Treating Schizophrenia and Bipolar I Disorder in the Real-World Setting: Effectiveness and Safety of Olanzapine/Samidorphan Combination

Maxwell Zachary Price, BA, and Richard Louis Price, MD

Olanzapine/samidorphan (OLZ/SAM) was released in October 2021 for adults with schizophrenia or bipolar I disorder in acute manic or mixed episodes and for maintenance to prevent manic and/or depressive episodes.[1] Samidorphan is a novel μ-opioid receptor antagonist and a κ-opioid and δ-opioid receptor partial agonist associated with regulation of appetite and metabolism.[2] Samidorphan has a longer half-life than naltrexone and 5 times the μ-opioid receptor blockade[3] that mitigates weight gain from olanzapine.[4] The following are representative cases drawn from a general pediatric and adult outpatient psychiatry practice located in Lower Hudson Valley, New York, demonstrating ancillary benefits we have consistently found.

Case 1

Gittel is a 45-year-old divorcee with bipolar I disorder, borderline personality disorder, compulsive skin picking, and cutting that led to multiple psychiatric hospitalizations. She failed lithium, lamotrigine, quetiapine, and clozapine for mood stabilization, with weight increase from 200 lb to 300 lb on olanzapine despite diet, exercise, melatonin, topiramate, metformin, naltrexone, and semaglutide, which caused nausea, gastroparesis, and suicidality. She directly switched from olanzapine 25 mg to OLZ/SAM 20 mg/10 mg plus 5 mg olanzapine, which was lowered to OLZ/SAM 20 mg/10 mg to alleviate sedation from samidorphan. Within 2 weeks, she lost 6 lb and weighed 150 lb a year later, with complete cessation of skin picking and cutting and no further hospitalizations. (Lower doses of OLZ/SAM may be substituted to alleviate sedation while maintaining efficacy, since olanzapine concentrations are highest for OLZ/SAM compared to its generic Apotex olanzapine component and even branded Zyprexa.[5])

Case 2

Pedro is an 18-year-old male with schizophrenia and autism spectrum disorder. He engaged in repetitive head banging that led to numerous emergency department visits despite trials of aripiprazole and risperidone together with naltrexone. During this time, he gained 100 lb and developed gynecomastia. He switched to OLZ/SAM 10 mg/10 mg, which was lowered to a half tablet to alleviate nausea from samidorphan. He lost 101 lb over the course of the year, with resolution of auditory hallucinations and head banging and no further emergency calls.

Case 3

Mike and Nick were 21-year-old college students with bipolar I disorder who liked to party but were not regular substance users. Mike was stable on olanzapine 5 mg. Nick was stable on OLZ/SAM 5 mg/10 mg. They attended the same party where fentanyl was laced into drugs that they both used. Mike is deceased. Nick is alive.

Discussion

Beyond OLZ/SAM for weight gain mitigation in adult olanzapine-naive patients with schizophrenia or bipolar I disorder,[4] and for potential weight loss in stable patients who have gained excessive weight on risperidone, quetiapine, clozapine, or olanzapine,[6] these cases illustrate where OLZ/SAM may be considered first-line treatment for a range of comorbid addictive/repetitive behaviors. In our humble opinion, OLZ/SAM can be helpful for non-suicidal self-injury in borderline personality disorder or autism spectrum disorder, cravings/urges, and accidental overdose, where an additional prescription for daily naltrexone or as-needed naloxone is less likely to be routinely utilized. Having a more potent opioid blocker already on board can be lifesaving.

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Author Affiliations: Hackensack Meridian School of Medicine, Nutley, New Jersey (MZ Price); Department of Psychiatry, Weill Cornell Medical College, New York, New York (RL Price).
Corresponding Author: Maxwell Z. Price, BA, Hackensack Meridian School of Medicine, Nutley, NJ 07110 (mzp2103@columbia.edu).
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