Physician's checklist:

Summary of recommendations

Gilenya®
0.5 mg hard capsules (fingolimod)

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA

GILENYA® (fingolimod) SFDA approved RMP Educational Materials V 20.2 May 2025

NOVARTIS

Considerations for Gilenya® (fingolimod) patient selection

Gilenya is suitable for adult and pediatric patients (≥10 years old) for the treatment of highly active relapsing remitting MS (RRMS).*

Considerations for treatment initiation

Gilenya is contraindicated in patients with cardiac condition. Do not initiate Gilenya in patients with cardiac condition or who are taking medicinal products for which Gilenya is contraindicated.

Gilenya causes transient heart rate reduction and may cause atrioventricular (AV) conduction delays following initiation of treatment. All patients should be monitored for a minimum of 6 hours on treatment initiation.

Monitoring requirements

Consider patients with the following conditions only after performing risk/benefit analysis and consulting a cardiologist.

Sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QT-interval prolongation†, history of cardiac arrest, uncontrolled hypertension or severe sleep apnea.

- At least overnight extended monitoring is recommended
- Consult cardiologist regarding appropriate first-dose monitoring

Taking beta-blockers, heart-rate–lowering calcium channel blockers‡, or other substances that are known to lower the heart rate§.

- Consult cardiologist regarding possibility of switching to non-heart-rate-lowering drugs
- If change in medication is not possible, extend monitoring to at least overnight
- Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines

It should also be followed at re-initiation of treatment if Gilenya is discontinued for:

- One day or longer within the first 2 weeks of treatment
- More than 7 days during weeks 3 and 4
- More than 2 weeks after the first month of treatment

Monitor for a minimum of 6 hours

After first dose and when re-initiating following discontinuation or increase in daily dose

- ☐ Perform baseline ECG and BP measurement
- ☐ Monitor for a minimum of 6 hours for signs and symptoms of bradycardia, with hourly pulse and BP checks. If patient is symptomatic, continue monitoring until resolution
  - Continuous (real-time) ECG is recommended throughout the 6-hour period
- ☐ Perform ECG at 6 hours

Treatment initiation algorithm

☐ Did the patient require pharmacologic intervention at any time during the monitoring period?
- No
- Yes → Monitor overnight in a medical facility. The first-dose monitoring should be repeated after the second dose of Gilenya

☐ Did third-degree AV block occur at any time during the monitoring period?
- No
- Yes → Extend monitoring at least overnight, until the findings have resolved

At the end of the monitoring period, did any of the following occur?

☐ HR <45 bpm, <55 bpm in pediatric patients aged ≥12 years old, or <60 bpm in pediatric patients aged 10 to <12 years of age

☐ ECG shows new-onset second-degree or higher AV block or QTc interval ≥500 msec

- No
- Yes → Extend monitoring at least overnight, until the findings have resolved

☐ At the end of the monitoring period, is the HR the lowest since the first dose was administered?
- No
- Yes → Extend monitoring by at least 2 hours and until the heart rate increases

First-dose monitoring is complete

BP=blood pressure; ECG=electrocardiogram; HR=heart rate; QTc=heart-rate–corrected QT interval.

*Gilenya is indicated as single disease modifying therapy in highly active relapsing remitting multiple sclerosis for the following groups of adult patients and pediatric patients aged 10 years and older: patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy, or patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI.

†QTc >470 msec (adult females), >460 msec (pediatric females), or >450 msec (adult and pediatric males).
‡Includes verapamil or diltiazem.
§Includes Class Ia and Class III antiarrhythmics, ivabradine, digoxin, anticholinesteratic agents, or pilocarpine.
Approved dose of 0.5 mg once daily to be used when restarting treatment as other dosing regimens have not been approved.

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Recommendations for managing patients on Gilenya

Key safety assessments and considerations before, during and after discontinuing treatment.

Prior to initiating treatment

- ☐ Gilenya is contraindicated in patients with severe liver impairment (Child-Pugh class C). Do not initiate Gilenya in patients with this condition
- ☐ Obtain recent (within 6 months) transaminase, and bilirubin levels
- ☐ Obtain recent (within 6 months or after discontinuation of prior therapy) full blood count
- ☐ Inform women of childbearing potential (including female adolescents and their parents/caregivers) that Gilenya is contraindicated in pregnant women and women of childbearing potential not using effective contraception, and about the serious risks of Gilenya to a fetus
- ☐ Gilenya is teratogenic. Confirm a negative pregnancy test result in women of childbearing potential (including female adolescents) prior to starting treatment and repeat at suitable intervals during treatment
- ☐ Provide all patients, parents (or legal representatives) and caregivers with the Pregnancy-Specific Patient Reminder Card
- ☐ Counsel women of childbearing potential (including female adolescents and their parents/caregivers) to avoid pregnancy and use effective contraception both during treatment and for 2 months after treatment discontinuation. Counselling should be facilitated by the Pregnancy-Specific Patient Reminder Card
- ☐ Gilenya is contraindicated in patients with immunodeficiency syndrome, increased risk for opportunistic infections including immunocompromised patients or severe active or active chronic infections (i.e. hepatitis or tuberculosis). Do not initiate Gilenya in patients with any of these conditions
- ☐ Delay initiation of treatment in patients with severe active infection until resolved
- ☐ Avoid co-administration of anti-neoplastic, immunomodulatory or immunosuppressive therapies due to the risk of additive immune system effects. For the same reason, a decision to use prolonged concomitant treatment with corticosteroids should be taken after careful consideration
- ☐ Human papilloma virus (HPV) infection, including papilloma, dysplasia, warts and HPV-related cancer, has been reported in the post-marketing setting. Cancer screening (including a Pap test) and vaccination for HPV-related cancer is recommended for patients as per standard of care
- ☐ Do not treat with Gilenya in patients with suspected or confirmed progressive multifocal leukoencephalopathy (PML)
- ☐ Ensure patients have a baseline MRI usually within 3 months before initiating Gilenya
- ☐ Check varicella zoster virus (VZV) antibody status in patients without a healthcare professional confirmed history of chickenpox or documentation of a full course of varicella vaccination. If negative, a full course of vaccination with varicella vaccine is recommended and treatment initiation should be delayed for 1 month to allow full effect of vaccination to occur
- ☐ Conduct an ophthalmologic evaluation in patients with history of uveitis or diabetes mellitus
- ☐ Conduct a dermatologic examination. The patient should be referred to a dermatologist in case suspicious lesions, potentially indicative of basal cell carcinoma, or other cutaneous neoplasms (including malignant melanoma, squamous cell carcinoma, Kaposi's sarcoma and Merkel cell carcinoma) are detected
- ☐ Provide patients, parents and caregivers with the Patient, Parent and Caregiver Guide

During treatment

- [ ] Obtain an ophthalmologic assessment in all patients:
  - 3–4 months after starting treatment for the early detection of visual impairment due to drug-induced macular edema
  - Discontinue Gilenya in patients who develop macular degeneration. Restart only after careful benefit-risk consideration
- [ ] Counsel patients to report signs and symptoms of infection immediately to their prescriber during and for up to 2 months after treatment with Gilenya has been discontinued
  - Symptoms such as fever, flu-like symptoms, headache accompanied by stiff neck, sensitivity to light, nausea, shingles and/or confusion, or seizures may be symptoms of meningitis and/or encephalitis
  - Perform prompt diagnostic evaluation in patients with symptoms and signs consistent with encephalitis, meningitis or meningoencephalitis and initiate appropriate treatment if diagnosed
    - Serious, life-threatening, and sometimes fatal cases of encephalitis, meningitis or meningoencephalitis caused by herpes simplex virus (HSV) and VZV were reported while on Gilenya treatment
    - Reports of cryptococcal meningitis (sometimes fatal) have been received after approximately 2–3 years of treatment, although an exact relationship with the duration of treatment is unknown
  - Gilenya should be discontinued in patients with CNS herpes and infections. Gilenya should be suspended in patients with cryptococcal meningitis with careful consideration with a specialist before reinitiating
  - Inform patients that during Gilenya treatment, they should not receive live attenuated vaccines and that other vaccines may be less effective
  - PML has been predominantly observed after 2 or more years of fingolimod treatment
  - Annual MRIs may be considered especially in patients with multiple risk factors generally associated with PML
  - If PML is suspected, perform a diagnostic MRI immediately and suspend Gilenya until PML has been excluded. Permanently discontinue Gilenya if PML is confirmed
  - Immune reconstitution inflammatory syndrome (IRIS) has been reported in patients treated with S1P receptors modulators, including fingolimod, who developed PML and subsequently discontinued treatment. The time to onset of IRIS in patients with PML was usually from weeks to months after S1P receptor modulator discontinuation. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken
  - For potentially serious infection, evaluate the patient promptly and consider an infectious disease referral. Consider suspending Gilenya and the benefit-risk of any subsequent reinitiation
- [ ] Monitor peripheral blood lymphocyte counts prior to and during treatment with Gilenya. Interrupt treatment for lymphocyte count<$0.2x10^9$/L until recovery
- [ ] Some cases of acute liver failure requiring liver transplant and clinically significant liver injury have been reported
  - In the absence of clinical symptoms:
    - Check liver transaminases and serum bilirubin at months 1, 3, 6, 9, and 12 on therapy and periodically thereafter until 2 months after Gilenya discontinuation
    - If liver transaminases are greater than 3 but less than 5 times the upper limit of normal (ULN) without increase in serum bilirubin, more frequent monitoring including serum bilirubin and alkaline phosphatase (ALP) measurements should be carried out to determine if further increases occur, and in order to discern if an alternative aetiology of liver dysfunction is present
    - Discontinue Gilenya if liver transaminases are at least 5 times the ULN or at least 3 times the ULN associated with any increase in serum bilirubin. Hepatic monitoring should be continued. Restart Gilenya only after careful benefit-risk consideration
- [ ] For patients with clinical symptoms of liver dysfunction, evaluate promptly and discontinue Gilenya if significant liver injury is confirmed. If serum levels return to normal (including if an alternative cause of the liver dysfunction is discovered), Gilenya may be restarted if the benefit-risk assessment is favorable for the patient
- [ ] While on treatment, women must not not become pregnant. Discontinue treatment if a woman becomes pregnant. Gilenya should be stopped 2 months before attempting to become pregnant, and the possible return of disease activity should be considered. An ultrasonography examination should be performed and medical advice about the harmful effects of Gilenya to a fetus should be provided
- [ ] Advise women of childbearing potential (including female adolescents and their parents/caregivers) that effective contraception must be used during treatment and for at least 2 months after treatment discontinuation. Pregnancy tests must be repeated at suitable intervals
- [ ] Women of childbearing potential (including female adolescents and their parents/legal representatives/caregivers) must be informed regularly about the serious risks of Gilenya to a fetus
- [ ] To help determine the effects of Gilenya exposure in pregnant women with MS, physicians are encouraged to report pregnant patients who may have been exposed to Gilenya at any time during pregnancy (from 8 weeks prior to last menstrual period onward) to Novartis by dialling +966112658100/ 8001240078 or visiting URL https://report.novartis.com/
- [ ] Vigilance for basal cell carcinoma and other cutaneous neoplasms is recommended with skin examination every 6 to 12 months and referral to a dermatologist if suspicious lesions are detected
  - Caution patients against exposure to sunlight without protection
  - Instruct patients to avoid concomitant phototherapy with UV-B-radiation or PUVA-photochemotherapy
- [ ] Consider suspending Gilenya and re-evaluate the benefit-risk to the patient of any subsequent re-initiation

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Summary guidance specifically for pediatric patients

All warnings, precautions and monitoring in adults also apply to pediatric patients. In addition:

Prior to initiating treatment

- ☐ Ensure that vaccination status is up to date before starting Gilenya
- ☐ Assess physical development (Tanner staging), and measure height and weight, as per standard of care

During treatment

- ☐ Perform first-dose monitoring on treatment initiation due to the risk of bradyarrhythmia
- ☐ Repeat first-dose monitoring in pediatric patients when the dosage is switched from 0.25 mg to 0.5 mg Gilenya once daily*
- ☐ Emphasize the importance of treatment compliance to patients, especially with regard to treatment interruption and the need to repeat first-dose monitoring
- ☐ Monitor the patient for signs and symptoms of depression and anxiety

*For pediatric patients (≥10 years old), the approved dosing for Gilenya is 0.5 mg once daily for patients weighing >40 kg.

Abbreviated Prescribing Information

You can report any problem or adverse events or request additional copies of the materials through:
Patient Safety Department Novartis Pharma AG - Saudi Arabia -.
Toll Free Number: 8001240078
Phone: +966112658100
Fax: +966112658107
Email: adverse.events@novartis.com
Or by online: https://report.novartis.com/

Saudi Food and Drug Authority National Pharmacovigilance Center
Unified Contact Center: 19999
Email: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

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