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Novartis announces FDA approval of Gilenya® as the first disease-modifying therapy for pediatric relapsing multiple sclerosis

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- - New approval for Gilenya (fingolimod) addresses strong unmet need for younger patients, who often experience more frequent relapses than adults with multiple sclerosis (MS)(1)
- - In a landmark controlled Phase III study of children and adolescents (ages 10 to less than 18) with relapsing forms of MS (RMS), Gilenya reduced the annualized relapse rate by approximately 82% vs. interferon beta-1a injections (p< 0.001)(2)
- - Gilenya is the most prescribed oral once-daily MS disease-modifying treatment, with a global exposure of more than 231,000 patients since its initial approval for adults with RMS(3)

EAST HANOVER, N.J., May 11, 2018 /PRNewswire/ -- Novartis today announced that the US Food and Drug Administration (FDA) has approved Gilenya® (fingolimod) for the treatment of children and adolescents 10 to less than 18 years of age with relapsing forms of multiple sclerosis, making it the first disease-modifying therapy indicated for these patients[2].

This approval expands the age range for Gilenya, which was previously approved for patients aged 18 years and older with RMS. Gilenya was granted Breakthrough Therapy designation by the FDA in December of 2017 for this pediatric indication.

"We now finally have an FDA-approved treatment for children and adolescents with relapsing MS," said Dr. Brenda Banwell, Chief of the Division of Neurology at Children's Hospital of Philadelphia, who served as co-Principal investigator of the pivotal study that supported the pediatric approval. "Repeated relapses are more common in young people with MS than in adults, so this is heartening news for patients and their families."

While MS is mostly diagnosed in adults, children and adolescents with the chronic disease often experience more frequent relapses and brain lesions than adults with MS[1].

"We have eagerly anticipated a proven treatment option for younger people living with MS," said Elin Phillips, President, Pediatric Multiple Sclerosis Alliance. "Until now, there have been no large clinical trials to assess treatment efficacy of disease-modifying therapies in children and adolescents. On behalf of the pediatric community, we would also like to thank the families and the clinical trial patients who made this progress possible."

The approval of Gilenya for the younger patient population was supported by PARADIGMS, a double-blind, randomized, multi-center Phase III safety and efficacy study of fingolimod vs. interferon beta-1a, designed specifically for children and adolescents with RMS[4]. The primary endpoint demonstrated that fingolimod reduced the rate of relapses (annualized relapse rate) by approximately 82% (p <0.001) over a period of up to two years compared to interferon beta-1a intramuscular injections in children and adolescents (ages 10 and older) with relapsing MS[2]. The safety profile of Gilenya in this study was overall consistent with that seen in previous clinical trials in adults[2]. In this study, while more adverse events (AEs) were reported in the interferon beta-1a group, severe AEs were reported at a higher frequency in fingolimod-treated patients[2].

"After becoming the first approved oral MS therapy in the US in 2010, we're proud this new approval represents another first for Gilenya," said Fabrice Chouraqui, US President of Novartis Pharmaceuticals Corporation. "It is the latest achievement in our ongoing commitment to drive innovation in MS and bring additional treatment options to more patients, including young people with MS."

About the Phase III PARADIGMS Study

The Phase III PARADIGMS study (NCT01892722) is a flexible duration (up to two years), double-blind, randomized, multi-center study to evaluate the safety and efficacy of oral fingolimod compared to interferon beta-1a in children and adolescents with a confirmed diagnosis of MS, followed by a five-year open label extension phase[5]. The study enrolled 215 children and adolescents with MS, 10 to less than 18 years of age with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5[5]. Patients were randomized to receive once-daily oral fingolimod (n=107, 0.5 mg or 0.25 mg, dependent on patients' body weight) or intramuscular interferon beta-1a (n=108) once weekly[5].

The primary endpoint of the study was the frequency of relapses in patients treated up to 24 months (annualized relapse rate)[5]. Secondary endpoints include the number of new or newly enlarged T2 lesions, Gadolinium enhancing T1 lesions, safety and the pharmacokinetic properties of fingolimod, all measured throughout the treatment period[5].

The Phase III PARADIGMS study was conducted in 87 sites over 26 countries, and was designed in partnership with the US Food and Drug Administration, European Medicines Agency and the International Pediatric Multiple Sclerosis Study Group.

About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic disorder of the central nervous system (CNS) that disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[6]. In adults, there are three types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)[7]. Approximately 85 percent of people with MS have relapsing-remitting MS, where the immune system attacks healthy tissue[8]. In children, RRMS accounts for nearly all cases (approximately 98 percent)[9].

In the US, MS affects around 400,000 people[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 decreases the frequency of MS flare-ups (relapses) and helps slow down the physical problems caused by RRMS.

Gilenya is the most prescribed oral once-daily DMT in the US, with approximately 79,800 patients having been exposed to Gilenya. Worldwide, Gilenya has been used to treat approximately 231,000 patients in both clinical trials and the post-marketing setting, with approximately 536,000 years of patient experience[3].

Indication

GILENYA is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS) in adults and children 10 years of age and older.

Important Safety Information

You should not take GILENYA if in the last 6 months you experienced heart attack, unstable angina, stroke or mini-stroke (transient ischemic attack or TIA), 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 serious side effects such as:

- Slow heart rate, especially after first dose. Adults and children will be monitored by a health care professional for at least 6 hours after the first dose or after a child takes the first dose of 0.5mg of GILENYA when switching from 0.25mg daily 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 dizziness, tiredness, feeling like your heart is beating slowly or skipping beats, or chest pain. 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, some of which could be life threatening and cause death. You should not receive live vaccines during treatment with GILENYA and for 2 months after you stop taking GILENYA. Vaccines may not work as well when given during treatment with GILENYA. 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 to check your white blood cells before you start GILENYA. Call your doctor right away if, while taking GILENYA or for 2 months after your last dose, 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 but has happened in people who do not have weakened immune systems. Call your doctor right away if you have any new or worsening symptoms of PML that have lasted several days, including changes in your thinking or memory, changes in your vision, decreased strength, problems with balance, weakness on 1 side of your body, loss of coordination in your arms and legs, confusion or changes in your personality.
- 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 is 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 happened rarely in adults 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 severe headache, sudden confusion, seizures, or sudden loss of vision.
- 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.
- Skin cancers including basal and Merkel cell carcinoma and melanoma. Tell your doctor if you have any changes in the appearance of your skin, including changes in a mole, new darkened area in your skin, a sore that does not heal, or growths on your skin such as a bump that may be shiny, pearly white, skin colored, or pink. While taking GILENYA, limit the amount of time you spend in sunlight and ultraviolet (UV) light as well as use sunscreen with a high sun protection factor and wear protective clothing.

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. It is not known if GILENYA passes into breast milk. Talk to your doctor about the best way to feed your baby if you take GILENYA. 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; stroke or mini-stroke; 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. Children 10 years and older should complete their vaccination schedule 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.

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.

In the pediatric study:

- The safety in children 10 years and older receiving GILENYA was similar to that seen in adults.
- The rate of seizures was higher in GILENYA-treated patients compared to that of a leading injectable.

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:
https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gilenya.pdf

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References

1. National Multiple Sclerosis Society. Pediatric MS. http://www.nationalmssociety.org/What-is-MS/Who-Gets-MS/Pediatric-MS. Accessed April 2018.
2. Gilenya® (fingolimod) Full Prescribing Information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation; May 11, 2018
3. Novartis Pharmaceuticals. Data on file.
4. Chitnis T et al. PARADIGMS: A Randomised Double-blind Study of Fingolimod Versus Interferon β-1a in Paediatric Multiple Sclerosis. Abstract no. 276. Oral presentation at 7th Joint ECTRIMS-ACTRIMS Meeting, Paris, France, October 25-28, 2017.
5. Clinical Trials. Safety and efficacy of fingolimod in pediatric patients with multiple sclerosis. https://clinicaltrials.gov/ct2/show/NCT01892722. Accessed April 2018.
6. PubMed Health. Multiple Sclerosis (MS). https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0024311/. Accessed April 2018.
7. Multiple Sclerosis Society. Types of MS. https://www.mssociety.org.uk/what-is-ms/types-of-ms. Accessed April 2018.

8. Multiple Sclerosis International Federation. Atlas of MS 2013. https://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf. Accessed April 2018.
9. Waldman A et al. Pediatric multiple sclerosis: Clinical features and outcome. Neurology 2016;87 (Suppl 2):S74-S81.
10. Tullman M. Overview of the epidemiology, diagnosis and disease progression associated with multiple sclerosis. Am J Managed Care. 2013 Feb;19(2 Suppl):S15-20.

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