

Drug to treat movement symptoms of HD approved by FDA

The FDA has approved valbenazine, also known as INGREZZA, as a treatment for the movement symptoms of Huntington's disease

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The vast majority of people with Huntington's disease experience movement symptoms known as chorea. Valbenazine, also known as INGREZZA, has recently been approved by the United States Food and Drug Administration (FDA), allowing doctors in the USA to prescribe this medicine for Huntington's disease (HD) chorea. In this article we go through the key points of this announcement and what it means for HD family members.

Background on valbenazine

INGREZZA is the trade name of valbenazine, a drug developed by the company Neurocrine Biosciences. It works similarly to tetrabenazine and deutetabenazine (Austedo), drugs commonly prescribed to help control the involuntary twitching or jerking movements that people with HD experience.



The United States Food and Drug Administration (FDA) is responsible for approving medicines which are shown to be safe in people and effective at treating different diseases.

Treatment with these drugs blocks a protein called VMAT2 that is responsible for packaging certain types of chemicals that brain cells use to communicate. VMAT2 helps to put the chemical messenger dopamine (among others) into bubbles that cross from cell to cell.

Dopamine plays a role in the movement circuits of our brain, and it's thought that blocking VMAT2 can quiet down the cross-talk. Exactly why this improves irregular and involuntary movements is not clear, but these drugs work for many people with HD chorea.

Valbenazine has been approved in the USA since 2017 for the treatment of tardive dyskinesia (TD), involuntary movements that stem from use of medications known as neuroleptics or antipsychotics. Antipsychotics are taken by many people worldwide to treat the psychiatric and behavioral symptoms of bipolar disorder, schizophrenia, and other diseases (including HD). After using these medications for a long time, some people develop TD, which often involves twitches in the muscles of the mouth and face. Valbenazine (INGREZZA) can be helpful to control those involuntary movements, so Neurocrine began studying whether it could also be effective for chorea caused by Huntington's disease.

Testing and approval of valbenazine for people with HD

Because valbenazine had been tested in people with TD and prescribed for several years, we already knew that it was safe in humans. However, a clinical trial was still needed to understand if it could effectively treat Huntington's disease chorea. In collaboration with the Huntington Study Group, Neurocrine ran a Phase 3 clinical trial called KINECT-HD, beginning in 2020. 128 people participated; half were given once-a-day capsules of valbenazine for 12 weeks, and half took a placebo (a pill with no drug). Participants were invited to continue in a longer, ongoing trial called KINECT-HD2, in which everyone receives valbenazine.

KINECT-HD was a success, reaching its primary endpoint, meaning that valbenazine decreased the severity of HD chorea compared to the placebo. It improved the Total Maximal Chorea (TMC) score, a metric clinicians use to monitor chorea symptoms. That "top-line" result was made public in 2021, and since then Neurocrine has continued its studies, analyzing, presenting, and preparing the data from the two HD trials of valbenazine. They presented it to the FDA in December of 2022, and on August 18th 2023, Neurocrine announced that INGREZZA had been FDA approved, meaning that it can now be officially prescribed to people in the USA to treat HD chorea.

"KINECT-HD was a success, reaching its primary endpoint, meaning that valbenazine decreased the severity of HD chorea compared to the placebo "

It can take some time for drugs to go from approval to launch to common prescription, especially for a rare disease. Once they get the green light, companies can devote more energy to educating medical professionals and the community about a new therapy. By the end of September, awareness among US doctors is likely to have ramped up, but there are already resources for family members to learn more.

What else do we know about valbenazine?

It is important to note that INGREZZA does not slow or halt the progression of HD. However, taking medication to improve involuntary movements and other HD symptoms can have a major impact on quality of life. For some people with HD and their loved ones, chorea isn't bothersome, but for others, it can interfere with day-to-day activities and even safety, and treatment can make a big difference.

INGREZZA is taken as a single capsule which is swallowed once a day. This is a positive feature of this medication, as for many people with HD, remembering to take a complex array of tablets throughout the course of the day can be difficult. Similar to valbenazine's "chemical cousins," there may be ways to modify delivery for people who have swallowing issues or use a feeding tube. The dose can also be altered over time depending on how well someone responds to the drug and any side effects they might experience. Neurocrine hopes that this means side effects will be more manageable for a larger number of people taking this medication compared to other VMAT2 targeting drugs.



INGREZZA is taken as a single pill, once daily, which can make it easier for folks with HD to keep on top of their medications

Image credit: [Rodrigo Senna](#)

Balancing side effects, cost, and other factors

Like all drugs, valbenazine has some downsides. VMAT2 inhibitors have common side effects, like sleepiness. They can also have very serious side effects which include depression as well as suicidal thoughts or actions. Therefore, it is very important that people with HD who are considering INGREZZA accurately relay their past medical history to their healthcare provider and alert them as soon as possible if they experience any side effects.

In addition to VMAT2 inhibitors, there are a variety of drugs that doctors prescribe to treat chorea alongside other symptoms. For example, some antipsychotics used for mental health and behavior in HD can also have the effect of calming movements. There are also considerations around cost, especially in countries like the US, where insurance coverage can differ or be absent entirely due to a lack of universal healthcare. Companies like Neurocrine with new drugs on the market aim to alleviate this issue through different channels including assistance programs.

It should be noted that a once-daily version of deutetrabenazine (Austedo XR) was introduced by Teva in the USA this May, which is likely not a coincidence - companies with drugs that treat the same disorder will often tailor their research strategies around public knowledge, like another company's impending FDA approval. The reasons for prescribing or taking one medication over another diverge from doctor to doctor and patient to patient. Everyone responds to drugs differently, and coverage and approvals vary wildly from place to place.

“The availability of multiple treatments for HD chorea raises public awareness of HD...and increases choice for HD family members in their healthcare decisions ”

Take home message

While we wait for treatments that can slow disease progression, drugs like INGREZZA can improve quality of life, and it is a welcome addition to our arsenal of tools to battle HD. The approval of valbenazine in the USA is good news for the HD community. It raises public awareness of Huntington's disease, and creates healthy competition to keep costs low. Most importantly, the availability of multiple treatments for chorea increases choice for HD family members in their healthcare decisions.

That said, outside of the USA, only study participants of KINECT-HD trials will be able to get access to this drug, and Neurocrine has not yet confirmed their commitment to seeking regulatory approval in other countries. They do plan to address the community directly in the near future via a public webinar aimed at HD family members. HDBuzz hopes that all companies developing HD therapies will work towards global access to drugs that can improve quality of life for people with HD.

Leora Fox works at the Huntington's Disease Society of America which has relationships and nondisclosure agreements with companies working on drugs for HD, including Neurocrine Biosciences. This article was written based on public information. Rachel Harding has no conflicts to declare. [For more information about our disclosure policy see our FAQ...](#)

Food and Drug Administration The government regulatory authority in the US responsible for approving new drugs

primary endpoint The main question asked in a clinical trial

clinical trial Very carefully planned experiments designed to answer specific questions about how a drug affects human beings

dopamine A signaling chemical (neurotransmitter) involved in movement control, mood and motivation

placebo A placebo is a dummy medicine containing no active ingredients. The placebo effect is a psychological effect that causes people to feel better even if they're taking a pill that doesn't work.

chorea Involuntary, irregular 'fidgety' movements that are common in HD

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