INDICATION
PONVORY® is a sphingosine 1-phosphate receptor modulator indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
PONVORY® is contraindicated in patients who:
• In the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III or IV heart failure.

PROVEN RESULTS
Superior efficacy in relapses and lesions; no disability progression for ~9 out of 10 patients.
More than 10 years of safety data spanning multiple studies; no known food restrictions or drug interactions with SSRIs.

AGILITY TO PAUSE IF NEEDED
For patients considering pregnancy, PONVORY® leaves the body naturally in ~1 week.

Fastest lymphocyte recovery in the S1P class: ~7-day recovery of lymphocyte counts allows you to pause therapy, if needed for infections or vaccines, and then restart.

S1P = sphingosine-1-phosphate; SSRI = selective serotonin reuptake inhibitor.
*In the phase 3 ~108-week OPTIMUM study vs Aubagio® (teriflunomide), PONVORY® was shown to reduce the average number of relapses per year and the average number of new gadolinium-enhancing T1 and new or enlarging T2 lesions.
†As measured by time to 3-month confirmed disability progression. There was no statistically significant difference between the PONVORY® and Aubagio® groups.
‡Includes the OPTIMUM study and the phase 2, 6-month, placebo-controlled study and the uncontrolled extension studies.
§PONVORY® must be stopped in cases of pregnancy. Advise a female patient to immediately inform you if she is pregnant or planning to become pregnant.
¶No elimination procedure required.
#As seen in pharmacokinetic-pharmacodynamic assessments.
||If 4 or more consecutive doses of PONVORY® are missed, treatment should be reinitiated with Day 1 of the titration regimen using a new 14-Day Starter Pack. First dose monitoring should also be completed in patients for whom it is recommended.

Please see additional Important Safety Information throughout and the full Prescribing Information and Medication Guide.
GET YOUR PATIENTS STARTED
IN 2 SIMPLE STEPS WITH
JANSSEN CAREPATH

ONCE YOU HAVE DECIDED TO PRESCRIBE PONVORY®

1 Fill out the Prescription Enrollment Form (PEF) in the Provider Portal or fax completed form to Janssen CarePath

2 Confirm assessments are completed

Learn more about PONVORY® [here](#)

PONVORY® is covered for ~80% of commercially eligible patients**

*Collected in 3/22 and is subject to change. Within 2% of access being stated. This information does not provide advice or guarantee coverage or payment, is not intended to provide reimbursement advice, and is not intended to increase or maximize reimbursement by any payer. Legal requirements and plan information can be updated frequently. We strongly recommend contacting the plan for more information about current coverage, restrictions, or prerequisites that may apply. This may not represent 100% of formulary lives due to data limitations.*

**Not an actual patient.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Herpes Viral Infections

Cases of herpes viral infection have been reported in the development program of PONVORY®, herpes simplex encephalitis and varicella zoster meningitis have been reported with other S1P receptor modulators. Patients without a healthcare professional confirmed history of varicella (chickenpox) or without documentation of a full course of vaccination should be tested for antibodies to VZV prior to initiating PONVORY®.

Cryptococcal Infections

Cases of fatal cryptococcal meningitis (CM) and disseminated cryptococcal infections have been reported with other S1P receptor modulators. Physicians should be vigilant for clinical symptoms or signs of CM. Patients with symptoms or signs consistent with a cryptococcal infection should undergo prompt diagnostic evaluation and treatment. PONVORY® treatment should be suspended until a cryptococcal infection has been excluded. If CM is diagnosed, appropriate treatment should be initiated.

Progressive Multifocal Leukoencephalopathy (PML)

PML has been reported in patients treated with a S1P receptor modulator and other multiple sclerosis (MS) therapies and has been associated with some risk factors (e.g., immunocompromised patients, polytherapy with immunosuppressants). Physicians should be vigilant for clinical symptoms or magnetic resonance imaging (MRI) findings that may be suggestive of PML. MRI findings may be apparent before clinical signs or symptoms. If PML is suspected, treatment with PONVORY® should be suspended until PML has been excluded. If PML is confirmed, treatment with PONVORY® should be discontinued.

Prior and Concomitant Treatment with Anti-neoplastic, Immune-Modulating, or Immunosuppressive Therapies

Anti-neoplastic, immune-modulating, or immunosuppressive therapies (including corticosteroids) should be co-administered with caution because of the risk of additive immune system effects.

Please see additional Important Safety Information throughout and the full Prescribing Information and Medication Guide.
Vaccinations

Patients without a confirmed history of chickenpox or without documentation of a full course of vaccination against VZV should be tested for antibodies to VZV before initiating PONVORY® treatment. A full course of vaccination for antibody-negative patients with varicella vaccine is recommended prior to commencing treatment with PONVORY®, following which initiation of treatment should be postponed for 4 weeks to allow the full effect of vaccination to occur.

No clinical data are available on the efficacy and safety of vaccinations in patients taking PONVORY®. Vaccinations may be less effective if administered during PONVORY® treatment. If live attenuated vaccines are required, administer at least 1 month prior to initiation of PONVORY®. Avoid the use of live attenuated vaccines during and for 1 to 2 weeks after treatment of PONVORY®.

Bradycardia and Atrioventricular Conduction Delays

Since initiation of PONVORY® treatment results in a transient decrease in heart rate and atrioventricular (AV) conduction delays, an up-titration scheme must be used to reach the maintenance dosage of PONVORY® (20 mg).

Reduction in Heart Rate

Initiation of PONVORY® may result in a transient decrease in heart rate. After the first titration dose of PONVORY®, the decrease in heart rate typically begins within an hour and reaches its nadir within 2–4 hours. The heart rate typically recovers to baseline levels 4–5 hours after administration.

Atrioventricular Conduction Delays

Initiation of PONVORY® treatment has been associated with transient atrioventricular conduction delays that follow a similar temporal pattern as the observed decrease in heart rate during dose titration. If treatment with PONVORY® is considered, advice from a cardiologist should be sought for individuals:

• With significant QT prolongation (QTc greater than 500 msec).
• With atrial flutter/fibrillation or arrhythmia treated with Class Ia or Class III anti-arrhythmic drugs.
• With unstable ischemic heart disease, cardiac decompensated failure occurring more than 6 months prior to treatment initiation, history of cardiac arrest, cerebrovascular disease (TIA, stroke occurring more than 6 months prior to treatment initiation), or uncontrolled hypertension.
• With a history of Mobitz Type II second degree AV block or higher-grade AV block, sick-sinus syndrome, or sino-atrial heart block.

Obtain an ECG in all patients to determine whether preexisting conduction abnormalities are present. For patients taking other drugs that decrease heart rate, treatment with PONVORY® should generally not be initiated without consultation from a cardiologist because of the potential effect on heart rate.

In all patients, a dose titration is recommended for initiation of PONVORY® treatment to help reduce cardiac effects.

Respiratory Effects

Dose-dependent reductions in forced expiratory volume over 1 second (FEV₁) and reductions in diffusion lung capacity for carbon monoxide (DLCO) were observed in PONVORY®-treated patients mostly occurring in the first month after treatment initiation. Spirometric evaluation of respiratory function should be performed during therapy with PONVORY® if clinically indicated.

Liver Injury

Elevations of transaminases may occur in PONVORY®-treated patients. Obtain transaminase and bilirubin levels, if not recently available (i.e., within last 6 months) before initiation of PONVORY® therapy.

Patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, rash with eosinophilia, jaundice and/or dark urine during treatment, should have hepatic enzymes checked. PONVORY® should be discontinued if significant liver injury is confirmed.

No dosage adjustment is necessary in patients with mild hepatic impairment (Child–Pugh class A). PONVORY® is not recommended in patients with moderate or severe hepatic impairment (Child–Pugh class B and C, respectively).

Increased Blood Pressure

PONVORY®-treated patients had an average increase of 2.9 mmHg in systolic blood pressure and 2.8 mmHg in diastolic blood pressure. Blood pressure should be monitored during treatment with PONVORY® and managed appropriately.

Cutaneous Malignancies

Cases of basal cell carcinoma and other skin malignancies have been reported in patients treated with S1P receptor modulators, including PONVORY®. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer. Providers and patients are advised to monitor for suspicious skin lesions. If a suspicious skin lesion is observed, it should be promptly evaluated. As usual for patients with increased risk for skin cancer, exposure to sunlight and ultraviolet light should be limited by wearing protective clothing and using a sunscreen with a high protection factor. Concomitant phototherapy with UV-B radiation or PUVA—photochemotherapy is not recommended in patients taking PONVORY®.

Fetal Risk

Based on animal studies, PONVORY® may cause fetal harm. Because it takes approximately 1 week to eliminate PONVORY® from the body, women of childbearing potential should use effective contraception to avoid pregnancy during and for 1 week after stopping PONVORY® treatment.
Macular Edema in Patients with a History of Uveitis or Diabetes Mellitus

Patients with a history of uveitis and patients with diabetes mellitus are at increased risk of macular edema during therapy with SIP receptor modulators, including PONVORY®. Therefore, these patients should have regular follow-up examinations of the fundus, including the macula, during treatment with PONVORY®.

Unintended Additive Immunosuppressive Effects from Prior Treatment with Immunosuppressive or Immune–Modulating Therapies

When switching from drugs with prolonged immune effects, the half-life and mode of action of these drugs must be considered in order to avoid unintended additive effects on the immune system while at the same time minimizing risk of disease reactivation, when initiating PONVORY®. Initiating treatment with PONVORY® after treatment with alemtuzumab is not recommended.

Severe Increase in Disability After Stopping PONVORY®

Severe exacerbation of disease, including disease rebound, has been rarely reported after discontinuation of a SIP receptor modulator. The possibility of severe exacerbation of disease should be considered after stopping PONVORY® treatment. Patients should be observed for a severe increase in disability upon PONVORY® discontinuation and appropriate treatment should be instituted, as required.

OVERDOSAGE

In patients with overdosage of PONVORY®, especially upon initiation/re-initiation of treatment, it is important to observe for signs and symptoms of bradycardia as well as AV conduction blocks, which may include overnight monitoring. Regular measurements of pulse rate and blood pressure are required, and ECGs should be performed.

There is no specific antidote to ponesimod. Neither dialysis nor plasma exchange would result in meaningful removal of ponesimod from the body. The decrease in heart rate induced by PONVORY® can be reversed by atropine.

In the event of overdose, PONVORY® should be discontinued, and general supportive treatment given until clinical toxicity has been diminished or resolved. It is advisable to contact a poison control center to obtain the latest recommendations for the management of an overdose.

ADVERSE REACTIONS

Most common adverse reactions (incidence at least 10%) are upper respiratory tract infection, hepatic transaminase elevation, and hypertension.


Please see additional Important Safety Information throughout and the full Prescribing Information and Medication Guide.

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