ACH-Fingolimod
healthcare professional
information

ACH-Fingolimod prescriber's checklist

Important points to remember before, during and after treatment

Considerations in ACH-Fingolimod patient selection

ACH-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 ACH-Fingolimod is contraindicated or not recommended.

ACH-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

ACH-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 ACH-Fingolimod, women should not become pregnant. If a woman becomes pregnant while taking ACH-Fingolimod, discontinuation of ACH-Fingolimod is recommended. Women receiving ACH-Fingolimod should not breastfeed.

Not recommended

Consider ACH-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] or >450 msec [adult 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.

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Patient's name: .....

Date of birth: .....

Consultant: .....

Hospital number: .....

Prior to initiating treatment

☐	Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines
☐	Conduct baseline electrocardiogram (ECG) and blood pressure measurement
☐	Treatment with ACH-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] or >450 msec [adult 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 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, including female adolescents
☐	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
☐	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 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 a patient reminder card

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 discontinue treatment if macular oedema is confirmed
☐	Counsel patients to report signs and symptoms of infection immediately to their prescriber • 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 ACH-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 $<0.2 \times 10^9$/L*
☐	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 • 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
☐	Women of child-bearing potential, including adolescent females, their parents (or legal representatives), and caregivers, should be informed about the serious risks of ACH-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 ACH-Fingolimod exposure in pregnant women with multiple sclerosis (MS), physicians are encouraged to report pregnant patients who may have been exposed to ACH-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 ACH-Fingolimod pregnancy registry by calling 1-866-296-0354 or emailing safety@accordhealth.ca
☐	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
☐	ACH-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 ACH-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
☐	Reassess on an annual basis the benefit of ACH-Fingolimod treatment versus risk in each patient

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

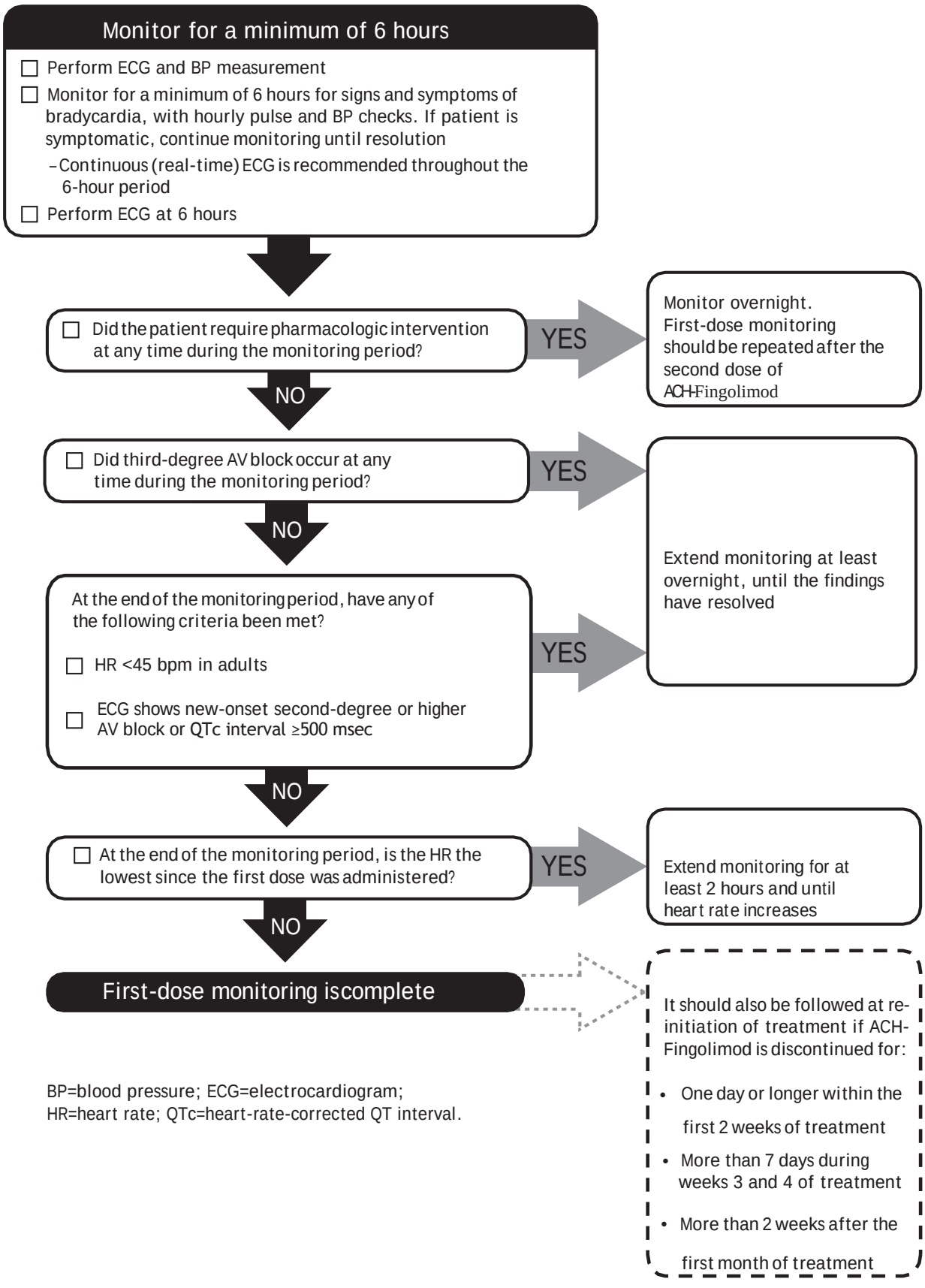
After treatment discontinuation	
☐	Repeat first-dose monitoring as for treatment initiation when treatment is interrupted for: • One day or more during the first 2 weeks of treatment • More than 7 days during weeks 3 and 4 of treatment • More than 2 weeks after 1 month of treatment
☐	Counsel patients 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	
☐	Assess physical development (Tanner staging), and measure height and weight
☐	Consider a complete vaccination schedule before starting ACH-Fingolimod
☐	Counsel patients and their parents/caregivers on ACH-Fingolimod's immunosuppressive effects
☐	On treatment initiation, perform first-dose monitoring due to the risk of bradyarrhythmia
☐	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

* 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 ACH-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.