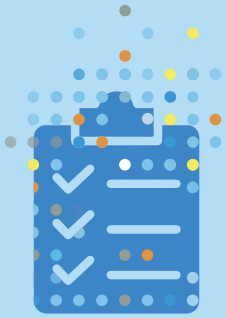

Finolim 0.5 mg

0.5 mg hard capsules (fingolimod)

PHYSICIAN'S CHECKLIST:

SUMMARY OF RECOMMENDATIONS

Rafa.

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CONSIDERATIONS IN FINOLIM (FINGOLIMOD) PATIENT SELECTION

Finolim is suitable for adult patients for the treatment of relapsing remitting MS (RRMS)*. While many patients may be suitable for treatment, the following section highlights patients in whom Finolim is contraindicated or not recommended.

Considerations for treatment initiation

Finolim may cause fetal harm when administered to a pregnant woman, Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

Finolim 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.

Appropriate

Eligible adult patients with RRMS *.

Contraindications

Finolim is contraindicated in patients who have:

- In the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization or Class III/IV heart failure
- A history or presence of Mobitz Type II second-degree or third-degree atrioventricular (AV) block or sick sinus syndrome, unless patient has a functioning pacemaker
- A baseline QTc interval ≥ 500 msec
- Cardiac arrhythmias requiring anti-arrhythmic treatment with Class Ia or Class III anti-arrhythmic drugs
- Had a hypersensitivity reaction to fingolimod or any of the excipients in Finolim. Observed reactions include rash, urticaria and angioedema upon treatment initiation

Not recommended

Consider 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 such as Digoxin.

- 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

*Finolim is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

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

‡Includes verapamil or diltiazem.

RECOMMENDED STEPS TO MANAGING PATIENTS ON FINOLIM

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

Prior to initiating treatment

- Treatment with Finolim 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*, history of cardiac arrest, uncontrolled hypertension, or severe sleep apnea
    - – 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, or other substances which may decrease heart rate (e.g. digoxin)
    - – 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
- Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines
- Conduct baseline electrocardiogram (ECG) and blood pressure (BP) measurement
- 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
- Inform WOCBP (Women Of Childbearing Potential) about the potential for a serious risk to the fetus and the need for effective contraception during treatment with Finolim
- Finolim may cause fetal harm when administered to a pregnant woman Confirm a negative pregnancy test result in WOCBP prior to starting treatment and repeat at suitable intervals during treatment
- Inform WOCBP about the serious risks of Finolim to the fetus
- Provide all patients and caregivers with the Pregnancy-Specific Patient Reminder Card
- Counsel WOCBP to avoid pregnancy and use effective contraception both during treatment and for 2 months after treatment discontinuation. Counseling should be facilitated by the Pregnancy-Specific Patient Reminder Card
- 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
- Perform an examination of the fundus, including the macula in all patients before starting treatment
- 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
- Ensure a baseline magnetic resonance imaging (MRI) is available (usually within 3 months) as a reference. MRI findings may be apparent before clinical signs or symptoms of Progressive Multifocal Leukoencephalopathy (PML)
- Provide patients and caregivers with the Patients and Caregiver's Guide

*QTc >470 msec (adult females), or >450 msec (adult males).

TREATMENT INITIATION ALGORITHM

All patients, need to be monitored for at least 6 hours during treatment initiation, as described in the algorithm below.
It should also be followed at re-initiation of treatment if Finolim 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

In addition, for patients in whom Finolim 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 6-hour period
- Perform ECG at 6 hours

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 Finolim

Did new onset second degree or higher AV block occur at any time during the monitoring period?

▼

NO

► YES

Additional observation should be instituted until the finding has resolved

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

- HR <45 beats per minute (bpm)
- ECG shows new-onset second-degree or higher AV block

▼

NO

► YES

Additional observation should be instituted until the finding has resolved

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

▼

NO

► YES

Additional observation should be instituted until the finding has resolved

First-dose monitoring is complete

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

DURING TREATMENT

- A full ophthalmologic assessment should be considered:
  - ► 3–4 months after starting treatment for the early detection of visual impairment due to drug-induced macular edema
  - ► During treatment in patients with diabetes mellitus or with a history of uveitis
- Counsel patients to report signs and symptoms of infection immediately to their prescriber during, and for up to 2 months after, treatment
  - ► Perform prompt diagnostic evaluation in patients with symptoms and signs consistent with encephalitis, meningitis and initiate appropriate treatment if diagnosed
    - – Serious, life-threatening, and sometimes fatal cases of encephalitis, meningitis caused by herpes simplex virus (HSV) and VZV were reported while on Finolim 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
  - ► Be vigilant for clinical symptoms or MRI findings suggestive of progressive multifocal leukoencephalopathy (PML). If PML is suspected, treatment with Finolim should be suspended until PML has been excluded. If PML is confirmed, treatment with FINOLIM should be discontinued
    - – Cases of PML have occurred after approximately 2–3 years of monotherapy treatment although an exact relationship with the duration of treatment is unknown
  - ► 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 $<0.2x10^9/L$*
- 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 Finolim 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) measurement should be instituted to determine if further increases occur and in order to discern if an alternative aetiology of hepatic dysfunction is present
    - – If liver transaminases are at least 5 times the ULN or at least 3 times the ULN associated with any increase in serum bilirubin, Finolim should be discontinued. Hepatic monitoring should be continued. If serum levels return to normal (including if an alternative cause of the hepatic dysfunction is discovered), Finolim may be restarted based on a careful benefit-risk assessment of the patient*
- While on treatment, women should not become pregnant. Discontinue treatment if a woman becomes pregnant. Finolim should be stopped 2 months before planning a pregnancy, and the possible return of disease activity should be considered. An ultrasonography examination should be performed and medical advice about the harmful effects of Finolim to the fetus should be provided.
- Advise WOCBP that effective contraception should be used during treatment and for at least 2 months after treatment discontinuation. Pregnancy tests should be repeated at suitable intervals
- WOCBP should be informed regularly about the serious risks of Finolim to the fetus.
- Ensure WOCBP, and caregivers receive regular counseling facilitated by the Pregnancy-Specific Patient Reminder Card
- To help determine the effects of Finolim exposure in pregnant women with MS, physicians are encouraged to report pregnant patients who may have been exposed to Finolim at any time during pregnancy (from 8 weeks prior to last menstrual period onward) to Rafa at drugsafety@rafa.co.il in order to allow monitoring of these patients through the Pregnancy Outcomes Intensive Monitoring Program (PRIM).
- 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
- Finolim 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. Surveillance should include vigilance for both skin malignancies and mycosis fungoides. Closely monitor patients during treatment, especially those with concurrent conditions, or known factors, such as previous immunosuppressive therapy; and discontinue treatment if a risk is suspected
- 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
- Reassess on an annual basis the benefit of Finolim treatment versus risk in each patient

*Approved dose of 0.5 mg once daily to be usued when restarting treatment as other dosing regimens have not been approved

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 encephalitis, meningitis infection and PML
- Monitor for development of immune reconstitution inflammatory syndrome (PML-IRIS) after stopping FINOLIM in the setting of PML
  - ► Immune reconstitution inflammatory syndrome (IRIS) has been reported in patients treated with S1P receptor modulators, including FINOLIM, who developed PML and subsequently discontinued treatment. IRIS presents as a clinical decline in the patient's condition that may be rapid, can lead to serious neurological complications or death, and is often associated with characteristic changes on MRI. The time to onset of IRIS in patients with PML was generally within a few months after S1P receptor modulator discontinuation. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken
- Inform WOCBP that effective contraception is needed for 2 months after discontinuation because of the serious risks of Finolim to the fetus
- Advise women who stop treatment with Finolim because they are planning a pregnancy that their disease activity may return
- Vigilance for the possibility of severe exacerbation of disease following discontinuation of treatment is recommended
  - ► In cases of severe exacerbation appropriate treatment should be initiated as required

For further information, please refer to the Prescribing Information.

REPORTING ADVERSE EVENTS

Adverse drug reactions

Adverse events can be reported to the Ministry of Health via

https://sideeffects.health.gov.il

You may also report to the registration holder, Rafa Laboratories LTD. at:

drugsafety@rafa.co.il

This document was approved according to the guidelines of the ministry of health on March 2024.