

Three Recent Cases of Likely Methadone Cross-Reactivity With Vortioxetine

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Dear Editor,

Trintellix, or vortioxetine (originally branded Brintellix), has been tested for cross-reactivity on urine testing with morphine and opiates. Our hospital uses the screening assay Methadone II, which is from Roche Diagnostics GmbH, Mannheim, Germany. The package insert for this testing shows a direct cross-reactivity of 4.1%, so that a concentration of 7339 ng/mL vortioxetine is equivalent to 300 ng/mL of methadone in the assay, just at the cutoff of our screening test. However, a metabolite of vortioxetine, Lu AA34443, has a cross-reactivity of around 11%, where a concentration of 2622 ng/mL of Lu AA34443 is equivalent to 300 ng/mL of methadone in the assay, meaning potentially around 10% of patients may screen positive for methadone while taking vortioxetine, the most significant cross-reactivity found by the manufacturer (Roche Diagnostics, 2017).

When tested recently in our laboratory, three cases of varying age, dose, and concurrently administered prescriptions tested positive for methadone on screening and negative on confirmation, suggesting that providers who work with populations who are often drug screened for work or to gauge adherence to their prescribed opioid regimens should be alert to this possibility. The confirmation testing used was at Mayo Medical Laboratories, Rochester, MN, using the gas chromatography-mass spectrometry, solid phase extraction method (Mayo Medical Laboratories, 2018).

The first case was of a Caucasian female in her early 30s, body mass index (BMI) of 29.8, who presented with a self-reported history of cannabis abuse and taking Adderall XR 30 mg daily, Trintellix 20 mg daily, Junel BCP 1 tablet daily, Trazodone 100 mg qHS, and occasional ibuprofen for musculoskeletal pain; her toxicology screen was positive for amphetamines and THC as expected, but also morphine on April 5, 2018. A repeat test with morphine confirmation send-out was performed on April 6, 2018, and showed negative for morphine confirmation. A repeat screen on April 10, 2018, showed consistent results with positive amphetamine, THC, and methadone screening.

The second case involved woman of Asian ancestry in her early 20s, BMI of 19, who presented reporting no history of illicit substance abuse. She was also taking an Adderall product, Vyvanse 50 mg daily, Lamotrigine 125

mg daily, Provigil 200 mg daily, Trintellix at only 5 mg daily, and vitamin D supplementation at 50,000 IU once weekly, as well as Fiorinal for occasional migraine. On April 10, 2018, her toxicology screen was positive for amphetamines as expected, and morphine. A confirmation send-out of this sample was negative. Trintellix was reduced on April 19, 2018, to 2.5 mg, and the plan was to discontinue after discharge.

The third case is of a Caucasian woman in her late 50s whose height and weight were unrecorded. She presented reporting a remote history of marijuana use. She was prescribed and reported taking regularly Wellbutrin 450 mg daily, vitamin B₁₂, a weekly vitamin D supplement 50,000 IU, melatonin 5 mg occasionally for sleep, multivitamin, and Trintellix 20 mg daily. On April 20, 2018, her toxicology report came back positive for methadone and opiates. This sample was sent out for confirmation and was negative; a repeat urine screening was still positive for methadone, but not opiates, on April 24, 2018.

The differences in age, body size, dose of the medication, and co-administered medications lead us to believe this issue may be more widespread than initially thought, and certainly bears considering when starting medication in individuals who receive regular toxicology screening.

Sincerely,

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