



Fingolimod  
healthcare professional  
information

# Fingolimod prescriber's checklist

Important points to remember before,  
during and after treatment

# Considerations in fingolimod patient selection

Fingolimod is suitable for adult 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.

**Appropriate:** Eligible adult 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 RRMS.

## 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  $\geq 500$  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.

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| <h3>Not recommended</h3> <p>Consider fingolimod only after performing risk/benefit analysis and consulting a cardiologist</p>  |  |
| <p>Consult cardiologist regarding appropriate first-dose monitoring</p>  |  |
| <p>Sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QT-interval prolongation (QTc <math>&gt;470</math> msec [adult females] or <math>&gt;450</math> msec [adult males]), history of cardiac arrest, uncontrolled hypertension or severe sleep apnoea.</p> | <p><b>At least overnight extended monitoring is recommended</b></p>                            |
| <p>Consult cardiologist regarding possibility of switching to non-heart-rate-lowering drugs</p>  |  |
| <p>Taking beta-blockers, heart-rate-lowering calcium channel blockers<sup>§</sup>, or other substances that are known to lower the heart rate<sup>  </sup></p>   | <p><b>If change in medication is not possible, extend monitoring to at least overnight</b></p> |

§ Includes verapamil or diltiazem.

|| Includes ivabradine, digoxin, anticholinesteratic agents, or pilocarpine.

# Fingolimod Prescriber's checklist

|                  |       |
|------------------|-------|
| Patient's name:  | ..... |
| Date of birth:   | ..... |
| Consultant:      | ..... |
| Hospital number: | ..... |

## Prior to initiating treatment

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|--------------------------|--|
| <input type="checkbox"/> | Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines  |
| <input type="checkbox"/> | Conduct baseline electrocardiogram (ECG) and blood pressure measurement  |
| <input type="checkbox"/> | <p>Treatment with fingolimod is not recommended in the following patients, unless anticipated benefits outweigh the potential risks:</p> <ul style="list-style-type: none"> <li>Those with sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QT-interval prolongation (QTc &gt;470 msec [adult females] or &gt;450 msec [adult males]), history of cardiac arrest, uncontrolled hypertension or severe sleep apnoea. <ul style="list-style-type: none"> <li><input type="checkbox"/> Seek advice from a cardiologist regarding the most appropriate monitoring at treatment initiation; at least overnight extended monitoring is recommended</li> </ul> </li> <li>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) <ul style="list-style-type: none"> <li><input type="checkbox"/> Seek advice from a cardiologist regarding a switch to non-heart-rate-lowering medicinal products prior to initiation of treatment</li> <li><input type="checkbox"/> 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</li> </ul> </li> </ul> |
| <input type="checkbox"/> | 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   |
| <input type="checkbox"/> | Obtain recent (within 6 months) transaminase, and bilirubin levels   |
| <input type="checkbox"/> | Obtain recent (within 6 months or after discontinuation of prior therapy) full blood count   |
| <input type="checkbox"/> | Confirm a negative pregnancy test result in women of childbearing potential, including female adolescents  |
| <input type="checkbox"/> | Counsel on the need for effective contraception in women of childbearing age. Confirm a negative pregnancy test result in women of childbearing potential, including female adolescents, due to teratogenic risk to foetus   |
| <input type="checkbox"/> | Delay initiation of treatment in patients with severe active infection until resolved  |
| <input type="checkbox"/> | 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   |
| <input type="checkbox"/> | 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   |
| <input type="checkbox"/> | Conduct an ophthalmologic evaluation in patients with history of uveitis or diabetes mellitus  |
| <input type="checkbox"/> | 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   |
| <input type="checkbox"/> | Provide patients, parents and caregivers with a patient reminder card  |

## During treatment

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|--------------------------|---|
| <input type="checkbox"/> | <p>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</p> <ul style="list-style-type: none"> <li>• Conduct periodic ophthalmologic evaluations in patients with history of uveitis or diabetes mellitus</li> <li>• Counsel patients to immediately report any visual disturbance during treatment</li> <li>• Evaluate the fundus, including the macula, and discontinue treatment if macular oedema is confirmed</li> </ul>   |
| <input type="checkbox"/> | <p>Counsel patients to report signs and symptoms of infection immediately to their prescriber</p> <ul style="list-style-type: none"> <li>• Prompt antimicrobial treatment should be initiated if indicated</li> <li>• Perform prompt diagnostic evaluation in patients with symptoms and signs consistent with cryptococcal meningitis, and initiate appropriate treatment if diagnosed</li> <li>• 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</li> <li>• Suspend treatment during serious infections</li> </ul>   |
| <input type="checkbox"/> | <p>Check full blood count periodically during treatment, at month 3 and at least yearly thereafter, and interrupt treatment if lymphocyte count is confirmed as <math>&lt;0.2 \times 10^9/L</math>*</p>   |
| <input type="checkbox"/> | <p>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</p> <ul style="list-style-type: none"> <li>• 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*</li> </ul>   |
| <input type="checkbox"/> | <p>During treatment and for up to 2 months after discontinuation</p> <ul style="list-style-type: none"> <li>• Vaccinations may be less effective</li> <li>• Live attenuated vaccines may carry a risk of infection and should be avoided</li> </ul>   |
| <input type="checkbox"/> | <p>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</p> <ul style="list-style-type: none"> <li>• 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 Accord by calling 1-866-296-0354, in order to allow monitoring of these patients through the ACH-Fingolimod Pregnancy Registry. Physicians may also enrol a pregnant MS patient under their care in the fingolimod pregnancy registry by calling 1-866-296-0354 or emailing <a href="mailto:safety@accordhealth.ca">safety@accordhealth.ca</a></li> </ul> |
| <input type="checkbox"/> | <p>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</p> <ul style="list-style-type: none"> <li>• Caution patients against exposure to sunlight without protection</li> <li>• Ensure patients are not receiving concomitant phototherapy with UV-B-radiation or PUVA-photochemotherapy</li> </ul>   |
| <input type="checkbox"/> | <p>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.</p>  |
| <input type="checkbox"/> | <p>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</p>   |
| <input type="checkbox"/> | <p>Reassess on an annual basis the benefit of fingolimod treatment versus risk in each patient</p>  |

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

### After treatment discontinuation

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|--------------------------|---|
| <input type="checkbox"/> | Repeat first-dose monitoring as for treatment initiation when treatment is interrupted for: <ul style="list-style-type: none"><li>• One day or more during the first 2 weeks of treatment</li><li>• More than 7 days during weeks 3 and 4 of treatment</li><li>• More than 2 weeks after 1 month of treatment</li></ul> |
| <input type="checkbox"/> | Counsel patients to report signs and symptoms of infection immediately to their prescriber for up to 2 months after discontinuation   |
| <input type="checkbox"/> | Instruct patients to be vigilant for signs of meningitis infection  |
| <input type="checkbox"/> | 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.   |
| <input type="checkbox"/> | Vigilance for the possibility of severe exacerbation of disease following discontinuation of treatment is recommended   |

### Summary guidance specifically

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| <input type="checkbox"/> | Assess physical development (Tanner staging), and measure height and weight   |
| <input type="checkbox"/> | Consider a complete vaccination schedule before starting fingolimod   |
| <input type="checkbox"/> | Counsel patients and their parents/caregivers on fingolimod's immunosuppressive effects   |
| <input type="checkbox"/> | On treatment initiation, perform first-dose monitoring due to the risk of bradyarrhythmia   |
| <input type="checkbox"/> | 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 |
| <input type="checkbox"/> | Monitor patients for signs and symptoms of depression and anxiety   |
| <input type="checkbox"/> | Provide guidance on seizure monitoring  |

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

# 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.

