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, fingolomod should be suspended and appropriate treatment should be initiated. A multidisciplinary consultation (i.e. infectious disease specialist) should be undertaken if re-initiation of Fegona 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 9 ,6 ,3 ,1, 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 SAJA Pharmaceuticals by dialing **+966 12 606 6667** or emailing **drugsafety@sajapharma.com**
- ☐ 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

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 SmPC for more Information

For any information about this medicine, please contact Saudi Arabian Japanese pharmaceutical company limited Jeddah – Saudi Arabia
P.O. Box: 42600, Jeddah 21551, KSA
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www.sajapharma.com

-To report any side effect (s)

• Saudi Arabia :
The National Pharmacovigilance and Drug Safety Centre (NPC)
o Fax: + 966 11 205 7662
o Toll free phone: 8002490000
o E-mail: npc.drug@sfda.gov.sa
o Website: www.sfda.gov.sa/npc

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FEGONA® (fingolimod) ▼

Prescriber's Checklist: Summary of Recommendations

▼ 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. See section 4.8 of the SmPC for how to report adverse reactions.

Considerations in FEGONA ®(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 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.

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)
- Severe active infections
- Active chronic infections
- Known active malignancies
- Severe liver impairment
- Hypersensitivity to the active substance or to any of the excipients.

The following patients should not be treated with fingolimod

- Those who are pregnant
- Those who are taking Class Ia or Class III antiarrhythmics

Not recommended

Consider only after performing risk/benefit analysis and consulting a cardiologist

Consult cardiologist regarding appropriate first-dose monitoring

Bradyarrhythmia (including the following: second-degree Mobitz type II or higher atrioventricular (AV) block, sick sinus syndrome, sinoatrial heart block, history of symptomatic bradycardia), significant QT-interval prolongation (>470 msec [females] or >450 msec [males]), severe untreated sleep apnoea, significant cardiovascular disease (including the following: ischaemic heart disease [including angina pectoris], history of myocardial infarction, congestive heart failure, history of cardiac arrest) , uncontrolled hypertension, cerebrovascular disease, or recurrent syncope.

→ 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 (including verapamil, diltiazem, or ivabradine) , or other substances that are known to lower the heart rate (including digoxin, anticholinesteratic agents, or pilocarpine).

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

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, unless anticipated benefits outweigh the potential risks:
  - Those with bradyarrhythmia[¶], significant cardiovascular disease[#], significant QT-interval prolongation, uncontrolled hypertension, cerebrovascular disease, severe untreated sleep apnoea, or a history of recurrent syncope
    - ☐ 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
- ☐ 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
- ☐ Counsel on the need for effective contraception in women of childbearing age due to teratogenic risk to 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 1 month to allow full effect of vaccination to occur
- ☐ Conduct an ophthalmologic evaluation in patients with history of uveitis or diabetes mellitus
- ☐ Provide patients with a Patient Reminder Card

[¶]Bradyarrhythmia includes the following: second-degree Mobitz type II or higher AV block, sick sinus syndrome, sinoatrial heart block, history of symptomatic bradycardia.
[#]Significant cardiovascular disease includes the following: ischaemic heart disease (including angina pectoris), history of myocardial infarction, congestive heart failure, history of cardiac arrest.

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 (see page 2), advice should be sought from a cardiologist regarding appropriate monitoring; at least overnight monitoring is recommended for this group.

Monitor for a minimum of 6 hours

- ☐ 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 -6hour period
- ☐ Perform ECG at 6 hours

↓

☐ Did the patient require pharmacologic intervention at any time during the monitoring period?

YES → Monitor overnight in a medical facility. The first-dose monitoring should be repeated after the second dose of fingolimod.

NO ↓

☐ Did third-degree AV block occur at any time during the monitoring period?

YES → Extend monitoring at least overnight, until the findings have resolved.

NO ↓

At the end of the monitoring period, have any of the following criteria been met?

- ☐ HR <45 bpm
- ☐ ECG shows new-onset second-degree or higher AV block or QTc interval ≥500 ms

YES → Extend monitoring at least overnight, until the findings have resolved.

NO ↓

☐ At the end of the monitoring period, is the HR the lowest since the first dose was administered?

YES → Extend monitoring by at least 2 hours and until the heart rate increases.

NO ↓

First-dose monitoring is complete.

The above first-dose monitoring procedure should also be followed at reinitiation of treatment if fingolimod therapy 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

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