PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr PONVORY®

ponesimod tablets

Read this carefully before you start taking PONVORY® 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 PONVORY®.

What is PONVORY® used for?
PONVORY® is used to treat adults with relapsing remitting Multiple Sclerosis (RRMS).

How does PONVORY® work?
PONVORY® contains ponesimod. Ponesimod binds to certain receptors on your white blood cells. This keeps the white blood cells in your body's lymph nodes and lowers the number of white blood cells circulating in your body. How exactly PONVORY® works is not known, but it may be due to less white blood cells entering your central nervous system where they could cause inflammation and damage to the protective coating around the nerves in the brain and spinal cord.

What are the ingredients in PONVORY® ?
Medicinal ingredient: ponesimod
Non-medicinal ingredients: croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone K30, silica colloidal anhydrous and sodium laurilsulfate

Tablet coating: Opadry II is used for the tablet coating and includes: hydroxypropyl methylcellulose, lactose monohydrate, polyethylene glycol 3350, titanium dioxide, and triacetin.

In addition, the following strengths include in their tablet coating:
- 3 mg, 4 mg, 7 mg, 8 mg, 9 mg and 10 mg: iron oxide red
- 4 mg, 5 mg, 8 mg and 9 mg: iron oxide black
- 3 mg, 5 mg, 7 mg, 9 mg, 10 mg and 20 mg: iron oxide yellow

PONVORY® comes in the following dosage forms:
Film-coated tablets

The Initiation Pack contains 14 tablets of different strengths of ponesimod: 2 tablets (2 mg), 2 tablets (3 mg), 2 tablets (4 mg), 1 tablet (5 mg), 1 tablet (6 mg), 1 tablet (7 mg), 1 tablet (8 mg), 1 tablet (9 mg) and 3 tablets (10 mg).

The Maintenance Pack contains only 20 mg tablets of ponesimod.

Do not use PONVORY® if:
- you are allergic to ponesimod or to any of the other ingredients of PONVORY® (listed in **What are the ingredients in PONVORY®**)
- 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 transplants)
    - disease (immunodeficiency syndrome)
- you currently have a severe bacterial, fungal or viral infection (such as hepatitis or tuberculosis)
- you currently have cancer (except for a type of skin cancer called basal cell carcinoma)
- if 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 you have been diagnosed with Class III or IV heart failure or certain types of heart failure
- you have or have had a history of certain types of irregular or abnormal heartbeat (arrhythmia) and do not have a pacemaker
- you have liver problems
- you are pregnant, think you may be pregnant or plan to get pregnant
- you are of childbearing age and not using an effective method of birth control

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

- have or had problems with your heart including:
    - an irregular or abnormal heartbeat (arrhythmia) and are taking medicines to treat it
    - a heart attack
    - severe heart disease
    - uncontrolled high blood pressure
    - a history of stroke or other diseases related to blood vessels in the brain
    - have a low resting heart rate
    - an abnormal heart rhythm or at a greater risk of having an abnormal heart rhythm due to an existing condition or factors such as gender and age
    - have low levels of electrolytes (such as potassium, magnesium or calcium), if you are at a higher risk, or you have heart rhythm disturbances or where an electrocardiogram (ECG) shows a prolonged QT interval
- have ever suddenly passed out or fainted
- have trouble breathing
- are taking medicines:
    - to lower your blood pressure
    - to treat an irregular heart beat (medicines that cause QT prolongation)
    - that slow your heart rate
- have a condition where you stop breathing while you sleep (sleep apnea)
- have severe lung disease including chronic obstructive pulmonary disease (COPD)
- have or have had seizures
- have a fever or infection

- have a weakened immune system and are unable to fight infections-due to a disease or from taking medicines that weaken your immune system (such as medicines that suppress or modulate the immune system, including other medicines used to treat MS, and medicines used to treat cancer, including corticosteroids).
- have had chicken pox or have received the chicken pox vaccine.
- have liver problems
- have diabetes
- have eye problems – especially an inflammation of the eye called 'uveitis'
- have high blood pressure.
- are breastfeeding or planning to breastfeed your baby. It is not known if PONVORY® can pass to your baby through your breast milk.
- you are allergic to lactose

Other warnings you should know about:

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 were reported with patients on PONVORY® . Your doctor should check for any abnormal skin growths before you start treatment and regularly during your treatment with PONVORY® 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. You should wear protective clothes and regularly apply sunscreen with a high degree of UV protection
- avoid "light therapy." This is a treatment where you are exposed to daylight or some form of light to treat seasonal affective disorder or to treat skin conditions

Risk of Infections: PONVORY® lowers the number of white blood cells in your blood. This can increase your risk of developing infections. These can be serious and life-threatening. Your doctor should do a blood test to check your white blood cell count before you start treatment, while you are taking PONVORY® and after you stop treatment. Your white blood cell levels will usually go back to normal within 1-2 weeks of stopping treatment.

If you have a fever, feel tired, have body aches, chills, nausea or vomiting during treatment or 1-2 weeks after your last dose of PONVORY®, call your doctor **right away. Also tell your doctor right away,** if you get any of the following symptoms **during your treatment** with PONVORY®. 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 along with a 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).

Herpes Zoster Virus: Cases of herpes viral infections have been reported in patients treated with PONVORY®.

Slow heart rate: PONVORY® can cause a slow heart rate– especially after you take your first dose. You should have a test to check the electrical activity of your heart called an 'electrocardiogram' (ECG) **before** you take your first dose of PONVORY®.

- If you are at increased risk for side effects due to a slowing of your heart rate, your doctor may ask you to stay at the doctor's office or clinic for at least 4 hours after your first dose.
- You will also have an ECG at the end of the 4 hours. If your ECG is not normal or you still have a very slow or decreasing heart rate, you may need to be monitored for a longer period.

The same may apply if you are restarting PONVORY® after taking a break in treatment.

Increase in blood pressure: PONVORY® can cause an increase in your blood pressure. Your doctor should check your blood pressure while you are taking PONVORY®.

Breathing problems: Some people who take PONVORY® have shortness of breath. Call your doctor **right away** if you have new or worsening breathing problems.

Vaccinations:

- Chickenpox: If you 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 get the vaccine, you will start treatment 1 month after the full course of the vaccination is completed.
- Human Papilloma Virus (HPV): If you have not been vaccinated for the HPV virus your doctor will decide whether you need to be vaccinated against HPV before starting treatment with PONVORY®.

If you are planning to get any other type of vaccine you should not get certain types of vaccines (called "live attenuated vaccines") while you are taking PONVORY® and for at least 2 weeks after stopping treatment. The use of live attenuated vaccines may increase your risk of infection and other vaccines may be less effective. Your doctor may want you to stop PONVORY® 1 week before you get a vaccine and for up to 4 weeks after you have received it.

Macular edema: PONVORY® can cause a problem with your vision called macular edema. The macula is a small area of the retina at the back of the eye. It allows you to see shapes, colours, and details clearly and sharply. PONVORY® may cause swelling in the macula. It usually happens within the first 6 months of starting treatment, but it can also happen at any time during treatment.

Your doctor should test your vision before you start taking PONVORY®. They should also test your vision any time you notice changes to your eyesight during treatment. Your risk of macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis.

Be sure to tell your doctor about any changes in your vision and if you notice:

- blurriness or shadows in the center of your vision

- a blind spot in the center of your vision
- sensitivity to light
- unusually colored (tinted) vision

Depression, thoughts of suicide and suicidal behaviour: These behaviours are known to occur in patients with MS. Tell your family if you have symptoms of depression, thoughts of suicide or thoughts about hurting yourself. If you, your caregiver, or family members notice changes in your mood contact your doctor **right away.**

Liver problems: PONVORY® may cause liver problems. Your doctor should do blood tests to check your liver within the first 3 months of starting treatment and regularly during your treatment with PONVORY®. Call your doctor **right away** if you have any of the following symptoms:

- yellowing of your skin or the whites of your eyes
- abnormally dark urine
- unexplained nausea and vomiting
- stomach pain
- feeling tired
- loss of appetite

Pregnancy and Contraception: You must not become pregnant while taking PONVORY® and for at least 2 weeks after you stop taking it. If you become pregnant while taking PONVORY®, stop taking it and tell your doctor right away. PONVORY® may harm your unborn baby.

If you are of childbearing age:

- your doctor should perform a pregnancy test to confirm that you are not pregnant **before** you start treatment with PONVORY®

- and you might get pregnant, you should use effective birth control methods during treatment and for at least **2 weeks** after stopping PONVORY®. Ask your doctor about options of effective birth control

Your doctor may enroll you in Janssen's PONVORY Pregnancy Outcomes Enhanced Monitoring (POEM) program. This program is designed to monitor you if you were exposed to PONVORY® during pregnancy.

After stopping treatment with PONVORY®:

- PONVORY® will stay in your body for about 1 week after you stop taking it. Your white blood cell count may remain low during this time and for up 1-2 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 PONVORY®.

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 PONVORY®:

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

- Medicines that slow down your heartbeat such as:
  - beta-blockers (such as atenolol or propranolol)
  - calcium channel blockers (such as verapamil or diltiazem)
  - other medicines that can decrease your heart rate (digoxin)

- Medicines that suppress or modulate the immune system, including other medicines used to treat MS

- Medicines to treat epilepsy such as phenytoin and carbamazepine

- Medicines used to treat tuberculosis such as rifampin

- Medicines used for chemotherapy and to treat cancer such as corticosteroids, methotrexate, camptothecin and tyrosine kinase inhibitors

- Medicines used to lower cholesterol such as rosuvastatin

- Medicines used to rheumatoid arthritis such as sulfasalazine

Vaccines: If you need to receive a vaccine, talk to your doctor first. For more information about vaccines see "**Other warnings you should know about**."

How to take PONVORY®:
You should only be prescribed PONVORY® by a neurologist who is experienced in the treatment of MS who can discuss the benefits, harms and the safe use PONVORY® with you.

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Before you start PONVORY®:

Your doctor may perform the following:

- an electrocardiogram (ECG) to check for any pre-existing heart conditions
- 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 of your antibody levels for the chickenpox virus (varicella zoster virus) or Human Papilloma Virus (HPV)
- a pregnancy test if you are a woman of childbearing age
- check if you currently have a severe infection
- check your medication history
- have you go for an eye exam

Patients with certain heart conditions or risk factors: If you have certain heart conditions or risk factors the first dose PONVORY® 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 4 hours.

Usual Adult Dose:

On Days 1 to 14 – Initiation Pack:

- When you start treatment with PONVORY® you will be given an Initiation Pack. The Initiation Pack contains 14 tablets of different strengths of ponesimod. Over a period of 14 days, you will slowly increase your dose. Carefully follow the directions in the table below and on the Initiation Pack.

- Write down the date on the blister card when you start taking the medicine

- **Only take 1 tablet each day** at about the same time each day**.** Swallow the tablet whole.

- It is important that you take your dose every day. If you miss a dose see "**Missed Dose**" below.

- When you finish the Initiation Pack switch to the Maintenance Pack (Day 15).

Initiation Pack Dosing Instructions

Day	Dose	Tablet Colour	Tablet Marking
1	2 mg	White	"2" on one side and an arch on the other side
2	2 mg	White	"2" on one side and an arch on the other side
3	3 mg	Red	"3" on one side and an arch on the other side
4	3 mg	Red	"3" on one side and an arch on the other side
5	4 mg	Purple	"4" on one side and an arch on the other side
6	4 mg	Purple	"4" on one side and an arch on the other side
7	5 mg	Green	"5" on one side and an arch and an "A" on the other side
8	6 mg	White	"6" on one side and an arch and an "A" on the other side
9	7 mg	Red	"7" on one side and an arch and an "A" on the other side
10	8 mg	Purple	"8" on one side and an arch and an "A" on the other side
11	9 mg	Brown	"9" on one side and an arch and an "A" on the other side
12	10 mg	Orange	"10" on one side and an arch and an "A" on the other side
13	10 mg	Orange	"10" on one side and an arch and an "A" on the other side
14	10 mg	Orange	"10" on one side and an arch and an "A" on the other side

<u>On Day 15 and after – Maintenance Pack Dosing Instructions:</u>

- Start the Maintenance Pack.
- Write down the date on the blister card when you start the Maintenance Pack.
- The recommended dose is 20 mg once a day at about the same time each day. Swallow the tablets whole.
- Continue taking PONVORY® every day for as long as your doctor tells you. Do not stop taking this medicine without talking to your doctor first.
- It is important that you take your dose every day. If you miss a dose see **"Missed Dose"** below.

Overdose:

If you think you, or a person you are caring for, have taken too much PONVORY®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
While taking the Initiation Pack or Maintenance Pack if you miss:

- 1, 2 or 3 doses in a row continue with your treatment by taking the first dose that you missed. Take it as soon as you remember. Then finish the Initiation Pack or Maintenance Pack as planned.
- 4 or more doses in a row, you will need to **restart treatment at Day 1 using a new Initiation Pack**. Call your doctor if this happens so that you can get a new Initiation Pack prescribed to you.

Do not take a double dose to make up for a forgotten dose.

What are possible side effects from using PONVORY®?
These are not all the possible side effects which you may feel when taking PONVORY®. If you experience any side effects not listed here, contact your healthcare professional.

Very common (may affect more than 1 in 10 people):

- infection of the nose, sinuses or throat (cold)
- increased level of liver enzymes in the blood

Common (may affect up to 1 in 10 people):

- a slower than normal heartbeat (bradycardia), especially when you start treatment with PONVORY®
- urinary tract infection
- bronchitis (inflammation of airways of the lungs)
- flu
- itchy, runny or blocked nose
- viral infection of nose, throat or chest

- viral infection
- infected or irritated throat
- sinus infection
- herpes zoster virus infection (shingles)
- depression
- feeling anxious
- difficulty sleeping
- feeling dizzy
- decreased feeling or sensitivity, especially on the skin
- feeling sleepy
- migraine
- spinning sensation (vertigo)
- high blood pressure
- being short of breath
- cough
- indigestion
- back pain
- joint pain
- arm or leg pain
- ligament sprain
- feeling very tired
- fever
- swollen hands, ankles or feet
- chest discomfort
- increased level of a protein in the blood that may indicate an infection or inflammation
- high level of cholesterol in the blood

Uncommon (may affect up to 1 in 100 people):
- swollen joint
- dry mouth
- sinus infection
- hay fever

Tell your doctor if you notice any of the above side effects. These are not all the possible side effects of PONVORY®. Tell your healthcare professional if you have any side effect that bothers you or that does not go away.

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**	
COMMON			
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,		✓	

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**	
colors may appear washed out or faded			
Herpes zoster (chickenpox): rash of small fluid-filled blisters, appearing on reddened skin		✓	
UNCOMMON			
Leukopenia (abnormally low number of lymphocytes – a type of white blood cells): get infections more easily, fever, sore throat or mouth ulcers due to infections		✓	
Atrioventricular block (irregular heartbeat)			✓
RARE			
Bradycardia (abnormally slow heartbeat): feeling dizzy, tired		✓	
Seizures (fit): loss of consciousness with uncontrollable shaking		✓	
Basal cell carcinoma (a type of skin cancer) a type of skin cancer (basal cell carcinoma, or colored skin bump or skin lesion)		✓	
FREQUENCY NOT KNOWN			
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			✓
Cryptococcal infections (a type of fungal infection) including cryptococcal meningitis: headache accompanied by stiff neck, sensitivity to light, nausea, and/or confusion		✓	
Progressive multifocal leukoencephalopathy (PML),		✓	

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	
(a rare brain infection): symptoms may include weakness on one side of your body, problems thinking, or vision changes			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell 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.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:

Store at room temperature (15-30ºC) in the original packaging.

Do not use PONVORY® after the expiry date which is stated on the label.

Keep out of reach and sight of children.

Proper disposal:
Medicines should not be discarded in the toilet or household garbage. Follow your local rules for discarding unused medicine. If you are not sure, ask your pharmacist how to throw away medicines you no longer need. This will help to protect the environment.

If you want more information about PONVORY®:

- 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://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html);
- For questions, concerns, or the full Product Monograph go to: www.janssen.com/canada or contact the manufacturer, Janssen Inc., at:1-800-567-3331 or 1-800-387-8781.

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