Novartis multiple sclerosis therapy fingolimod granted FDA Breakthrough Therapy designation for pediatric MS

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- - Breakthrough Therapy designation can expedite the development and review of therapies for serious conditions(1)
- - In a pivotal Phase III study, oral fingolimod significantly reduced relapses by 82% in a pediatric patient population vs. interferon beta-1a intramuscular injection(2)
- - Currently, no disease-modifying therapies are approved for pediatric patients with MS, who often have more frequent relapses than adults with early MS(3)

EAST HANOVER, N.J., Dec. 18, 2017 /PRNewswire/ -- Novartis today announced that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for fingolimod for the treatment of children and adolescents 10 years of age or older with relapsing multiple sclerosis (MS). Fingolimod, also known as Gilenya® in the US, is approved to treat relapsing forms of MS in adults. Gilenya is not currently approved for children and adolescents with relapsing MS.

The Breakthrough Therapy designation is based on data from the Phase III PARADIGMS study, which evaluated the safety and efficacy of fingolimod vs. interferon beta-1a in children and adolescents (ages 10 or older) with relapsing MS[4]. PARADIGMS, the first completed randomized, controlled clinical trial specifically designed for pediatric relapsing MS, found that treatment with fingolimod resulted in an 82% reduction in the rate of relapses (annualized relapse rate) in this patient population over a period of up to two years, compared to interferon beta-1a intramuscular injection ($p < 0.001$)[2]. The safety profile of fingolimod in this study was overall consistent with that seen in previous clinical trials in adults[5].

"Despite the fact that children experience approximately two to three times as many relapses as a typical adult onset MS patient, there are currently no disease-modifying therapies approved for the pediatric population," said Dr. Tanuja Chitnis, Director of the Partners Pediatric Multiple Sclerosis Center, Massachusetts General Hospital, Boston, US, and Scientist, Ann Romney Center, Brigham and Women's Hospital, Boston, US. "Children with MS differ from adults in important ways and additional treatment options for pediatric patients are needed," added Dr. Chitnis, who also served as principal investigator for the PARADIGMS study.

The FDA grants Breakthrough Therapy designation for therapies that are intended to treat a serious condition and that have preliminary clinical evidence indicating that the treatment may demonstrate substantial improvement over available therapy on one or more clinically significant endpoints. This designation is a process designed to expedite the development and review of such therapies[1].

"We're proud of this regulatory milestone, which represents part of our commitment to advance treatment options for young people with MS," said Fabrice Chouraqui, President of Novartis Pharmaceuticals Corporation. "Novartis is looking forward to working with the FDA to bring a therapy with a long track record in adults with relapsing MS to this younger patient population as soon as possible."

About Multiple Sclerosis

MS, a chronic disorder of the central nervous system, affects around 400,000 people in the US[6]. MS disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[7]. In adults, there are three types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)[8]. In children, RRMS accounts for nearly all cases of MS (approximately 98 percent)[9].

The progression of MS results in an increasing loss of both physical and cognitive (e.g., memory) function. This has a substantial negative impact on the lives of people affected by MS, of whom between three and five percent are estimated to be children[10].

About Gilenya® (fingolimod) in adults

Gilenya was the first once-a-day pill approved to treat relapsing multiple sclerosis (MS). Approved for first-line use, Gilenya is a disease-modifying therapy (DMT) that offers freedom from injections, which may fit many patients' lifestyles. Gilenya helps slow down the physical problems caused by RRMS and decreases the frequency of MS flare-ups (relapses).

Gilenya is the most prescribed oral once-daily DMT. In the US, approximately 73,000 patients have been exposed to Gilenya. Worldwide, Gilenya has been used to treat approximately 217,000 patients in both clinical trials and the post-marketing setting, with approximately 480,000 years of patient experience[5].

Indication

Gilenya is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS) in adults. Gilenya can decrease the number of MS flare-ups (relapses). Gilenya does not cure MS, but it can help slow down the physical problems that MS causes.

Important Safety Information

You should not take Gilenya if in the last 6 months you experienced heart attack, unstable angina, stroke or warning stroke, or certain types of heart failure. Do not take Gilenya if you have an irregular or abnormal heartbeat (arrhythmia), including a heart finding called prolonged QT as seen on an ECG, or if you take medicines that change your heart rhythm. Do not take Gilenya if you are allergic to fingolimod or any of the other ingredients.

Gilenya may cause side effects such as:

- Slow heart rate, especially after first dose. You will be monitored by a health care professional for at least 6 hours after your first dose. Your pulse and blood pressure will be checked hourly. You'll get an ECG before and 6 hours after your first dose. If any heart problems arise or your heart rate is still low, you'll continue to be monitored. If you have any serious side effects, especially those that require treatment with other medicines, or if you have certain types of heart problems, or if you're taking medicines that can affect your heart, you'll be watched overnight. If you experience slow heart rate, it will usually return to normal within 1 month. Call your doctor, or seek immediate medical attention if you have any symptoms of slow heart rate, such as feeling dizzy or tired or feeling like your heart is beating slowly or skipping beats. Symptoms can happen up to 24 hours after the first dose. Do not stop taking Gilenya without consulting with your doctor. Call your doctor if you miss 1 or more doses of Gilenya—you may need to repeat the 6-hour monitoring.
- Increased risk of serious infections. Gilenya lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 2 months of stopping Gilenya. Your doctor may do a blood test before you start Gilenya. Gilenya may decrease the way vaccines work in your body, especially

the chicken pox vaccine. Increased risk of infection was seen with doses higher than the approved dose (0.5 mg). Two patients died who took higher-dose Gilenya (1.25 mg) combined with high-dose steroids. Call your doctor right away if you have fever, tiredness, body aches, chills, nausea, vomiting, or headache accompanied by fever, neck stiffness, sensitivity to light, nausea, and/or confusion. These may be symptoms of meningitis.

- Progressive multifocal leukoencephalopathy (PML). PML is a rare brain infection that usually leads to death or severe disability. If PML happens, it usually happens in people with weakened immune systems. It is important that you call your doctor right away if you have any new or worsening medical problems that have lasted several days, including problems with thinking, eyesight, strength, balance, weakness on 1 side of your body, or using your arms and legs.
- Macular edema, a vision problem that can cause some of the same vision symptoms as an MS attack (optic neuritis), or no symptoms. If it happens, macular edema usually starts in the first 3 to 4 months after starting Gilenya. Your doctor should test your vision before you start Gilenya; 3 to 4 months after you start Gilenya; and any time you notice vision changes. Vision problems may continue after macular edema has gone away. Your risk of macular edema may be higher if you have diabetes or have had an inflammation of your eye (uveitis). Call your doctor right away if you have blurriness, shadows, or a blind spot in the center of your vision; sensitivity to light; or unusually colored vision.
- Swelling and narrowing of the blood vessels in your brain. A condition called PRES (Posterior reversible encephalopathy syndrome) has occurred rarely in patients taking Gilenya. Symptoms of PRES usually get better when you stop taking Gilenya. However, if left untreated, it may lead to a stroke. Call your doctor right away if you experience any symptoms, such as sudden headache, confusion, seizures, loss of vision, or weakness.
- Breathing problems. Some patients have shortness of breath. Call your doctor right away if you have trouble breathing.
- Liver problems. Your doctor should do blood tests to check your liver before you start Gilenya. Call your doctor right away if you have nausea, vomiting, stomach pain, loss of appetite, tiredness, dark urine, or if your skin or the whites of your eyes turn yellow.
- Increases in blood pressure (BP). BP should be monitored during treatment.
- A type of skin cancer called basal cell carcinoma (BCC). Talk to your doctor if you notice any skin nodules (shiny, pearly nodules), patches or open sores that do not heal within weeks. These may be signs of BCC.

Gilenya may harm your unborn baby. Talk to your doctor if you are pregnant or planning to become pregnant. Women who can become pregnant should use effective birth control while on Gilenya, and for at least 2 months after stopping. If you become pregnant while taking Gilenya, or within 2 months after stopping, tell your doctor right away. Women who take Gilenya should not breastfeed, as it is not known if Gilenya passes into breast milk. A pregnancy registry is available for women who become pregnant during Gilenya treatment. For more information, contact the Gilenya Pregnancy Registry by calling Quintiles at 1-877-598-7237, by e-mailing gpr@quintiles.com, or by going to www.gilenyapregnancyregistry.com.

Tell your doctor about all your medical conditions, including if you had or now have an irregular or abnormal heartbeat; heart problems; a history of repeated fainting; a fever or infection, or if you are unable to fight infections due to a disease or are taking medicines that lower your immune system, including corticosteroids, or have taken them in the past; eye problems; diabetes; breathing or liver problems; or uncontrolled high blood pressure. Also tell your doctor if you have had chicken pox or have received the chicken pox vaccine. Your doctor may test for the chicken pox virus, and you may need to get the full course of the chicken pox vaccine and wait 1 month before starting Gilenya.

If you take too much Gilenya, call your doctor or go to the nearest hospital emergency room right away.

Tell your doctor about all the medicines you take or have recently taken, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Tell your doctor if you have been vaccinated within 1 month before you start taking Gilenya. You should not get certain vaccines, called live attenuated vaccines, while taking Gilenya and for at least 2 months after stopping Gilenya treatment.

The most common side effects with Gilenya were headache, abnormal liver tests, diarrhea, cough, flu, sinusitis, back pain, abdominal pain, and pain in arms or legs.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/MedWatch or call 1-800-FDA-1088.

Please see full Prescribing Information, including Medication Guide at http://www.pharma.us.novartis.com/product/pi/pdf/gilenya.pdf.

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About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 121,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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