often irreversible, can affect any body region, and can be debilitating. In the ARM-TDand AIM-TD studies, deutetrabenazine treatment demonstrated statistically and clinically significant reductions in Abnormal Involuntary Movement Scale (AIMS) scores at Week 12 compared with placebo (primary endpoint).

**OBJECTIVE:** To evaluate the efficacy of deutetrabenazine, as measured by the Clinical Global Impression of Change (CGIC) scale, in patients with TD from the pooled ARM-TDand AIM-TD (24 and 36 mg/day doses) data sets, as compared with the pooled placebo cohort.

**METHODS:** ARM-TD and AIM-TD were 12-week, randomized, double-blind, placebo-controlled studies that evaluated the safety and efficacy of deutetrabenazine for thetreatment of TD. The key secondary endpoint of each study was the proportion of patients "much improved" or "very much improved" (treatment success) at Week 12 on theCGIC.

**RESULTS:** At Week 12, the odds of treatment success among patients treated with deutetrabenazine (n = 152) was more than double that of patients given placebo (n = 107; odds ratio: 2.12; P = 0.005). In a categorical analysis of CGIC ratings, patients treated with deutetrabenazine showed greater improvement than patients given placebo (P = 0.003). Patients treated with deutetrabenazine also had a significantly better treatment response than those given placebo (least-squares mean CGIC score treatment difference: –0.4; P = 0.006).

**CONCLUSIONS:** Deutetrabenazine treatment led to statistically and clinically significant improvements in TD symptoms based on the CGIC result, suggesting that clinicians were able to recognize the benefit in patients treated with deutetrabenazine.

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## Use of Pimavanserin in Combination With Selective Serotonin Reuptake Inhibitors (SSRIs)

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**ABSTRACT:** Study Objective: Psychosis is common in Parkinson's disease (PD) and increases in both frequency and severity with disease duration. It is associated withincreased morbidity/mortality, complicates management of motor symptoms and often leads to long-term care placement. Pimavanserin is a selective 5-HT2A inverse agonist/antagonist approved in the U.S. for treatment of hallucinations and delusions associated