Golimara® (Fingolimod)

Prescriber's Checklist

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA)

Prescriber's Checklist

Considerations in Golimara ®(fingolimod) Patient Selection

Fingolimod is suitable for adult patients for the treatment of highly active relapsing-remitting multiple sclerosis (RRMS). While many patients may be suitable for treatment, the following section highlights patients in whom fingolimod is contraindicated or not recommended.

Considerations for treatment initiation
Fingolimod is indicated as single disease modifying therapy in highly active relapsing-remitting multiple sclerosis for the following groups of adult patients and paediatric 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.

Appropriate
Eligible adult patients with highly active RRMS who have not responded to a full and adequate course of at least one disease modifying therapy or those with rapidly evolving, severe RMS.

Contraindications
- Known immunodeficiency syndrome.
- Patients with increased risk for opportunistic infections, including immunocompromised patients (including those currently receiving immunosuppressive therapies or those immunocompromised by prior therapies).
- Severe active infections, active chronic infections (hepatitis, tuberculosis).
- Known active malignancies.
- Severe liver impairment (Child-Pugh class C).
- Patients who in the previous 6 months had myocardial infarction (MI), unstable angina pectoris, stroke/transient ischaemic attack (TIA), decompensated heart failure (requiring inpatient treatment) or New York Heart Association (NYHA) class III/IV heart failure.
- Patients with severe cardiac arrhythmias requiring anti-arrhythmic treatment with class Ia or class III anti-arrhythmic medicinal products.
- Patients with second-degree Mobitz type II atrioventricular (AV) block or third-degree AV block, or sick-sinus syndrome, if they do not wear a pacemaker.
- Patients with a baseline QTc interval ≥ 500 msec.
- Hypersensitivity to the active substance or to any of the excipients.

Physician Checklist–Recommended Steps to Managing Patients on Fingolimod

The checklist and schematic that follow are intended to assist in the management of patients on fingolimod.
Key steps and considerations while starting, continuing, or discontinuing treatment are provided.

Prior to initiating treatment

- ☐ Before initiating treatment, a baseline MRI should be available (usually within three months) as a reference
- ☐ Medical evaluation of the skin is recommended at initiation of treatment as cases of BCC have been reported in patients receiving fingolimod
- ☐ Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines
- ☐ Conduct baseline electrocardiogram (ECG) and blood pressure measurement
- ☐ Treatment with fingolimod is not recommended in the following patients:
  - Sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QT-interval prolongation†, history of cardiac arrest, uncontrolled hypertension or severe sleep apnoea
- ☐ Seek advice from a cardiologist regarding the most appropriate monitoring at treatment initiation; at least overnight extended monitoring is recommended
  - Those receiving concurrent therapy with beta-blockers, heart-rate–lowering calcium channel blockers (eg, verapamil, diltiazem, ivabradine), or other substances which may decrease heart rate (eg, digoxin, anticholinesteratic agents, pilocarpine)
- ☐ Seek advice from a cardiologist regarding a switch to non-heart-rate–lowering medicinal products prior to initiation of treatment
- ☐ If heart-rate–lowering medication cannot be stopped, seek advice from a cardiologist regarding the most appropriate monitoring at treatment initiation; at least overnight extended monitoring is recommended

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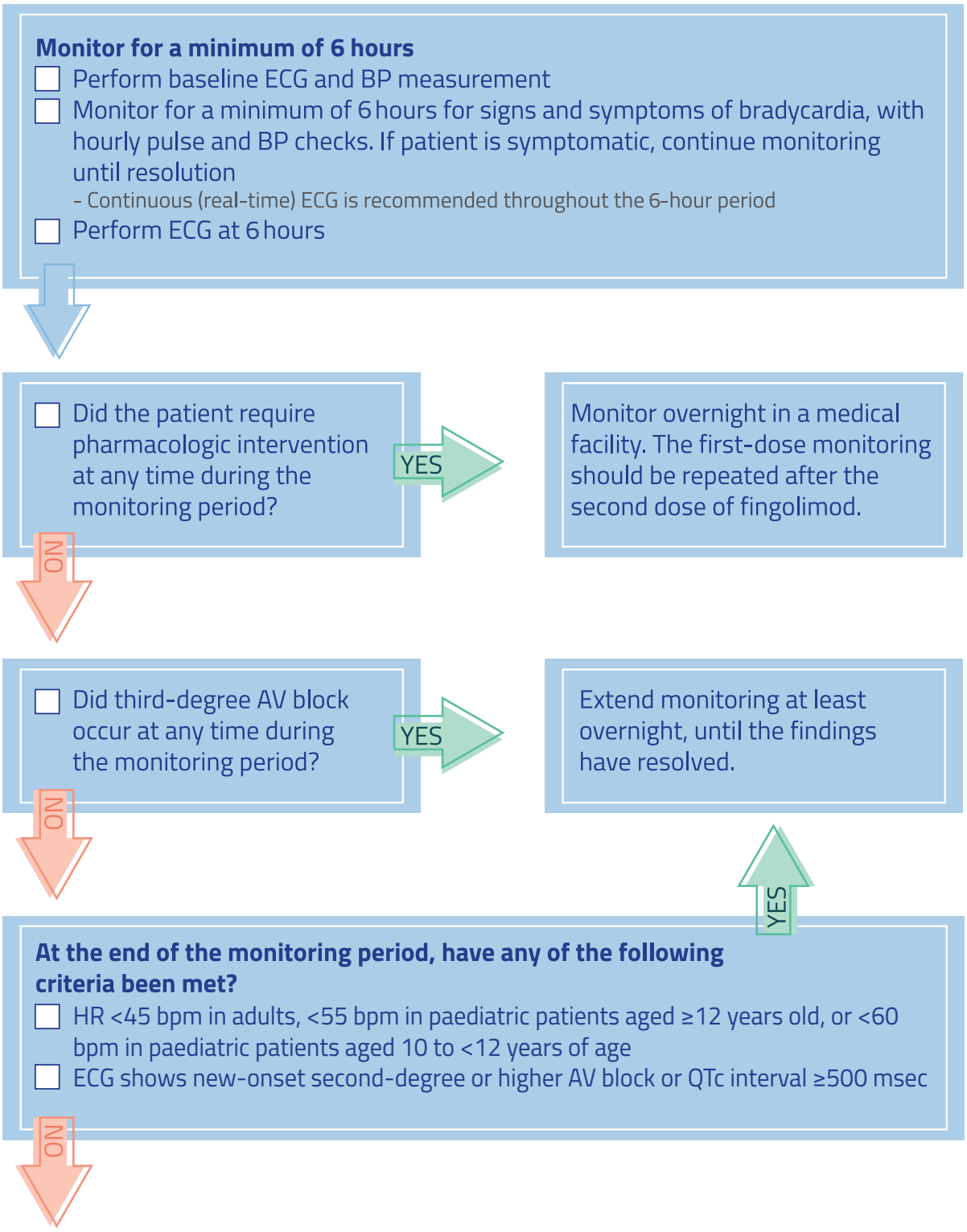
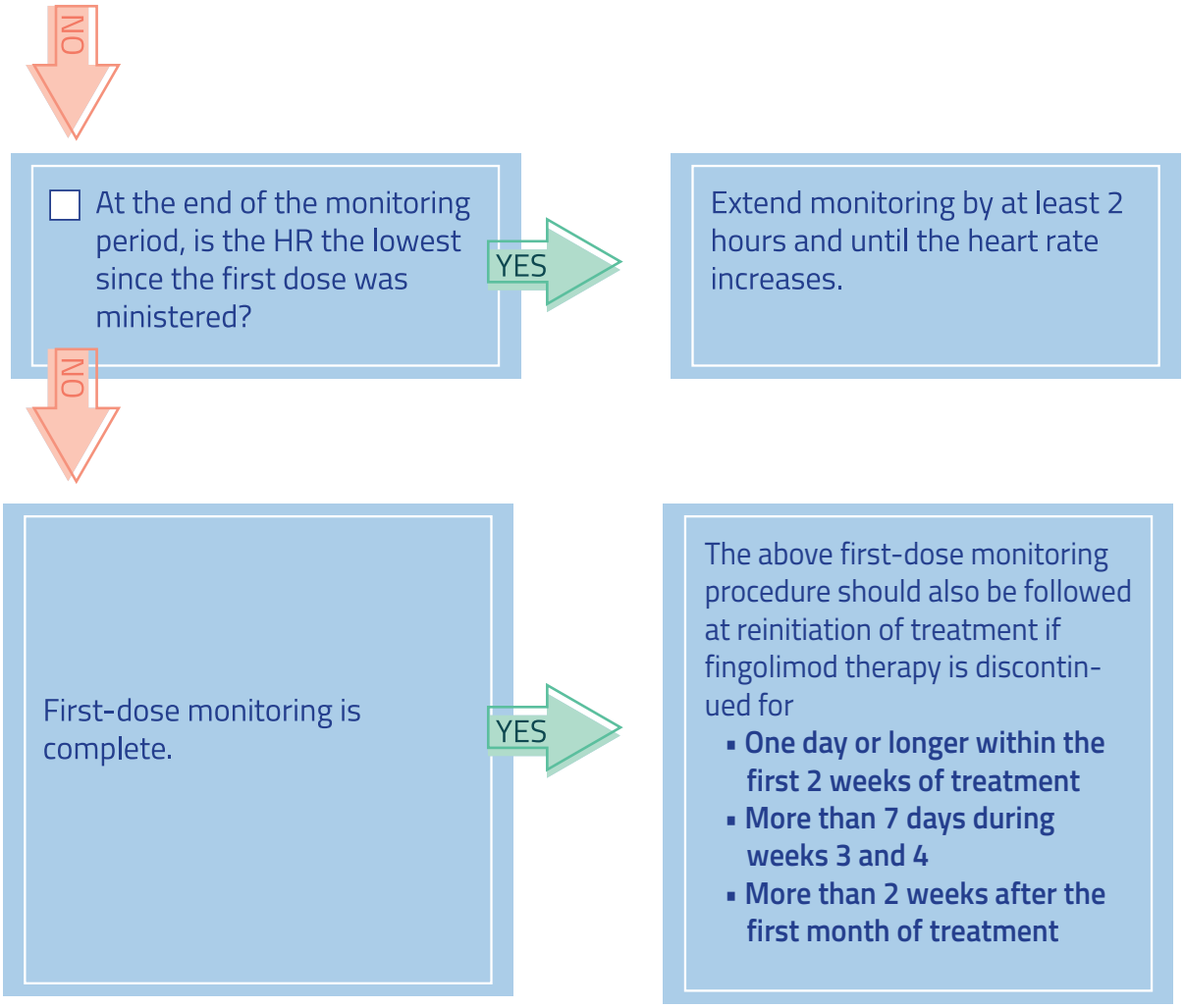
- [ ] Avoid co-administration of anti-neoplastic, immunomodulatory or immunosuppressive therapies due to the risk of additive immune system effects. For the same reason, a decision to use prolonged concomitant treatment with corticosteroids should be taken after careful consideration
- [ ] Obtain recent (within 6 months) transaminase, and bilirubin levels
- [ ] Obtain recent (within 6 months or after discontinuation of prior therapy) full blood count
- [ ] Confirm a negative pregnancy test result prior to starting treatment and repeat at suitable intervals during treatment
- [ ] Counsel on the need for effective contraception in women of childbearing age due to teratogenic risk to foetus, both during treatment and for 2 months after treatment discontinuation.
- [ ] Inform women of childbearing potential (including adolescents and their parents/caregivers) about the serious risks of fingolimod to the foetus.
- [ ] Delay initiation of treatment in patients with severe active infection until resolved
- [ ] 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
- [ ] 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
- [ ] For paediatric patients, assess Tanner staging, measure height and weight, and consider a complete vaccination schedule, as per standard of care
- [ ] Conduct an ophthalmologic evaluation in patients with history of uveitis or diabetes mellitus
- [ ] Provide patients with a Patient Reminder Card

†QTc >470 msec (adult females), >460 msec (paediatric females), or >450 msec (adult and paediatric males).

Treatment initiation algorithm

All patients will need to be monitored for at least 6 hours during treatment initiation, as described in the algorithm below. In addition, for patients in whom fingolimod is not recommended, advice should be sought from a cardiologist regarding appropriate monitoring; at least overnight monitoring is recommended for this group.





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

During treatment

☐ Conduct a full ophthalmologic evaluation at 3 to 4 months after starting treatment
- Conduct periodic ophthalmologic evaluations in patients with history of uveitis or diabetes mellitus
- Counsel patients to report any visual disturbance during treatment
- Evaluate the fundus, including the macula, and discontinue treatment if macular oedema is confirmed

☐ Counsel patients to report signs and symptoms of infection
- Prompt antimicrobial treatment should be initiated if indicated
- Perform prompt diagnostic evaluation in patients with symptoms and signs (e.g. headache accompanied by mental changes such as confusion, hallucinations, and/or personality changes) consistent with cryptococcal meningitis. If cryptococcal meningitis is diagnosed, fingolimod should be suspended and appropriate treatment should be initiated. A multidisciplinary consultation
(i.e. infectious disease specialist) should be undertaken if re-initiation of Golimara® is warranted
- Progressive multifocal leukoencephalopathy (PML) has been reported under fingolimod treatment
since marketing authorisation. Be vigilant for clinical symptoms or MRI findings that may be suggestive of PML. MRI imaging may be considered as part of increased vigilance in patients considered at increased risk of PML. If PML is suspected, MRI should be performed immediately for
diagnostic purposes and treatment with fingolimod should be suspended until PML has been excluded
- Suspend treatment during serious infections

☐ Check full blood count periodically during treatment, at month 3 and at least yearly thereafter, and interrupt treatment if lymphocyte count is confirmed as $<0.2x10^9/L$

☐ Check liver transaminases at months 1, 3, 6, 9 and 12 and periodically thereafter, or at any time there are signs or symptoms of hepatic dysfunction
- Monitor more frequently if liver transaminases rise above 5 times the ULN, and interrupt treatment if liver transaminases remain elevated above this level until recovery

☐ During treatment and for up to 2 months after discontinuation
- Vaccinations may be less effective
- Live attenuated vaccines may carry a risk of infection and should be avoided

- [ ] Pregnancy tests should be repeated at suitable intervals. Discontinue treatment if a patient becomes pregnant
  - To help determine the effects of fingolimod exposure in pregnant women with MS, physicians are encouraged to report pregnant patients who may have been exposed to fingolimod at any time during pregnancy (from 8 weeks prior to last menstrual period onward) to SPIMACO by dialing +966 11 252 3393 or emailing GPV@spimaco.sa

- [ ] Fingolimod should be stopped 2 months before planning a pregnancy. Medical advice about the harmful effects of Fingolimod to the foetus should be provided.

- [ ] Advise women of child-bearing potential that effective contraception must be used during treatment and for at least 2 months after treatment discontinuation.

- [ ] Cases of basal cell carcinoma (BCC) have been reported in patients receiving fingolimod. Vigilance for skin lesions is warranted and a medical evaluation of the skin is recommended after at least one year and then at least yearly taking into consideration clinical judgement. The patient should be referred to a dermatologist if suspicious lesions are detected

- [ ] Cases of seizure, including status epilepticus, have been reported. Vigilance for seizures, especially in those patients with underlying conditions or with a pre-existing history or family history of epilepsy, is recommended

- [ ] Monitor paediatric patients for signs and symptoms of depression and anxiety

- [ ] Reassess on an annual basis the benefit of Gilenya treatment versus risk in each patient, especially paediatric patients

After treatment discontinuation

- [ ] Repeat first-dose monitoring as for treatment initiation when treatment is interrupted for
  - One day or more during the first 2 weeks of treatment
  - More than 7 days during weeks 3 and 4 of treatment
  - More than 2 weeks after one month of treatment

- [ ] Counsel patients to report signs and symptoms of infection for up to 2 months after discontinuation

- [ ] Counsel patients that effective contraception is needed for 2 months after discontinuation

The information in this material has been approved by the Saudi Food and Drug Authority.
Please see the accompanying SPC for more Information

Any suspected adverse events should be reported to the national spontaneous reporting system according to the national regulations.

SFDA (National Pharmacovigilance and Drug Safety Center)
Email to: npc.drug@sfda.sa
Direct number: 19999

https://ade.sfda.gov.sa

Or Pharmacovigilance Department in SPIMACO
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