First approved medication for tardive dyskinesia demonstrates safety, study shows

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A recently FDA-approved medication for the movement disorder tardive dyskinesia is safe and well tolerated, according to neurologists presenting results from a yearlong monitoring study.

The results were presented this week at the American Academy of Neurology meeting in Los Angeles by Stewart Factor, DO, professor of neurology at Emory University School of Medicine and director of the Movement Disorders program at Emory Brain Health Center.

Valbenazine (commercial name: Ingrezza) was the first drug approved for the treatment of tardive dyskinesia in 2017, a disorder in which patients experience involuntary movements of the face, limbs or trunk.

Tardive dyskinesia is linked to the chronic treatment of conditions such as schizophrenia, bipolar disorder and depression with antipsychotic medications that act as dopamine antagonists, as well as treatment with other medications for gastrointestinal disorders.

"Receiving FDA approval of the first drug for the treatment of tardive dyskinesia is an important advance for patients with this condition. Our study is a valuable demonstration of its long-term safety, further validating the use of this medication," says Factor.

Before the FDA's fast track approval of valbenazine, physicians prescribed various medications "off label", including the drug tetrabenazine, which is similar to valbenazine. A review by Factor and Emory colleagues on this class of medications is available here, as well as their 2014 review on tardive dyskinesia.

Factor was presenting data from the KINECT 4 study, a yearlong open-label examination of movement outcomes as well as safety, with two different doses of valbenazine (40 vs 80 mg daily). 163 people, all previously diagnosed with tardive dyskinesia and previously schizophrenia, schizoaffective disorder or mood disorders, participated.

Investigators summarize their conclusions in the study poster:

- Sustained improvements in involuntary movement symptoms were observed, based on clinician- and patient-rated measures
- After stopping valbenazine, some loss of improvement was observed, suggesting that patients may require ongoing therapy with valbenazine to maintain effect
- Valbenazine was generally well tolerated and no unexpected safety signals were found

More than 60 percent of study participants did experience one or more "treatment-emergent adverse events," which could range from urinary tract infection or constipation to headaches or thoughts of suicide. However, the rates of these adverse events tended not to increase with the higher dose of valbenazine. About 15 percent of study participants discontinued because of adverse events.

According to the FDA, Ingrezza is known to cause side effects such as sleepiness and can disturb cardiac rhythms (QT prolongation), and should be avoided by patients with certain cardiac conditions.

Valbenazine's manufacturer, Neurocrine Biosciences, sponsored the study. In addition to Emory, other authors came from UCLA, University

of South Florida, and the Zucker School of Medicine at Hofstra/Northwell.

Factor is also a co-author on other presentations at the American Academy of Neurology meeting, studying a close chemical relative of tetrabenazine, deutetrabenazine.

Both valbenazine and deutetrabenazine are thought to work by reducing the amount of dopamine released in a region of the brain that controls movement and motor function. They target VMAT2, an enzyme involved in packaging dopamine and other neurotransmitters into vesicles.

More information: Laura M. Scorr et al. VMAT2 inhibitors for the treatment of tardive dyskinesia, *Journal of the Neurological Sciences* (2018). DOI: 10.1016/j.jns.2018.02.006

Leslie J. Cloud et al. Tardive Dyskinesia: Therapeutic Options for an Increasingly Common Disorder, *Neurotherapeutics* (2013). DOI: 10.1007/s13311-013-0222-5

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