Fingolimod
healthcare professional
information

Fingolimod SPC® (fingolimod) prescriber's checklist

Important points to remember before, during and after treatment

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

▼ **This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.**

SPC
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Considerations in fingolimod patient selection

Fingolimod is suitable for adult and paediatric patients (≥10 years old) 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.

Fingolimod causes transient heart rate reduction and may cause AV conduction delays following initiation of treatment.

All patients should be monitored for a minimum of 6 hours on treatment initiation. Below is a brief overview of monitoring requirements. Refer to page 4 for more information

Contraindications

Fingolimod is contraindicated in patients with known immunodeficiency syndrome, patients with increased risk for opportunistic infections (including immunocompromised patients), severe active infections, active chronic infections, known active malignancies, severe liver impairment, patients who in the last 6 months had myocardial infarction, unstable angina, stroke/transient ischaemia attack, decompensated heart failure, or New York Heart Association class III/IV heart failure, patients with severe cardiac arrhythmias requiring anti-arrhythmic treatment with Class Ia or Class III anti-arrhythmic drugs, patients with second-degree Mobitz type II atrioventricular block or third-degree AV block, or sick-sinus syndrome (if they do not wear a pacemaker), patients with a baseline QTc interval of ≥500 msec, and hypersensitivity to the active substance or to any of the excipients

While on fingolimod, women should not become pregnant. If a woman becomes pregnant while taking fingolimod, discontinuation of fingolimod is recommended. Women receiving fingolimod should not breastfeed.

Not recommended
Consider fingolimod only after performing risk/benefit analysis and consulting a cardiologist

Consult cardiologist regarding appropriate first-dose monitoring

Sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QT-interval prolongation (QTc >470 msec [adult females], >460 msec [paediatric females], or >450 msec [adult and paediatric males]), history of cardiac arrest, uncontrolled hypertension or severe sleep apnoea.

→ At least overnight extended monitoring is recommended

Consult cardiologist regarding possibility of switching to non-heart-rate-lowering drugs

Taking beta-blockers, heart-rate-lowering calcium channel blockers*, or other substances that are known to lower the heart rate**

→ If change in medication is not possible, extend monitoring to at least overnight

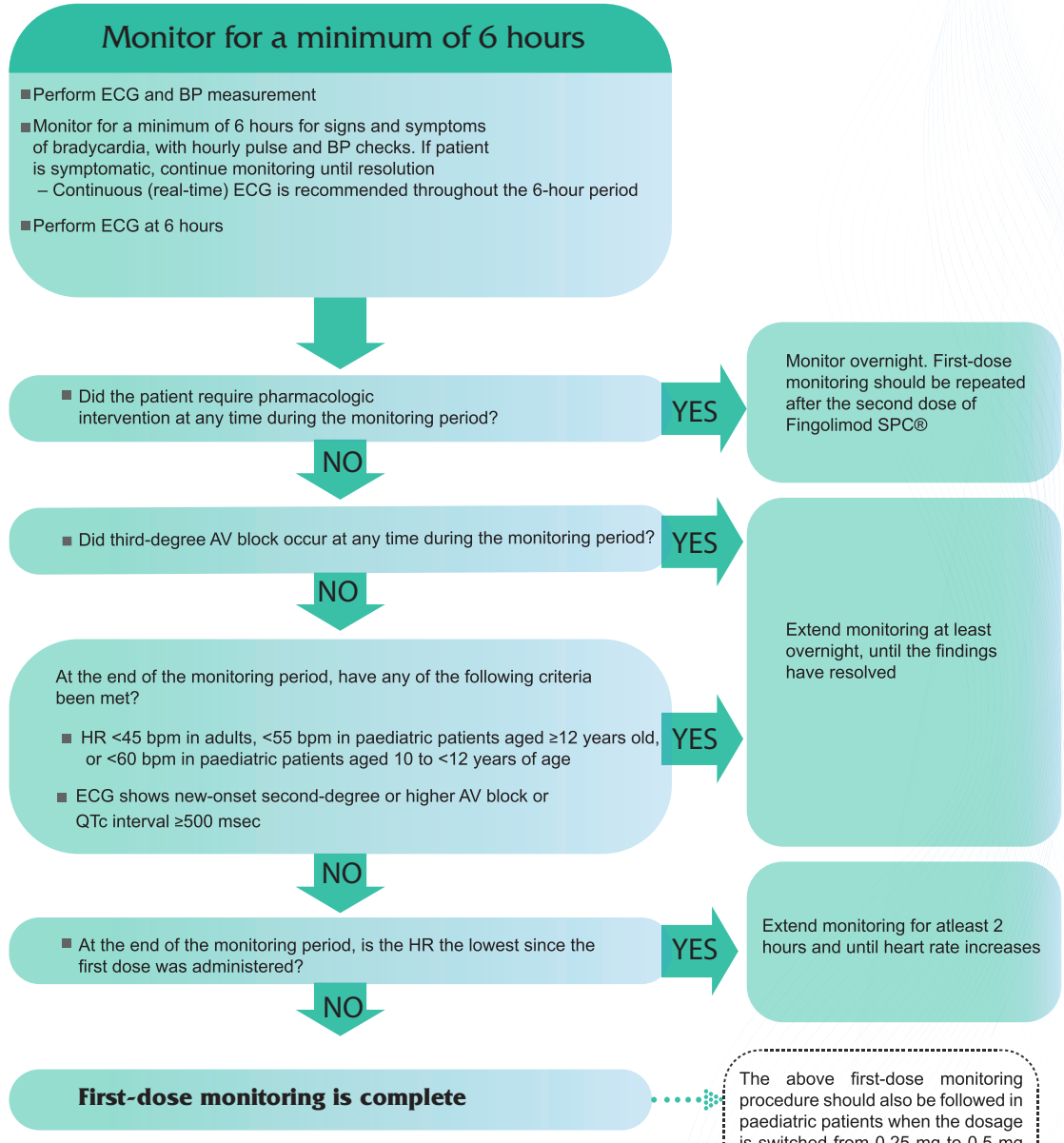
* Includes verapamil or diltiazem.
** Includes ivabradine, digoxin, anticholinesteratic agents, or pilocarpine.

Treatment initation algorithm

All patients, including paediatric patients will need to be monitored for at least 6 hours during treatment initiation, - as described in the algorithm below.

This procedure should also be followed in pediatric patients when the dosage is switched from 0.25 mg to 0.5 mg Fingolimod once daily*

In addition, for patients in whom fingolimod is not recommended (see page 2), 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.*For paediatric patients (≥10 years old), the approved dosing for fingolimod is 0.25 mg once daily for patients weighing ≤40 kg and 0.5 mg once daily for patients weighing >40 kg.

The above first-dose monitoring procedure should also be followed in paediatric patients when the dosage is switched from 0.25 mg to 0.5 mg fingolimod once daily*It should also be followed at re-initiation of treatment if fingolimod is discontinued for:• One day or longer within the first 2 weeks of treatment
• More than 7 days during weeks 3 and 4 of treatment
• More than 2 weeks after the first month of treatment

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Prescriber's checklist

Patient's name: _____

Date of birth: _____

Consultant: _____

Hospital number: _____

Prior to initiating treatment

- ☐ For paediatric patients, assess Tanner staging, measure height and weight, and consider a complete vaccination schedule
- ☐ Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines
- ☐ Conduct baseline electrocardiogram(ECG) and blood presure measurement.
- ☐ Treatment with fingolimod is not recommended in the following patients, unless anticipated benefits outweigh the potential risks:
  - Those with sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope,significant QT-interval prolongation QT-interval prolongation (QTc >470 msec [adult females],>460 msec [paediatric females], or >450 msec [adult and paediatric males]), 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), or other substances which may decrease heart rate (eg, ivabradine, 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
- ☐ Avoid co-administration of anti-neoplastic, immunomodulatory or immunosuppressive therapiesdue 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 in women of childbearing potential, and repeat at suitable intervals during treatment.
- ☐ Counsel on the need for effective contraception in women of childbearing ageboth during treatment and for 2 months after treatment discontinuation.
- ☐ Inform women of childbearing potential about the serious risks of fingolimod to the foetus
- ☐ Delay initiation of treatment in patients with severe active infection until resolved
- ☐ 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 1month to allow full effect of vaccination to occur
- ☐ 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 is recommended for patients as per standard of care
- ☐ 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 if 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 Patients, Parents and caregivers Guide

During treatment

☐ Conduct a full ophthalmologic evaluation at 3 to 4 months after starting treatment for the early detection of visual impairment due to drug-induced macular oedema

Conduct periodic ophthalmologic evaluations in patients with history of uveitis or diabetes mellitus.

- Counsel patients to immediately report any visual disturbance during treatment
- Evaluate the fundus, including the macula, and it is recommended to discontinue treatment if macular oedema is confirmed.

☐ Counsel patients to report signs and symptoms of infection immediately to their prescriber during, and for up to 2 months after, treatment

Prompt antimicrobial treatment should be initiated if indicated

- Perform prompt diagnostic evaluation in patients with symptoms and signs consistent with cryptococcal meningitis, and initiate appropriate treatment if diagnosed
- Be vigilant for clinical symptoms or MRI findings that may be suggestive of progressive multifocal leukoencephalopathy (PML). If PML is suspected, 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 $<0.2x10^9/L$

☐ Liver function tests including serum bilirubin should be performed before starting treatment and at months 1, 3, 6, 9 and 12 on therapy and periodically thereafter until 2 months after fingolimod discontinuation.

- In case of absence of clinical symptoms, if liver transaminases are:
  - ☐ Greater than 3 times the upper limit of normal (ULN) but less than 5 times ULN without increase in serum bilirubin, more frequent monitoring including serum bilirubin and alkaline phosphatase (ALP) should be instituted.
  - ☐ At least 5 times ULN or at least 3 times ULN associated with any increase in serum bilirubin, fingolimod should be discontinued. If serum levels return to normal, fingolimod may be restarted based on a careful benefit- risk assessment of the patient.
- In case of presence of clinical symptoms suggestive of hepatic dysfunction, the Liver enzymes and bilirubin should be checked immediately and fingolimod should be discontinued if significant liver injury is confirmed.

☐ 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

☐ Women of child-bearing potential, including adolescent females, their parents (or legal representatives), and caregivers, should be informed about the serious risks of fingolimod to the foetus. Effective contraception during treatment and for at least 2 months after treatment discontinuation should be recommended. 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 multiple sclerosis (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 Sudair Pharma by calling 920001432 Ext.107, visiting http://www.sudair-pharma.com/pharmacvigilance , or emailing Pharmacovigilance@sudairpharma.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
- Ensure patients are not receiving concomitant phototherapy with UV-B-radiation or PUVA-photochemotherapy

☐ Fingolimod has an immunosuppressive effect and can increase the risk of developing lymphomas (including mycosis fungoides), and other malignancies, particularly those of the skin and serious opportunistic infections. Closely monitor patients during treatment, especially those with concurrent conditions or known factors, such as previous immunosuppressive therapy. Surveillance should include vigilance for both skin malignancies and mycosis fungoides.If this risk is suspected, discontinuation of fingolimod should be considered by the physician on a case-by-case basis.

☐ 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 fingolimod 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 1 month of treatment
- ☐ Counsel patients to report signs and symptoms of infection immediately to their prescriber for up to 2 months after discontinuation
- ☐ Instruct patients to be vigilant for signs of meningitis infection
- ☐ Inform women of childbearing potential, including female adolescents, that effective contraception is needed for 2 months after discontinuation. For female adolescents, please also inform their parents and other caregivers.
- ☐ Vigilance for the possibility of severe exacerbation of disease following discontinuation of treatment is recommended.

Summary guidance specifically for paediatric patients

- ☐ Assess physical development (Tanner staging), and measure height and weight
- ☐ Consider a complete vaccination schedule before starting fingolimod
- ☐ Counsel patients and their parents/caregivers on fingolimod's immunosuppressive effects
- ☐ Perform cardiovascular monitoring
- ☐ On treatment initiation, perform first-dose monitoring due to the risk of bradyarrhythmia
- ☐ First-dose monitoring must be repeated in paediatric patients when the dosage is switched from 0.25 mg to 0.5 mg fingolimod once daily*.
- ☐ Emphasize the importance of treatment compliance to patients, their parents and other caregivers, especially with regard to treatment interruption and the need to repeat first-dose monitoring.
- ☐ Monitor patients for signs and symptoms of depression and anxiety.
- ☐ Provide guidance on seizure monitoring.
- ☐ Provide patients, parents and caregivers with the Patients, Parents and caregivers Guide

*Approved dose of 0.5 mg once daily (or 0.25 mg once daily in paediatric patients [≥10 years old] with a body weight of ≤40 kg) to be used when restarting treatment as other dosing regimens have not been approved.

National Pharmacovigilance Center reporting information:

SFDA Call Center: 19999
Free Phone: 8002490000
Website: https://ade.sfda.gov.sa
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