Huntington's Disease Chorea Gets New Treatment

The FDA expanded the label for valbenazine (Ingrezza) capsules to include chorea associated with Huntington's disease, [Neurocrine Biosciences announced](https://neurocrine.gcs-web.com/news-releases/news-release-details/neurocrine-biosciences-announces-fda-approval-ingrezzar%22%20%5Co%20%22Opens%20in%20a%20new%20tab%20or%20window%22%20%5Ct%20%22_blank) Friday.

Valbenazine is an inhibitor of the vesicular monoamine 2 transporter (VMAT2) pathway, which plays a role in regulating dopamine levels in the brain. The drug is also approved for tardive dyskinesia.

"Clinical results that led to this important approval showed reduction in the severity of chorea as early as 2 weeks after starting Ingrezza at an initial dose of 40 mg, with consistently greater improvements versus placebo seen at all subsequent visits," said Erin Furr Stimming, MD, who led the phase III study of the drug, in a statement.

"Data also demonstrated Ingrezza was generally well tolerated and showed clinically meaningful improvement in adults with chorea associated with Huntington's disease," added Furr Stimming, a professor of neurology at the McGovern Medical School at UTHealth in Houston.

The FDA approval was supported by data from the phase III [KINECT-HD](https://classic.clinicaltrials.gov/ct2/show/NCT04102579) study and the ongoing [KINECT-HD2](https://classic.clinicaltrials.gov/ct2/show/NCT04400331?term=valbenazine&draw=3) open-label extension trial.

In [KINECT-HD](https://www.medpagetoday.com/neurology/generalneurology/104846), Unified Huntington's Disease Rating Scale Total Maximal Chorea scores decreased by 4.6 points with once-daily valbenazine and by 1.4 with placebo -- a difference of 3.2 points on the 28-point scale (*P*<0.0001) -- over 12 weeks. Patients in the valbenazine group reported greater reductions in disease burden related to mobility, abnormal movements, and hand and arm function than those in the placebo group.

The most common treatment-emergent adverse events with valbenazine were somnolence and sedation, urticaria, rash, and insomnia. No suicidal behavior or worsening of suicidal ideation was observed in the valbenazine-treated participants.

Earlier research, however, has linked [VMAT2 inhibition](https://onlinelibrary.wiley.com/doi/full/10.1002/pcn5.79#pcn579-bib-0002) with suicide-related events. Like other FDA-approved treatments for Huntington's chorea, [valbenazine's label](https://www.neurocrine.com/assets/2023/08/INGREZZA-Full-Prescribing-Information_PPI_Approved.pdf%22%20%5Co%20%22Opens%20in%20a%20new%20tab%20or%20window%22%20%5Ct%20%22_blank) carries a box warning for depression, suicidal thoughts, or suicidal behavior in Huntington's disease. Patients and clinicians should pay close attention to changes, especially when the drug is started or the dose is changed. The drug's prescribing information also indicates that patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval should not use the drug. Treatment should be discontinued if neuroleptic malignant syndrome occurs.

Valbenazine's pharmacokinetic profile allows for once-daily dosing and a relatively short titration period. Two other VMAT2 inhibitors, tetrabenazine (Xenazine) and deutetrabenazine (Austedo), are also approved for treating Huntington's-related chorea.