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Testimony Before the Psychopharmacologic Drug and Drug Safety and Risk Management Advisory Committees

Topic: Olanzapine/samidorphan (OLZ/SAM)
NDA 213,378 (ALK3831) for schizophrenia or bipolar

U.S. Food and Drug Administration, Via Webinar

October 9, 2020

Presentation by Michael T. Abrams, M.P.H., Ph.D.

First slide

I'm Michael Abrams a health researcher at Public Citizen. I have no financial conflicts of interest.

Slide 2

Regarding efficacy, the primary endpoint for this medication is weight gain. Evidence presented shows that the addition of samidorphan does not eliminate the weight gain associated with olanzapine administration, it only reduces that weight gain by an absolute amount of approximately 2% (well below the 5% goal for weight loss drugs cited in the FDA briefing document on page 8). Additionally, this small effect was not coupled with same-direction significant differences across a number of metabolic and cardiovascular health indicators, including: mixed results regarding waist circumference and blood pressure changes, and unfavorable glycemic trends, summarized by these two slides from the sponsor and the FDA…

Slide 3

… and unfavorable or null results regarding lipid parameters (left panel), and unfavorable glycemic trends are highlighted in the center graph of the right panel, both slides taken directly from the sponsor.

Slide 4

Regarding safety, there is clear concern noted by both the sponsor and the FDA that use of the opioid receptor antagonists, samidorphan, comes with substantial risk for opioid overdose and death as persons with psychosis have especially high risk of substance use disorders (slide on the left), and I must add substantial risk for medication discontinuity. Additionally, use of samidorphan carries with it the risk of inadequate pain control from opioids when such pain

control is needed. The right-hand slide from the FDA reminds us that over 1 in 5 adults on olanzapine concurrently uses opioid analgesia.

Slide 5

Moreover, data on Quality of Life, a key patient-reported outcome, does not support this medication's benefit-to-risk profile over that of olanzapine alone.

Slide 6

Accordingly, Public Citizen concludes that this application for olanzapine/samidorphan as a treatment for schizophrenia or bipolar offers marginal benefits in weight gain reductions, at best, with no other physiologic or patient-oriented improvements demonstrated. Moreover, it intensifies real risks of opioid overdose and death.

We thus recommend that the advisory committee vote "No" on these three basic questions of safety and efficacy, and that the FDA not approve this combination medication

Thank you.