

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

PrMAYZENT™
Siponimod tablets

Read this carefully before you start taking **MAYZENT™** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **MAYZENT**.

What is MAYZENT used for?

MAYZENT is used to treat adults with a form of multiple sclerosis (MS) known as secondary progressive MS (SPMS), specifically SPMS with active disease. This means that patients still have relapses or signs of inflammation that can be seen in scans (MRI – magnetic resonance imaging).

MAYZENT is used to slow down the progression of physical disability.

How does MAYZENT work?

Siponimod, the ingredient in MAYZENT, binds to selective receptors on your white blood cells and keeps them in your body's lymph nodes. This lowers the number of your white blood cells circulating in your body. How MAYZENT works is not known, but it may be due to less white blood cells entering your central nervous system.

What are the ingredients in MAYZENT?

Medicinal ingredient: siponimod.

Non-medicinal ingredients: Colloidal silicon dioxide, crospovidone, glyceryl behenate, lactose monohydrate, microcrystalline cellulose. The tablet coating consists of iron oxide (red and black iron oxides for the 0.25 mg strength and red and yellow iron oxides for the 2 mg strength), lecithin (soya), polyvinyl alcohol, talc, titanium dioxide, xanthan gum.

MAYZENT comes in the following dosage forms:

Film-coated tablets: 0.25 mg and 2 mg.

Do not use MAYZENT if:

- you are allergic to:
 - siponimod
 - peanut
 - soya or
 - to any of the other ingredients in MAYZENT (see **What are the ingredients in MAYZENT** above)
- you have a CYP2C9*3*3 genotype

- you are at an increased risk of opportunistic infection, i.e. if you have a weakened immune system due to:
 - treatments that suppress the immune system (cancer treatments, immunosuppressive or immune modulating therapies, total lymphoid irradiation or bone marrow transplantation)
 - disease (immunodeficiency syndrome)
- you currently have a bacterial, fungal or viral infection (such as hepatitis, tuberculosis). You should not take MAYZENT until your infection is treated and resolved.
- you currently have cancer (except for a type of skin cancer called basal cell carcinoma)
- you have had in the last 6 months a:
 - heart attack
 - unstable angina
 - stroke or warning signs of a stroke
 - a sudden worsening of the signs and symptoms of heart failure that required treatment or have been diagnosed with Class III or IV heart failure
- you have certain types of second or third degree atrioventricular (AV) heart block or certain heart rhythm problems and do not have a pacemaker
- you are pregnant, think you may be pregnant or plan to get pregnant
- you are of childbearing age and not using an effective methods of birth control
- you are of childbearing age and your doctor has not performed a pregnancy test to confirm that you are not pregnant before you start treatment, as MAYZENT may harm your baby.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take MAYZENT. Talk about any health conditions or problems you may have, including if you:

- have or had problems with your heart:
 - an irregular or abnormal heartbeat
 - a heart attack
 - severe heart disease
 - uncontrolled high blood pressure
 - a history of stroke or other diseases related to blood vessels in the brain
 - a risk for, or if you have heart rhythm disturbances
 - where an electrocardiogram (ECG) shows a prolonged QT interval
- have severe sleep apnea (a disorder where you breathing repeatedly starts and stop while you sleep) that is not being treated
- have or had a history of fainting
- have difficulty breathing

Your doctor may decide not to use MAYZENT if you have or have had one of these conditions, or may refer you to a cardiologist before you start treatment.

- are taking medications:
 - to lower your blood pressure
 - to treat an irregular heartbeat (medicines that cause QT prolongation)
 - that slow your heart rate

Depending on the medications you are taking, your doctor may decide not to use MAYZENT or refer you to a cardiologist to change your medication (see **The following may interact with MAYZENT** below for more information).

- suffer from a slow heart rate or you have a history of fainting. MAYZENT can cause your heart rate to slow down especially at beginning of treatment (in the first 6 days). MAYZENT can also cause an irregular heartbeat. If your heart rate slows down at the beginning of treatment, you may feel dizzy or tired.
 - the heart rate usually returns to normal within 10 days after start of treatment
 - an irregular heartbeat usually returns to normal in less than one day after you start treatment
- have an infection. MAYZENT lowers your white blood cell count. This may increase your risk of infections including serious and life-threatening infections. This can occur while you are being treated with MAYZENT and up to 1 month after you stop treatment. Your doctor should do a complete blood test to check your white blood cell count before you start treatment if you have not had one done within the last 6 months, during treatment and after you stop treatment.
- have never had chickenpox or have not been vaccinated against chickenpox (varicella zoster virus). Your doctor will check your antibody levels and may decide to vaccinate you if you do not have enough antibodies against the virus. If you get the vaccine, you will start treatment 1 month after the full course of the vaccination is completed.
- have not been vaccinated against:
 - Human Papilloma Virus (HPV). Your doctor will decide whether you need to be vaccinated against HPV before starting treatment. For female patients, your doctor may also recommend HPV screening. HPV infection, including papilloma, dysplasia, warts and HPV-related cancer, has been reported in patients treated similar medicines like MAYZENT.
 - Herpes Zoster Virus. Cases of herpes viral infections have been reported in patients treated with similar medicines like MAYZENT.
- plan to receive a vaccine:
 - you should not receive certain types of vaccines (called “live attenuated vaccines”) while you are being treated with MAYZENT and for up to 4 weeks after stopping treatment
 - other vaccines can be less effective. Your doctor may want you to stop MAYZENT one week before the vaccination and for up to 4 weeks after vaccination.
- have a weakened immune system due to a disease or from medicines that suppress the immune system. You may get infections more easily or an infection you already have may get worse. MAYZENT lowers your white blood cell count during treatment and for up to 1 month after you stop taking it.
- have not had a test to check your liver function within the last 6 months
- if you have a history of seizures. MAYZENT may cause you to have seizures more often.
- have breathing problems. MAYZENT can have a slight effect on your lung function.
- have an allergy to:
 - lactose or
 - have a rare hereditary problem of galactose intolerance, total lactose deficiency or glucose-galactose malabsorption.

You should not take MAYZENT if you have any of these conditions.

- have or have had:

- changes in your vision or other signs of swelling in the central vision area at the back of the eye - a condition known as macular edema
- disease of the retina
- inflammation or infection of the eye (uveitis) or
- have diabetes

The macula is a small area of the retina at the back of the eye. It allows you to see shapes, colors, and details clearly and sharply. MAYZENT may cause swelling in the macula and it usually happens during the first 3 to 4 months treatment.

Your chance of developing macular edema is higher if you have diabetes, have had an inflammation or infection of the eye or are on long-term treatment with MAYZENT.

Your doctor may want you to undergo an eye examination:

- before you start MAYZENT
 - 3 to 4 months after starting treatment
 - during treatment and
 - at anytime throughout your treatment if you notice changes in your vision. Tell your doctor about any changes in your vision.
- have liver problems. MAYZENT may affect your liver function. If you notice any of the following symptoms, tell your doctor **right away**:
 - yellowing of your skin or the whites of your eyes
 - abnormally dark urine
 - unexplained nausea or vomiting
 - tiredness

Your doctor may carry out blood tests to check your liver function and may consider stopping MAYZENT treatment if your liver problem is serious.

Other warnings you should know about:

After you stop treatment:

- MAYZENT will stay in your body for about 10 days after you stop taking it. Your white blood cell count may remain low during this time and for up to 3 to 4 weeks after. The side effects described in this leaflet may still occur.
- your symptoms of MS can return and may become worse compared to before you started treatment or during treatment. Tell your doctor if MS symptoms become worse after you stop taking MAYZENT.

Patients taking immunosuppressive or immune modulating medicines: you could be at an increased risk for developing cancer, particularly skin cancer. Basal cell carcinoma, malignant melanoma *in situ* and squamous cell carcinoma were reported with patients on MAYZENT therapy. Your doctor should check for any abnormal skin growths before you start treatment and regularly during your treatment with MAYZENT especially if you are at a higher risk for skin cancer. During treatment you should:

- check your skin regularly for unusual changes
- limit how much time you are exposed to the sun and UV rays. Wear protective clothes and regularly apply sunscreen with a high degree of UV protection.

Depression, thoughts of suicide and suicidal behaviour: are known to occur in patients with MS. Thoughts of suicide and suicidal behaviour have been reported with patients taking

MAYZENT. Tell your family you are taking this medicine. If you, your caregiver or family members notice changes in your mood, or you start to have thoughts about hurting yourself, **contact your doctor right away.**

Pregnancy: You should avoid becoming pregnant while taking MAYZENT and for at least 10 days after you stop taking it before planning a pregnancy. MAYZENT may harm your unborn baby. Female patients who might become pregnant should use effective birth control methods during treatment and for at least 10 days after stopping MAYZENT. Ask your doctor about options of effective birth control.

- If you become pregnant or think you are pregnant, tell your doctor **right away.** You and your doctor will decide what is best for you and your baby.

Breast-feeding: You should not breast-feed while you are taking MAYZENT. MAYZENT can pass into breast milk and there is a risk of serious side effects for a breast-fed baby. Talk with your doctor before breast-feeding while you take MAYZENT.

Laboratory Tests:

- **Abnormal liver function test results:** a high level of an enzymes called alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT) and aspartate aminotransferase (AST) have been reported in MS patients taking MAYZENT.
- **Lower lung function test results:** decreases in lung function (breathing) tests were have been reported in MS patients taking MAYZENT.

Tell your doctor right away, if you get any of the following symptoms **during your treatment** with MAYZENT. It could be serious:

- if you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms. These may be the symptoms of **progressive multifocal leukoencephalopathy (PML).** This is a rare brain disorder caused by an infection.
- if you have fever, feel like you have a flu, or have a headache accompanied by stiff neck, sensitivity to light, nausea, and/or confusion. These may be symptoms of **cryptococcal meningitis** caused by a fungal infection.
- if you have symptoms such as the sudden start of a severe headache, confusion, seizures, changes in your behaviour and changes to your vision. These may be symptoms of a condition called **posterior reversible encephalopathy syndrome (PRES).**

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with MAYZENT:

- **Medicines that treat an irregular heartbeat (medicines that cause QT prolongation)**
 - quinidine
 - procainamide
 - amiodarone
 - sotalol

Your doctor may decide not to use MAYZENT if you are taking these medicines to reduce the possible additive effect of an irregular heartbeat.

- **Medicines that slow down your heartbeat** such as:

- beta-blockers (such as atenolol or propranolol)
- calcium channel blockers (such as verapamil or diltiazem)
- cholinomimetics
- other substances that can decrease your heart rate (ivabradine or digoxin)

MAYZENT can slow your heartbeat when you first start treatment. Your doctor may decide to refer you to a cardiologist to change your medicine before you start treatment.

If you are taking a beta-blocker, your doctor will check your resting heart rate before deciding if you can start treatment. When MAYZENT is taken with a beta-blocker the effects of a slow heartbeat are more noticeable.

- **Medicines that suppress or modulate the immune system, including other medicines used to treat MS and medicines used to treat cancer:**
 - beta-interferons
 - glatiramer acetate
 - natalizumab
 - mitoxantrone
 - dimethyl fumarate
 - teriflunomide
 - alemtuzumab
 - corticosteroids
 - ocrelizumab

MAYZENT should not be started while you are taking these medicines or you are switching to or from other therapies used to treat MS with immunosuppressive or immune modulating effects. Your doctor may want to wait for several weeks after you stop taking these medicines before starting you on MAYZENT to reduce the possible additive effect on your immune system. MAYZENT can generally be started immediately after discontinuation of beta interferon or glatiramer acetate.

- **Vaccines.** If you need to receive a vaccine, talk to your doctor first. For more information about vaccines see **To help avoid side effects and ensure proper use** above.
- **Treatment with medicines such as carbamazepine and rifampin (strong CYP3A4/moderate CYP2C9 dual inducers)** is not recommended. These types of medicines can lower the level of MAYZENT in your blood.
- **If you have the CYP2C9 *1*3 or *2*3 genotype:** treatment with medicines such as modafinil and efavirenz (moderate CYP3A4 inducers) or with strong CYP3A4 inducers is not recommended. These types of medicines can lower the level of MAYZENT in your blood.
- **Treatment with medicines such as fluconazole (moderate CYP2C9/CYP3A4 dual inhibitors)** is not recommended. These types of medicines can increase the level of MAYZENT in your blood.

How to take MAYZENT:

You should only be prescribed MAYZENT by a neurologist who is experienced in the treatment of multiple sclerosis who can discuss the benefits, harms and the safe use MAYZENT with you.

Before you start treatment:

Your doctor will:

- confirm your CYP2C9 genotype:
 - If you have the CYP2C9*3*3 genotype: **Do not** take MAYZENT
- conduct an electrocardiogram (ECG) to check for any pre-existing heart conditions
- perform:
 - liver tests if you have not had one within the last 6 months
 - a complete blood test if you have not had one in the last 6 months
 - a check your antibody levels for the chickenpox virus (varicella zoster virus)
 - a pregnancy test if you are a woman of childbearing potential
- check if you currently have a severe infection
- check your medication history

Your doctor may also:

- have you go for an eye exam if you have or had uveitis (a swelling in the middle layer of tissue in the eye wall) a history of retinal disorders or diabetes

Patients with certain heart conditions or risk factors:

If you have certain heart conditions or risk factors the first dose MAYZENT will have to be taken in your doctor’s office or hospital where your heart rate and blood pressure can be monitored (hourly blood pressure and pulse measurements, ECG monitoring) for at least 6 hours.

Adult dose:

On Days 1 to 5 (Titration doses):

When you start treatment with MAYZENT you will be given a starter pack. The starter pack contains 12 tablets. Over a period of 5 days you will slowly increase (titrate) your dose. Follow the directions on the starter pack and the table below.

Take your titration doses once a day in the **morning**. Swallow the tablets whole with water.

Starter pack dosing schedule:

Day	Daily Dose	Directions	Starter Pack
Day 1	0.25 mg	Take 1 (one) 0.25 mg tablet	
Day 2	0.25 mg	Take 1 (one) 0.25 mg tablet	
Day 3	0.5 mg	Take 2 (two) 0.25 mg tablets	
Day 4	0.75 mg	Take 3 (three) 0.25 mg tablets	
Day 5	1.25 mg	Take 5 (five) 0.25 mg tablets	
Day 6	Switch to your maintenance dose		

On Day 6 (Maintenance dose):

Switch to your maintenance dose. Depending on the results of your genotype test your doctor will either prescribe a 1 mg dose or a 2 mg dose.

- If dose is 1 mg: Take 4 (four) 0.25 mg tablets
- If your dose is 2 mg: Take 1 (one) 2 mg tablet

Take your maintenance dose once a day **at about the same time each day**. Swallow the tablets whole with water.

Continue taking MAYZENT every day for as long as your doctor tells you. Do not stop taking this medicine without talking to your doctor.

IMPORTANT – Missed Doses:

If you miss a dose during the first 6 days of treatment:

- If you **miss 1** of your doses during the first 6 days of treatment, contact your doctor **right away** before you take the next dose. You will have to re-start treatment (from Day 1) using a new starter pack.

If you miss a dose after the first 6 days of treatment (Day 7 and onwards):

- if you miss taking your dose for 1, 2 or 3 days in row, take the missed dose as soon as you remember. Then take your next dose as usual.
- if you miss taking your dose for **4 or more days in a row**, you will have to re-start treatment using a new starter pack. Contact your doctor **right away** if this happens.

If you have questions about how long to take MAYZENT, talk to your doctor or your pharmacist.

Overdose:

If you think you have taken too much MAYZENT, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose: see **How to take MAYZENT** above for missed dose information.

What are possible side effects from using MAYZENT?

These are not all the possible side effects you may feel when taking MAYZENT. If you experience any side effects not listed here, contact your healthcare professional.

Side effects include:

- Headache.
- Dizziness.
- Involuntary shaking of the body (tremors).
- Diarrhea.
- Nausea.
- Pain in the hands and feet.
- Swollen hands, ankles, legs or feet.
- Weakness / lack of energy.

If these side effects become severe, please tell your doctor, pharmacist or healthcare provider. These are not all the possible side effects you may feel when taking MAYZENT. If you experience any side effects not listed here, contact your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		√	
COMMON			
Herpes zoster (chickenpox): rash of small fluid-filled blisters, appearing on reddened skin		√	
Melanocytic nevus (a type of tumors - moles)		√	
Lymphopenia (low white blood cells: lymphocytes): get infections more easily, fever, sore throat or mouth ulcers due to infections		√	
Seizures (fit): loss of consciousness with uncontrollable shaking		√	
Macular edema (swelling and build-up of fluid in the center of the retina): blurry vision, blurry or wavy vision near or in the center of your field of vision, colors may appear washed out or faded		√	
Atrioventricular block (irregular heartbeat)		√	
Bradycardia (abnormally slow heartbeat): feeling dizzy, tired		√	
Trouble breathing		√	
FREQUENCY NOT KNOWN			
Cryptococcal infections (a type of fungal infection), including cryptococcal meningitis: headache accompanied by stiff neck, sensitivity to light, nausea, and/or confusion		√	
Herpes zoster meningitis: headache, repeated vomiting			√
Cerebrovascular accident, ischemic stroke, transient ischemic attack (stroke): Sudden numbness or weakness of your arm, leg or face,			√

<p>especially if only on one side of the body; sudden confusion, difficulty speaking or understanding others; sudden difficulty in walking or loss of balance or coordination; suddenly feeling dizzy or sudden severe headache with no known cause.</p>			
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If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

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.

Storage:

- Do not take this medicine after the expiry date, which is stated on the box.
- Store in the refrigerator (between 2 to 8°C).
- Keep in the original package.
- Keep out of reach and sight of children.

Ask your pharmacist how to dispose of medicines you no longer use.

If you want more information about MAYZENT:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>); the manufacturer's website (www.novartis.ca), or by calling 1-800-363-8883.

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

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