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Healthcare Professional Information

Eligon®(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

Date: Aug.2023
Version: 3.0

Considerations in Eligon® patient selection

Eligon® is suitable for adult and pediatric patients (≥10 years old) for the treatment of highly active relapsing remitting MS (RRMS)*. While many patients may be suitable for treatment, the following section highlights patients in whom Eligon® is contraindicated or not recommended.

Eligon® 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. Below is a brief overview of monitoring requirements. Refer to page 4 for more information.

Contraindications

Eligon® 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 chronic infections, unstable angina, stroke / transient ischaemia attack, decompensated heart failure, or New York Heart Association class III / IV heart failure, severe cardiac arrhythmias treatment with Class Ia or Class III anti-arrhythmic drugs, patients with second-degree Mobitz type II AV atrioventricular block, or sick-sinus syndrome (if they do not wear a pacemaker), patients with a baseline QTc interval of ≥ 500 msec, and patients with hypersensitivity to the active substance or to any of the excipients.

while on Eligon® women should not become pregnant. if a woman become pregnant while taking Eligon®, discontinuation of Eligon® is recommended. Women receiving Eligon® should not breastfeed.

Not recommended

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

Consult cardiologist regrding the 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 (pediatric females), or >450 msec (adult and pediatric males), history of cardiac arrest, uncontrolled hypertension or severe sleep apnea

→ 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

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

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Treatment initiation algorithm

All patients, including pediatric patients, 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 Eligon® once daily*

In addition, for patients in whom Eligon® 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.

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

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Eligon® 0.5mg Fingolimod (For Oral Use)

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 6-hour period
- Perform ECG at 6 hours

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

Yes → *At least overnight extended monitoring is recommended*

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, <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

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 Eligon® 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.

** For pediatric patients (≥10 years old), the approved dosing for Eligon® is 0.25 mg once daily for patients weighing ≤40 kg, and 0.5 mg once daily for patients weighing >40 kg.*

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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 hight 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 pressure (BP) measurement.`
¤	Treatment with Eligon® 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 (QTc >470 msec (adult females), >460 msec (pediatric females), or >450 msec (adult and pediatric males)), history of cardiac arrest, uncontrolled hypertension or severe sleep apnea • treatment as other dosing regimens have not been approved. - 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 (e.g. verapamil or diltiazem), or other substances which may decrease heart rate (e.g. ivabradine, digoxin, anticholinesteratic agents, or 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 in women of childbearing potential, and repeat at suitable intervals during treatment.
¤	Counsel on the need for effective contraception in women of childbearing age both during treatment and for 2 months after treatment discontinuation
¤	Inform women of childbearing potential about the serious risks of fingolimond to the fetus
¤	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.
¤	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.
¤	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 Patients, Parent's and Caregiver's Guide.

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During Treatment

- Conduct full ophthalmologic evaluation at 3 to 4 months after starting treatment for the early detection of visual impairment due to drug-induced macular edema.
  Conduct periodic ophthalmologic evaluation in patients with history of uveitis or diabetes mellitus.
  - counsel patients to immediately report any visual disturbance during treatmment
  - 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 i itiated if indicated
  - Perform prompt diagnostic evaluation in patients with symptoms and signs consistent with encephalitis, meningitis or meningoencephalitis and initiate appropriate treatment if diagnosed
  - Be vigilant for clinical symptoms or MRI findings suggestive of PML. If PML is suspected, treatment with Eligon® 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 prefomed before starting treatment and at months 9 ,6 ,3 ,1, and 12 on therapy and periodically thereafter until 2 months after Eligon® 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, Eligon® should be discontinued. If serum levels return to normal, Eligon® 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 Eligon® 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 oof infection and should be avoided
- Women of child-bearing potential. Including adolescent females, there parents (or legal representative), and caregivers, should be informed about the serious risks of Eligon® to the fetus. effective contraception must be used during treatment and for at least 2 months after treatment discontinuation. Pregnancy tests must be repeated at suitable intervals. Discontinue treatment if a woman becomes pregnant.
- To help determine the effects of Eligon® exposure in pregnant women with MS, physicians are encouraged to report pregnant patients who may have been exposed to Eligon® at any time during pregnancy (from 8 weeks prior to last menstrual period onward) to Sudair Pharma by calling 9200001432 Ext:107, visiting http://www.saudairpharma.com/pharmacvigilance, or emailing pharmacovigilance@saudairpharma.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.
- Eligon® has an immunosuppressive effect and can increase the risk of developing lymphomas (including mycosis fungoids), 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 is suspected, discontinuation of Eligon® should be considered by the physician on 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 pediatric patients for signs and symptoms of depression and anxiety.
- Reassess on an annual basis the benefit of Eligon® treatment versus risk in each patient, especially pediatric patients.

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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 immediately to their prescriber for up to 2 months after discontinuation.
- Instruct patients to be vigilant for signs of meningitis infection
- Inform Women of child-bearing potential, Including adolescent females, that effective contraception is needed for 2 months after discontinuation. For females adolescent, 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 pediatric patients

- Assess physical development (Tanner staging), and measure height and weight
- Consider a complete vaccination schedule before starting Figolimod.
- Counsel patients and their parents/caregivers on Figolimod immunosuppressive effects.
- Perform first-dose monitoring
- on treatment initiation preform first-dose monitoring due to the risk of bradyarrhythmia
- first-dose monitoring must be Repeated in pediatric patients when the dosage is switched from 0.25 mg to 0.5 mg Figolimod once daily*.
- Monitor the patient for signs and symptoms of depression and anxiety.
- Provide guidance on seizure monitoring
- Provide patients and their parents and caregivers with the patients. Parents and caregivers Guide

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approved dose of 0.5mg daliy (or 0.25 once daliy in paediatric patients (≥10 years old) with a body weight of ≤ 40kg) 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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Sudair Pharma Company reporting information.

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