PART III: CONSUMER INFORMATION

[Pr]ACH-FINGOLIMOD
Fingolimod (as fingolimod hydrochloride)

This leaflet is part III of a three-part "Product Monograph" published when ACH-Fingolimod was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ACH-Fingolimod. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

ACH-Fingolimod is used to treat:

- Adult patients with the relapsing and remitting form of multiple sclerosis (MS). ACH-Fingolimod is generally recommended for MS patients who have not responded well to, or cannot tolerate one or more of the other therapies for multiple sclerosis.

What it does:

ACH-Fingolimod does not cure MS, but it helps to reduce the number of attacks (relapses) that occur, reduce inflammation in the brain (brain lesions identified seen on MRI scans), and slow the build-up of physical problems due to MS (disability progression).

ACH-Fingolimod changes how the body's immune system works by decreasing the ability of lymphocytes to move freely within the body. This lowers the number of lymphocytes in the blood and prevents them from reaching the brain and spinal cord. This may reduce the inflammation and nerve damage that happens in MS.

When it should not be used:

You should not take ACH-Fingolimod if you:

- are allergic (hypersensitive) to fingolimod or to any of the other ingredients listed in this leaflet.
- immune system is weakened (immunocompromised) due to disease (immunodeficiency syndrome) or medicines or treatments that suppress the immune system, such as medicines used to treat cancer or bone marrow transplantation.
- have a severe active infection or an active chronic infection such as hepatitis or tuberculosis.
- have an active cancer (except for a type of skin cancer called basal cell carcinoma).
- have severe liver disease.
- **have had a heart attack, angina, stroke or warning of a stroke or certain types of heart failure in the last 6 months**.
- **have certain types of irregular or abnormal heartbeat** (arrhythmia), or your electrocardiogram (ECG) shows prolonged QT interval before starting ACH-Fingolimod.
- **are taking or have recently taken medicine for irregular heartbeat** such as quinidine, disopyramide, amiodarone or sotalol (due to a possible added effect on irregular heartbeat).
- **are pregnant, suspect you may be pregnant or plan to get pregnant.**
- **are of childbearing age not using effective methods of birth control.**
- **are of childbearing age, until it is confirmed with a pregnancy test that you are not pregnant. This is done just before you begin treatment with ACH-Fingolimod.**

What the medicinal ingredient is:

The active substance of ACH-Fingolimod is fingolimod.

What the nonmedicinal ingredients are:

The nonmedicinal ingredients of ACH-Fingolimod hard capsules are: Pregelatinized starch, magnesium stearate, Gelatin, titanium dioxide, iron oxide yellow, propylene glycol, black iron oxide, potassium hydroxide.

What dosage forms it comes in:

ACH-Fingolimod is supplied as hard capsules. Each hard capsule contains 0.5 mg of fingolimod (as fingolimod hydrochloride).

WARNINGS AND PRECAUTIONS

Chickenpox vaccine
Patients who have not had chickenpox or have not had the chickenpox vaccine are at risk of having a serious and life-threatening chickenpox infection during treatment with ACH-Fingolimod. There have been very rare fatal cases of chickenpox infection reported in patients treated with ACH-Fingolimod, who also received a relatively long course of corticosteroid therapy.

If you are not protected against chickenpox, your doctor may recommend that you receive the chickenpox vaccine 1 month before starting treatment with ACH-Fingolimod.

BEFORE you use ACH-Fingolimod talk to your doctor or pharmacist if:

- you have heart problems, such as **high blood pressure, or severe untreated sleep apnea**
- **you are taking medicines for an irregular heartbeat** such as quinidine, disopyramide, amiodarone or sotalol. (see "When it should not be used")
- **you suffer from slow heart rate, you are already taking other medicines that slow your heart rate or you have a history of sudden loss of consciousness (fainting)**.
- you have a weakened immune system (due to a disease or medicines that suppress the immune system).
- you have been vaccinated within 1 month before you start taking ACH-Fingolimod or you plan to receive a vaccine. You should not receive certain types of vaccines (called "live attenuated vaccines") during and for up to 2 months after treatment with ACH-Fingolimod.
- you have never had chickenpox or have not been vaccinated for chickenpox.
- you have or have had visual disturbances or other signs of swelling in the central vision area at the back of the eye (a condition known as macular edema), inflammation or infection of the eye (uveitis).
- you have diabetes. Diabetes increases the risk of having macular edema during ACH-Fingolimod treatment.
- you have liver problems. ACH-Fingolimod may affect your liver function.
- you have low or high blood pressure. ACH-Fingolimod causes a mild increase in blood pressure.
- you have high cholesterol or triglyceride levels. ACH-Fingolimod may increase blood levels of cholesterol and triglycerides.
- you have kidney problems.
- you have breathing problems. ACH-Fingolimod has a slight effect on lung function.
- you are pregnant, think you may be pregnant or are trying to become pregnant.
- you are breast feeding.

Your doctor will consider **whether you need to have a vaccination against Human Papilloma Virus** (HPV) before starting treatment. If you are a female, your doctor will also recommend HPV screening. HPV infection, including papilloma, dysplasia, warts and HPV-related cancer, has been reported in patients treated with fingolimod.

Monitoring: Before you start treatment and periodically during treatment, your doctor may want you to undergo several tests to help monitor side-effects of ACH-Fingolimod. These will include:
blood tests (to check your white blood cell counts, liver function), eye examination (to monitor for macular edema), checks of your heart rhythm and blood pressure, and possibly lung function.

Slow heart rate and irregular heart beat

ACH-Fingolimod causes the heart rate to slow down, especially during the first month of treatment. ACH-Fingolimod can also cause an irregular heartbeat, especially after the first dose. Irregular heartbeat usually returns to normal in less than one day. Slow heart rate usually returns to normal within one month. These heart rhythm disturbances may be more likely in patients with risk factors, such as heart disease, or when certain interacting drugs are taken. In general, people more than 65 years of age are at higher risk.

If you have an irregular or abnormal heartbeat or a history of sudden loss of consciousness (fainting), your condition may worsen temporarily with ACH-Fingolimod. The same applies if you have a slow heart rate or if you are taking medicines which slow the heartbeat.

If you experience any symptoms of a possible heart rhythm disturbance, such as dizziness, palpitations (sensation of rapid, pounding, or irregular heart beat), fainting, or seizures, at any time during treatment with ACH-Fingolimod, you should seek immediate medical attention.

Because fingolimod has side effects on the heart, you will be required to have an electrocardiogram (ECG) to check the health of your heart before you start fingolimod. Your doctor will ask you to stay in the clinic or office for at least 6 hours after taking the first dose of fingolimod so your heart rate and blood pressure can be checked each hour and appropriate measures can be taken if heart-related side effects occur at the start of treatment. A second ECG will be done 6 hours after taking the first dose. Depending on the results of the ECG, blood pressure checks and how you are feeling, you may need to be observed for longer, possibly overnight, in a health care facility. The same observation process may apply if you are starting

treatment again after a break from fingolimod therapy.

Infections

The effects of ACH-Fingolimod on your body's immune system may reduce your body's ability to fight infections and you may get infections more easily while you are taking ACH-Fingolimod (and for up to 2 months after you stop taking it). If you have an infection, tell your doctor before you take ACH-Fingolimod. Any infection that you already have may get worse. Infections could be serious and sometimes life-threatening. Before you start taking ACH-Fingolimod, your doctor will confirm whether you have enough white blood cells in your blood.
During your treatment with ACH-Fingolimod, if you think you have an infection, have fever, feel like you have the flu, or have a headache with a stiff neck, sensitivity to light, nausea, and / or confusion (these may be caused by a serious fungal infection and may be symptoms of cryptococcal meningitis), contact your doctor right away. If you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms, talk to your doctor as soon as possible, because these may be the symptoms of a rare brain disorder caused by infection and called progressive multifocal leukoencephalopathy (PML). Your doctor will consider performing an MRI scan to evaluate this condition and will decide whether you need to stop taking ACH-Fingolimod.

The use of other medications and treatments that suppress or change how the immune system works is not recommended during treatment with ACH-Fingolimod because the risk of infections can be increased further.

Macular edema
A problem with your vision, called macular edema, can occur during treatment with ACH-Fingolimod. Macular edema can cause some of the same vision symptoms as an MS attack (optic neuritis), but you also may not notice any symptoms. Macular edema usually starts in the first 3 to 4 months after you start taking ACH-Fingolimod. Your doctor should therefore test your vision 3 to 4 months after you start taking ACH-Fingolimod, or any time you notice vision changes during treatment.

Your risk of macular edema may be higher if you have diabetes or have had an inflammation of your eye called uveitis. If you have or have had visual disturbances or other signs of swelling in the central vision area (macula) at the back of the eye, uveitis or diabetes, your doctor should test your vision before you start taking ACH-Fingolimod.

Seizures:
Some patients have had seizures while taking ACH-Fingolimod. It is not known whether the seizures were related to the effects of their MS, ACH-Fingolimod, or to a combination of both. If you have a seizure while taking ACH-Fingolimod, you should call your doctor right away.

Depression and Suicidal Ideation:
Are known to occur in the MS population. Patients, families and caregivers of patients being treated with ACH-Fingolimod should watch for these symptoms. Contact your health care professional **right away** if any of these symptoms occur.

Other warnings you should know about:
The effects of ACH-Fingolimod on the body's immune system may increase the risk of developing lymphoma and other cancers such as skin cancer. Lymphoma and skin cancer, mostly basal cell carcinoma, have been reported in patients treated with fingolimod.

If you already have moles or open sores before starting treatment with ACH-Fingolimod, pay attention for changes in the size, shape or color of moles or the healing of open sores (not healing within weeks) after you start treatment. These may be signs of skin cancer that you should talk to your doctor about.

A type of skin cancer called basal cell carcinoma (BCC) and other cutaneous neoplasms such as malignant melanoma, squamous cell carcinoma, Kaposi's sarcoma and Merkel cell carcinoma have has been reported in MS patients treated with fingolimod. During treatment with ACH-Fingolimod you should check your skin regularly for unusual changes. Symptoms of BCC may include skin nodules (e.g. shiny pearly nodules), patches or open sores that do not heal within weeks. Symptoms of other skin cancers may include abnormal growth or changes of skin, such as unusual moles, that may change in color, shape or size over time. Your doctor will also do regular skin examinations during your treatment with ACH-Fingolimod.

Long- term exposure to the sun and a weak immune system can affect the risk of developing Merkel cell carcinoma. You should limit your exposure to the sun and UV rays by: wearing appropriate protective clothing and regularly applying sunscreen with a high degree of UV protection.

After ACH-Fingolimod treatment is stopped, symptoms of MS can return and may become worse compared to before or during treatment. Tell your doctor if you have worsening of MS symptoms after stopping ACH-Fingolimod.

A condition with unusually large brain lesions associated with MS relapse has been rarely reported in patients treated with fingolimod (a condition called tumefactive lesions). In case of severe relapse, your doctor will consider performing an MRI scan to evaluate this condition and will decide whether you need to stop taking ACH-Fingolimod.

Older people (over 65 years old)
Fingolimod was studied in very few MS patients over 65 years old. Treatment with ACH-Fingolimod requires extra caution in older patients due to the greater likelihood of having other medical problems in addition to MS.

Children and adolescents (under 18 years old)
ACH-Fingolimod is not indicated for use in children and adolescents under 18 years of age.

Pregnancy and breast-feeding

ACH-Fingolimod can harm the unborn baby if used during pregnancy. If you are a female who could become pregnant or if you are a female planning to become pregnant, before you start treatment with ACH-Fingolimod your doctor

- will tell you about the risk to an unborn baby,
- will ask you to do a pregnancy test in order to ensure that you are not pregnant.

and

- you must use effective contraception while taking ACH-Fingolimod and for two months after you stop taking it.

You must avoid becoming pregnant while taking ACH-Fingolimod and in the two months after you stop taking it because of the risk of harming your unborn child. Talk with your doctor about the associated risk and about reliable methods of birth control that you must use during treatment and for 2 months after you stop treatment.

If you do become pregnant while taking ACH-Fingolimod tell your doctor right away. You and your doctor will decide what is best for you and your baby. . If you become pregnant while taking ACH-Fingolimod, you can call the ACH-Fingolimod Pregnancy Registry at 1-866-296-0354.

You should not breast-feed while you are taking ACH-Fingolimod. Fingolimod can pass into breast milk and there is a risk of serious side effects for a breast-fed baby.

Driving and using machines

After the first dose of ACH-Fingolimod, you will need to stay at the doctor's office or clinic for at least 6 hours to have your heart rate checked. Your ability to drive and use machines may be affected during and potentially after this period.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking or have recently taken any of the following medicines:

- **Medicines for heart problems or high blood pressure**.
- **Medicines for an irregular heartbeat** such as, quinidine, disopyramide, amiodarone or sotalol. (see "When it should not be used")
- **Medicines that slow down heartbeat** such as atenolol or metoprolol (called beta-blockers), such as verapamil, or diltiazem (called calcium channel blockers) or digoxin.
- **Medicines that suppress or modulate the immune system including other medicines used to treat MS** (beta-interferon, glatiramer acetate, natalizumab, mitoxantrone, dimethyl fumarate, teriflunomide, alemtuzumab or corticosteroids) **or medicines used to treat cancer**. ACH-Fingolimod should not be started while you are on these medications. ACH-Fingolimod can usually be started immediately after stopping beta interferon, glatiramer acetate or dimethyl fumarate provided that immune effects from these therapies have resolved. If switching to ACH-Fingolimod from other disease modifying treatments for MS (listed above), your health care provider may want to wait for several months to reduce the possible added effect on the immune system and potential for increased risk of serious infections. However, starting treatment with ACH-Fingolimod after alemtuzumab is not recommended.

When corticosteroids were used for a few days to treat relapses in the multiple sclerosis studies with fingolimod this did not result in increased infections. However, because there is the potential for increased risk of infection, extra caution is recommended if corticosteroids are used.

- **Vaccines.** If you need to receive a vaccine, seek your doctor's advice first. During and for up to 2 months after stopping treatment with ACH-Fingolimod, administration of some vaccines containing live virus (live attenuated vaccines) may result in the infection that the vaccination should prevent, while other vaccines may not work well enough to protect you.
- **Antifungal drugs** (such as ketoconazole).
- **Antibiotics** (such as erythromycin).
- **Drugs to treat HIV infection.**
- **Asthma drugs**.

PROPER USE OF THIS MEDICATION

Always take ACH-Fingolimod exactly as your doctor has told you.

Usual adult dose:

The dose is one capsule per day (0.5 mg of fingolimod) taken orally (by mouth).

Take ACH-Fingolimod once a day, at the same time each day with half a glass of water. ACH-Fingolimod can be taken with or without food.

Do not stop taking ACH-Fingolimod or change your dose without talking with your doctor.

ACH-Fingolimod will stay in your body for up to 2 months after you stop taking it, the side effects described in this leaflet may still occur during that time.

Overdose:

If you think you have taken too much ACH-Fingolimod contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms. Take the medication package with you when you go to the hospital.

Missed Dose:

If you forget a dose, take the next dose as planned. Do not take a double dose to make up for a forgotten dose.

If you missed a dose on one day during the first 2 weeks, or if you stop taking ACH-Fingolimod for more than 7 days during weeks 3 and 4 of treatment, contact your doctor right away. Your doctor may decide to observe you at the time you take the next dose.

If you start ACH-Fingolimod again after stopping for 2 weeks or more, you will start taking ACH-Fingolimod again in your doctor's office or clinic. Do not restart ACH-Fingolimod after stopping it for more than two weeks without seeking advice from your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with all medicines, patients treated with ACH-Fingolimod may experience side effects, although not everybody gets them.

Very common side effects (affect more than 1 in 10 patients):

- Flu virus infection
- Headache
- Diarrhea
- Back pain
- Cough

Common side effects (affect between 1 and 10 in every 100 patients):

- Sinusitis
- Fungal infections affecting skin, nails or hair
- Dizziness
- Migraine
- Weakness
- Mild increase in blood pressure
- Skin rash
- Hair loss
- Itchy skin
- Weight loss
- Blurred vision
- Breathlessness
- Tingling or numbness
- Depression
- Eye pain

Uncommon side effects (affect between 1 and 10 in every 1,000 patients):

- Depressed mood.

Frequency not known:

- Nausea.
- Muscle pain
- Joint pain

If any of these side effects affects you severely, tell your doctor.

If you notice any other side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

	Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency help
		Only if severe	In all cases	
Common	Symptoms of bronchitis such as cough with phlegm, chest pain, fever		✓	
Common	Symptoms of gastroenteritis such as vomiting, nausea, diarrhea, fever		✓	
Common	Symptoms of shingles (or herpes zoster) such as blisters, burning, itching or pain of the skin, typically on the upper body or the face. Other symptoms may be fever followed by numbness, itching or red patches with severe pain		✓	
Common	Symptoms of slow heartbeat (bradycardia) such as feeling dizzy, tired, awareness of own heartbeat, decrease in blood pressure		✓	
Common	Symptoms of a type of skin cancer called basal cell carcinoma (BCC), which often appears as a pearly nodule, though it can also take other forms		✓	
Common	Symptoms of low level of white blood cells such as fever, sore throat or mouth ulcers due to infections		✓	
Uncommon	Symptoms of pneumonia such as fever, cough, difficulty breathing		✓	
Uncommon	Symptoms of macular edema (swelling in the central vision area of the retina at the back of the eye) such as shadows or blind spot in the center of the vision, blurred vision, problems seeing colors or fine details		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

	Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency help
		Only if severe	In all cases	
	Liver disorder (symptoms include feeling nauseous, , or throwing up, loss of appetite, swelling and/or pain in the abdomen, feeling tired, itching, yellowing of the skin or eyes, dark urine)		✓	
	Trouble breathing		✓	
	Melanoma, a type of skin cancer that usually develops from an unusual mole. New moles or moles that may change in size, shape, height or colour over time as well, may be signs of melanoma. The moles may itch, bleed or form a sore.		✓	
	Convulsions, fits (more frequent in children and adolescents than in adults)			✓
Rare	Stroke (symptoms include weakness and/or loss of feeling of limbs or face, difficulty speaking, clumsiness, vision loss)			✓
Rare	Peripheral artery disease (symptoms include cold, painful, discolored limb, fingers or toes)			✓
Rare	Posterior reversible encephalopathy syndrome (PRES) (symptoms may include sudden severe headache, feeling nauseous or throwing up confusion, drowsiness, personality change, paralysis, abnormal speech, convulsions and vision changes)			✓
Rare	Cancer of the lymphatic system (lymphoma) (symptoms may include painless swelling of lymph node swollen tonsils, fever, chills, night sweats, feeling tired, itching, unexplained weight loss, loss of appetite, persistent coughing/ difficulty		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

	Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency help
		Only if severe	In all cases	
	breathing or not being able to breathe, and headache)			
Very Rare	Tumour related to infection with human herpes virus 8 called Kaposi's sarcoma (symptoms may include purple, red or brown blotches or tumours, usually on the skin of the legs or face)		✓	
Isolated cases	Temporary but serious abnormal heart beat			✓
Frequency not known	Cryptococcal infections (a type of fungal infection), including meningitis with symptoms such as headache with a stiff neck, sensitivity to light, feeling nauseous and/or confusion		✓	
	Progressive multifocal leukoencephalopathy (PML), a rare brain infection (symptoms may include) weakness on one side of your body, problems thinking, or vision changes)		✓	
	Return of disease activity after stopping treatment (worsening of symptoms of MS compared to before and during treatment)		✓	
	Human Papilloma Virus (HPV) infection, including papilloma, dysplasia, warts and HPV-related cancer		✓	
	Allergic reactions, including symptoms of rash or itchy hives, swelling of lips, tongue or face, which are more likely to occur on the day you start ACH-Fingolimod treatment.		✓	

This is not a complete list of side effects. For any unexpected effects while taking ACH-Fingolimod, contact your doctor or pharmacist.

HOW TO STORE IT

- Do not use ACH-Fingolimod after the expiry date shown on the box.
- Store at 15-25°C.
- Store in the original package, protect from moisture.
- Keep out of the reach and sight of children.

REPORTING SIDE EFFECTS

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

If you want more information about ACH-Fingolimod:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); or by calling the sponsor Accord Healthcare Inc. at 1-866-296-0354.

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