Novartis Australia announces TGA approval of Gilenya® (fingolimod), the first licenced oral treatment for paediatric MS

May 01, 2019

- *Gilenya® (fingolimod) is the first licenced oral treatment for paediatric patients with multiple sclerosis in Australia*
- *Children and young people diagnosed with multiple sclerosis (MS) typically relapse two-to-three times more frequently than adults, causing increased symptom severity[i]*
- *TGA approval is supported by the results of the PARADIGMS study[ii]*

Sydney, May 1, 2019 – Novartis today announced that the Therapeutic Goods Administration (TGA) has approved Gilenya® (fingolimod) for the treatment of children and adolescents 10-17 years old with relapsing forms of multiple sclerosis. The registration makes Gilenya the first licenced disease-modifying treatment for children and adolescents in Australia.

MS is the most commonly acquired disease of the central nervous system among young adults in Australia[iii]. Approximately 5% of people with MS experience disease onset before they reach the age of 18[iv].

Compared to adults, children and adolescents experience two-to-three times as many relapses[1]. With each relapse, MS can severely impact a young person's mobility, balance, co-ordination and sensation[v]. Thirty percent (30%) of those diagnosed experience significant cognitive impairment[vi] and it is thought that around half will experience depression within two years of disease onset[vii].

"The debilitating symptoms of MS can severely limit children and adolescents' ability to participate in normal day-to-day activities such as going to school," said Paediatric Neurologist Associate Professor Andrew Kornberg. "Today's milestone is welcome news to both the medical community and those affected by the disease."

The TGA approval of Gilenya is based on the results of the PARADIGMS Phase III study, published in the New England Journal of Medicine (NEJM) in 2018[2].

"The recent approval marks a significant milestone in our journey to change the course of MS," said Richard Tew, General Manager of Novartis Pharmaceuticals Australia and New Zealand. "Novartis are committed to reimagining the care of people affected by MS and we will work closely with all stakeholders to help improve the lives of young Australians living with this disease."

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[i] Gorman MP et al. Increased relapse rate in pediatric-onset compared with adult-onset multiple sclerosis. Arch Neurol. 2009; 66: 54-59.

[ii] Chitnis T et al. Fingolimod versus Interferon Beta-1a in Pediatric Multiple Sclerosis. NEJM 2018; 379: 1017-1027.

[iii] MS Australia. Key facts and figures about multiple sclerosis. Available at:

msaustralia.org.au/file/1276/download?token=1KgyRQBY (link is external). Accessed April 2019.

[iv] Patel Y et al. Pediatric multiple sclerosis. Ann Indian Acad Neurol. 2009; 12(4): 238-245.

[v] Patel Y et al. Pediatric multiple sclerosis. Ann Indian Acad Neurol. 2009;12(4):238-245.

[vi] Amato MP et al. Cognitive and psychosocial features of childhood and juvenile MS. Neurology. 2008; 70: 1891-1897.

[vii] Bigi S and Banwell B. Pediatric multiple sclerosis. J Child Neurol. 2012;27(11):1378-1383. Epub 2012 Aug 21.

Minimum Product Information

See approved Product Information before prescribing. Approved Product Information available on request. For the most up to date Product Information go to https://www.novartis.com/au-en/products/consumer-information

GILENYA® (fingolimod)

Indication: *Treatment of adult and paediatric patients of 10 years of age and above with relapsing forms of Multiple Sclerosis to reduce the frequency of relapses and delay the progression of disability.*

Dosage and administration: To be taken orally with or without food**. Adults:** One 0.5 mg capsule taken once daily. ***Children and Adolescents:*** *body weight ≤ 40 kg: one 0.25 mg capsule per day; weight > 40 kg: one 0.5 mg capsule per day.* Special patient population: No dosage adjustment needed for renal impairment, mild to moderate hepatic impairment or elderly patients (caution as experience is limited). Caution in patients with severe hepatic impairment and diabetes mellitus.

Contraindications: Patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization or Class III/IV heart failure. History or presence of Mobitz Type II second-degree or third-degree atrioventricular (AV) block or sick-sinus syndrome, unless patient has a functioning pacemaker. Baseline QTc interval ≥ 500 msec. Concomitant treatment with Class Ia or Class III anti-arrhythmic drugs during Gilenya initiation. Known hypersensitivity to fingolimod or any of the excipients.

Precautions: First dose monitoring: ECG to be performed, heart rate, blood pressure to be monitored, same recommendation applies after interruption of treatment. **Bradyarrhythmia:** Due to the risk of serious cardiac rhythm disturbances, Gilenya should not be used in patients with sino-atrial heart block, a history of symptomatic bradycardia or recurrent syncope, significant QT prolongation, (QTc >470 msec (adult females), *QTc >460 msec (paediatric females),* or >450 msec (adult *and paediatric* males)) relevant risk factors for QT prolongation, concurrent therapy with QT prolonging drugs with a known risk of torsades de pointes. Gilenya should also not be used in patients with history of cardiac arrest, uncontrolled hypertension or severe untreated sleep apnoea since significant bradycardia may not be well tolerated in these patients; Concurrent therapy with beta-blockers, heart rate lowering calcium channel blockers or other substances that may decrease heart rate. **Vaccination** may be less effective during and for up to two months after treatment with Gilenya. The use of live attenuated vaccines should be avoided. Varicella zoster virus (VZV) vaccination is recommended in antibody-negative patients. *In paediatric patients, a complete vaccination schedule is recommended before starting Gilenya.* **Infections:** Lymphocyte count is decreased during Gilenya therapy and up to two months after stopping Gilenya therapy. Do not start Gilenya in patients with active acute or chronic infections until this has resolved. Consider discontinuing therapy if a serious infection develops, and re-evaluate benefit-risk before restarting. Cases of progressive multifocal leukoencephalopathy (PML) and cryptococcal meningitis have been reported in the post-marketing setting. **Macular oedema:** Patients with

history of uveitis and diabetes mellitus are particularly at risk of developing macular oedema. An ophthalmic examination is recommended before Gilenya therapy initiation and regularly during Gilenya therapy in patients at risk. Discontinuing therapy should be considered if macular oedema develops. **Liver Function:** Recent transaminase and bilirubin levels should be available before initiation of treatment. A liver function test is recommended in patients who develop symptoms of hepatic dysfunction during treatment or with a history of significant liver disease. Gilenya should be discontinued if significant liver injury is confirmed. **Posterior reversible encephalopathy syndrome (PRES):** Discontinue Gilenya treatment if PRES is suspected. **Immunosuppressive or immune-modulating therapies:** Caution when switching patients from natalizumab or teriflunomide to Gilenya. Initiating treatment with Gilenya after alemtuzumab is not recommended unless the benefits clearly outweigh the risks. **Skin cancers:** Basal cell carcinoma (BCC) *and other cutaneous neoplasms* are associated with use of Gilenya. Healthcare professionals and patients are advised to monitor for suspicious skin lesions. ***Return of disease activity:*** *severe exacerbation of disease has been reported after discontinuation of Gilenya, usually within 12 weeks,but in some cases up to and beyond 24 weeks. Patients should be monitored for relevant signs and symptoms, initiate appropriate treatment as required.* (See full PI for details.)

Pregnancy: Category D. Adequate contraceptive measures in women of childbearing potential are needed during treatment with Gilenya and for at least 2 months following discontinuation of treatment.

Breastfeeding: Women receiving Gilenya should not breast feed.

Interactions: At treatment initiation concomitant use with beta-blockers, heart rate lowering calcium channel blockers (e.g. verapamil, diltiazem) or other drugs that may lower heart rate (e.g. ivabradine or digoxin) is not recommended. Caution is required in concomitant use of anti-neoplastic, immunosuppressive or immune modulating therapies (including corticosteroids) during and for up to two months after stopping Gilenya treatment. Caution is required when switching therapy from drugs with a long-acting immune effect such as natalizumab, teriflunomide or mitoxantrone. Concomitant use is not recommended with live attenuated vaccines; other vaccines may have reduced efficacy during and for up to two months after stopping Gilenya therapy. Patients who use Gilenya and systemic ketoconazole concomitantly should be closely monitored.

Adverse effects: Very common (>10%): Influenza, sinusitis, headache, diarrhoea, back pain, hepatic enzymes increased, cough. Common (1 to 10%): Bronchitis, herpes zoster, tinea versicolour, basal cell carcinoma, bradycardia, dizziness, migraine, asthenia, eczema, pruritus, hepatic enzyme increased, blood triglycerides increased, liver function test abnormal, dyspnoea, vision blurred, hypertension, leucopenia, lymphopenia. Uncommon (<0.1 to 1%): Pneumonia, macular oedema, *melanoma, seizures including status epilepticus.* Rare (0.01 to 0.1%): Posterior reversible encephalopathy syndrome. *Very rare (<0.01%):Kaposi's sarcoma*. Frequency not known: Hypersensitivity reactions, including rash, urticaria and angioedema upon treatment initiation. *Severe exacerbation of disease after Gilenya discontinuation.* Nausea*. Myalgia, arthralgia.* Thrombocytopenia. Post-marketing setting: Cases of opportunistic infections, some of which were serious, (viral infections such as PML, encephalitis and meningitis (herpes simplex and varicella zoster), fungal infections including cryptococcal meningitis and atypical mycobacterial skin and lung infections). Isolated cases of transient spontaneously resolving complete AV block during the six hour observation period. (gil090419m.doc based on gil090419i). Novartis Pharmaceuticals Australia Pty Limited ABN 18 004 244 160. 54 Waterloo Road, Macquarie Park NSW 2113. Ph (02) 9805 3555. ® = Registered Trademark.

**Please note changes in Product Information*

PBS Information: The 0.5 mg capsule is Authority Required. For use in patients with relapsing-remitting multiple sclerosis who meet certain criteria. Refer to PBS Schedule for full Authority Required information. The 0.25 mg capsule is not listed on the PBS.

About Multiple Sclerosis

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

The evolution of MS results in an increasing loss of both physical and cognitive (e.g. memory) function. It is estimated that over 25,600 people in Australia are living with MS[3], and it is believed that 85% are diagnosed with relapse remitting MS[3], a form of the disease that brings unpredictable symptom flares that are challenging to manage and significantly impact quality of life [v]. Approximately 5% of people with MS will experience symptom onset before the age of 18[4].

About Gilenya

Gilenya® is indicated for the treatment of adult and paediatric patients of 10 years of age and above with relapsing forms of multiple sclerosis to reduce the frequency of relapses and to delay the progression of disability.[vi] To date, an estimated 267,000 adult patients worldwide have been treated with Gilenya, amounting to approximately 621,000 adult patient-years of experience.[vii]

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[i] PubMed Heath. Multiple Sclerosis (MS). ncbi.nlm.nih.gov/pubmedhealth/PMH0001747/. Accessed April 2019.

[ii] MS Australia. Types of MS. https://www.msaustralia.org.au/about-ms/types-ms. Accessed: April 2019.

[iii] Multiple Sclerosis International Federation. Atlas of MS 2013. Atlas-of-MS-3571 (PDF 3.5 MB) Accessed April 2019.

[iv] Waldman A et al. Pediatric multiple sclerosis. Neurology. 2016; 87(9): S74-S81.

[v] Kargiotis O et al. Quality of life in multiple sclerosis: effects of current treatment options. 2010; 22(1): 67-82

[vi] Gilenya TGA-approved Product Information. Novartis Pharmaceuticals Australia Pty Ltd 12th April 2019. https://www.guildlink.com.au/gc/ws/nv/pi.cfm?product=nvpgilor11115 Accessed: April 2019.

[vii] Data cut-off 30-11-2018, Novartis Pharmaceuticals Q4 2018 Financial Report dated January 2019

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