



INNOVATION

Janssen Announces U.S. FDA Approval of PONVORY™ (ponesimod), an Oral Treatment for Adults with Relapsing Multiple Sclerosis Proven Superior to Aubagio® (teriflunomide) in Reducing Annual Relapses and Brain Lesions

Head-to-head pivotal clinical trial results showed PONVORY™ treatment led to nearly a third fewer annual relapses than teriflunomide

PONVORY™ is the first and only FDA-approved oral disease modifying therapy studied against an established oral comparator

Approval follows more than 10 years of cumulative data demonstrating the treatment's efficacy and safety

TITUSVILLE, N.J. – (March 19, 2021) – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the U.S. Food and Drug Administration (FDA) approved PONVORY™ (ponesimod), a once-daily oral selective sphingosine-1-phosphate receptor 1 (S1P1) modulator, to treat adults with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease.^{1,2,3} PONVORY™ offers MS patients superior efficacy in reducing annualized relapse rates compared to an established oral therapy and a proven safety profile backed by over a decade of cumulative clinical research.^{3,4,5}

The FDA approval is based, in part, on a two-year, head-to-head Phase 3 clinical trial in which PONVORY™ 20 mg demonstrated superior efficacy in significantly reducing annual relapses by 30.5% compared to teriflunomide (Aubagio®) 14 mg in patients with relapsing MS.³ Over the study period, 71% of patients treated with PONVORY™ had no confirmed relapses, compared to 61% in the teriflunomide group.³ PONVORY™ was also superior to teriflunomide in reducing the number of new gadolinium-enhancing (GdE) T1 lesions and the number of new or enlarging T2 lesions by 59% and 56%, respectively.³ GdE T1 lesions and T2 lesions are identified using magnetic resonance imaging (MRI) technology and are recognized as classic measures of MS pathology that can provide insights into disease activity and disease burden, respectively.^{6,7}

Click-to-Tweet: #BREAKINGNEWS: @US_FDA approves a new #multiplesclerosis treatment from @JanssenUS proven to help reduce relapses and brain lesions, and backed by over a decade of clinical research. Learn more: <http://bit.ly/3vEIS74>

PONVORY™ also prevented disability from worsening for most people. Nine in 10 PONVORY™-treated patients did not have worsening of 3-month disability, and PONVORY™ showed a numerical benefit in delaying disability progression. The difference in rates of disability progression was not statistically significant between the PONVORY™ and teriflunomide groups.³

"MS is a complex disease, and any individual's response to MS disease-modifying therapy can vary," said Dr. Bruce Bebo, Executive Vice President of Research at the National MS Society. "It's so important that people living with MS have access to effective treatment options. We are pleased that there is a new therapy approved for relapsing MS."

If treatment needs to be stopped, PONVORY™ leaves the blood within one week, with effects on the immune system wearing off in one to two weeks for most patients.³ This may offer additional flexibility in treatment management if patients need to receive vaccines, address potential infections, or begin family planning. PONVORY™ has no known food restrictions and requires no genetic testing or first-dose monitoring for most patients.³

"In the pivotal study, ponesimod demonstrated superior clinical efficacy in reducing annual relapses and MRI activity compared against teriflunomide, another oral MS therapy. Those results, combined with a favorable side effect profile, make ponesimod a useful treatment option for people with relapsing MS," said Robert J. Fox, M.D., Staff Neurologist, Mellen Center for MS Treatment and Research, Vice-Chair for Research, Neurological Institute, Cleveland Clinic. Dr. Fox has served as a paid consultant to Actelion Pharmaceuticals Ltd and Janssen as a member of the ponesimod Advisory Board.

PONVORY™ has a proven safety profile and was generally well-tolerated over multiple clinical studies totaling more than 10 years, with overall adverse event rates similar to placebo in the Phase 2 and teriflunomide in the Phase 3 trials.^{3,4,5,8} The most common adverse events observed in the Phase 3 trial in PONVORY™-treated patients were upper respiratory infection, hepatic transaminase elevation (abnormal liver tests) and hypertension (high blood pressure).⁸

"Every person with multiple sclerosis is affected differently, given variability in both the underlying disease and emerging symptoms. Continued innovation in this space is critical, and we're committed to meeting patients' evolving healthcare needs," said Mathai Mammen, M.D., Ph.D., Global Head, Janssen Research & Development, Johnson & Johnson. "We are proud to offer PONVORY as a valuable new option for people with MS that may help them gain better control of their disease."

Janssen CarePath offers a comprehensive support program that helps patients get started on PONVORY™ and stay on track. Janssen CarePath provides information on insurance coverage, potential out-of-pocket costs and treatment support, and identifies options that may help make treatment more affordable, including the Janssen CarePath Savings Program for commercially insured patients who are eligible. For patients who are prescribed PONVORY™, the Wellness Companion Program by Janssen CarePath provides patients with one-on-one education to help them get started and continue treatment.

About the Phase 3 Study⁸

The Oral Ponesimod Versus Teriflunomide In Relapsing Multiple Sclerosis (OPTIMUM) trial was a head-to-head, prospective, multicenter, randomized, double-blind Phase 3 study comparing efficacy, safety and tolerability of PONVORY™ 20 mg versus teriflunomide 14 mg in adults with relapsing MS. The primary endpoint of the study, which included 1,133 participants, was the annualized relapse rate (ARR) from baseline through the study period. The study included several other important efficacy endpoints, including the number of new Gd-enhancing T1 lesions from baseline to Week 108, the number of new or enlarging T2 lesions from baseline to Week 108, and the time to 3-month and 6-month confirmed disability progression.

About Multiple Sclerosis (MS)

MS is a chronic autoimmune inflammatory disease of the central nervous system (CNS) in which immune cells attack myelin (the protective casing that insulates nerve cells), damaging or destroying it and causing inflammation.⁹ This affects how the CNS processes information and communicates with the rest of the body, causing the neurologic signs and symptoms of MS.¹⁰ Symptoms vary by person, but common symptoms include fatigue, balance and walking problems, numbness or tingling, dizziness and vertigo, vision problems, bladder and bowel problems and weakness.^{11,12,13}

About PONVORY™

PONVORY™ (ponesimod) is a daily oral selective sphingosine-1-phosphate receptor 1 (S1P1) modulator, indicated to treat adults with relapsing forms of multiple sclerosis (MS), to include clinically isolated

syndrome, relapsing-remitting disease and active secondary progressive disease.^{1,2,3} PONVORY™ is believed to work by keeping immune cells called lymphocytes out of the blood by trapping them in the lymph nodes.³ The way PONVORY™ exerts therapeutic effects in MS is unknown, but may help keep the lymphocytes out of the central nervous system, where they could cause damage.³

PONVORY™ does not require genetic testing or first-dose cardiac monitoring for most patients. Because initiation of PONVORY™ treatment results in a decrease in heart rate, first-dose monitoring is recommended in patients with certain preexisting cardiac conditions.³

It is not known if PONVORY™ is safe and effective in children.

Janssen submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for ponesimod for treatment of adults with relapsing multiple sclerosis in Q1 2020, which is currently under review.

A member of the Janssen Pharmaceutical Companies of Johnson & Johnson, Actelion Pharmaceuticals Ltd is party to a revenue sharing agreement with Idorsia Pharmaceuticals Ltd, which provides for certain payments to Idorsia related to the sales of ponesimod.

About the Wellness Companion Program

The Wellness Companion Program is limited to education for patients about their Janssen therapy, its administration and/or their disease. It is intended to supplement a patient's understanding of their therapy. It does not provide medical advice, health coaching or improved wellness as a result of engaging with the program, replace a treatment plan from the patient's doctor or nurse, provide case management services, or serve as a reason to prescribe.

**Aubagio® (teriflunomide) is a registered trademark of Sanofi Genzyme.*

IMPORTANT SAFETY INFORMATION

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT PONVORY™?

PONVORY™ may cause serious side effects, including:

· **Infections** - PONVORY™ can increase your risk of serious infections that can be life-threatening and cause death. PONVORY™ lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 1 to 2 weeks of stopping treatment. Your healthcare provider should review a recent blood test of your white blood cells before you start taking PONVORY™. Call your healthcare provider right away if you have any of these symptoms of an infection during treatment and for 1 to 2 weeks after your last dose of PONVORY™:

- fever
- tiredness
- body aches
- chills
- nausea
- vomiting
- headache with fever, neck stiffness, sensitivity to light, nausea, or confusion (these may be symptoms of meningitis, an infection of the lining around your brain and spine)

Your healthcare provider may delay starting or may stop your PONVORY™ treatment if you have an infection.

· **Slow heart rate (bradycardia or bradyarrhythmia) when you start taking PONVORY™.**

PONVORY™ can cause your heart rate to slow down, 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.

Only Start your treatment with PONVORY™ using the Starter Pack. You must use the PONVORY™ Starter Pack by slowly increasing the dose over a 14-day period to help reduce the effect of slowing of your heart rate. It is important to follow the recommended dosing instructions.

Call your healthcare provider if you experience the following symptoms of slow heart rate:

- dizziness
- lightheadedness
- feeling like your heart is beating slowly or skipping beats
- shortness of breath
- confusion
- chest pain
- tiredness

Do not take PONVORY™ if you:

- have had a heart attack, chest pain called unstable angina, stroke or mini-stroke (transient ischemic attack or TIA), or certain types of heart failure in the last 6 months.
- have certain types of heart block or irregular or abnormal heartbeat (arrhythmia) unless you have a pacemaker.

Talk to your healthcare provider if you have any of these conditions, or do not know if you have any of these conditions.

Before you take PONVORY™, tell your healthcare provider about all your medical conditions, including if you:

- have a fever or infection, or you are unable to fight infections due to a disease or taking medicines that lower your immune system.
- have had chicken pox or have received the vaccine for chicken pox. Your healthcare provider may do a blood test for chicken pox virus. You may need to get the full course of vaccine for chicken pox and then wait 1 month before you start taking PONVORY™.
- have slow heart rate.
- have an irregular or abnormal heartbeat (arrhythmia).

- have a history of stroke.
- have heart problems, including a heart attack or chest pain.
- have high blood pressure.
- have breathing problems, including during your sleep (sleep apnea).
- have liver problems.
- had or now have a type of skin cancer called basal cell carcinoma (BCC), melanoma, or squamous cell carcinoma
- have eye problems, especially an inflammation of the eye called uveitis.
- have diabetes.
- are pregnant or plan to become pregnant. PONVORY™ may harm your unborn baby. Talk with your healthcare provider if you are pregnant or plan to become pregnant. If you are a woman who can become pregnant, you should use effective birth control during your treatment with PONVORY™ and for 1 week after you stop taking PONVORY™. Talk to your healthcare provider about what method of birth control is right for you during this time. Tell your healthcare provider right away if you do become pregnant while taking PONVORY™ or within 1 week after you stop taking PONVORY™.
- are breastfeeding or plan to breastfeed. It is not known if PONVORY™ passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take PONVORY™.

Tell your healthcare provider about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.

Using PONVORY™ and other medicines together may affect each other causing serious side effects. Especially tell your healthcare provider if you take or have taken: Medicines to control your heart rhythm (antiarrhythmics), or blood pressure (antihypertensives), or heart-beat (such as calcium channel blockers or beta-blockers); medicines that affect your immune system, such as alemtuzumab; and medicines such as rifampin, phenytoin, or carbamazepine.

You should not receive **live** vaccines during treatment with PONVORY™, for at least 1 month before taking PONVORY™, and for 1 to 2 weeks after you stop taking PONVORY™. If you receive a live vaccine, you may get the infection the vaccine was meant to prevent. Vaccines may not work as well when given during treatment with PONVORY™.

Talk with your healthcare provider if you are not sure if you take any of these medicines.

HOW SHOULD I TAKE PONVORY™?

- Take PONVORY™ exactly as your healthcare provider tells you to take it.
- Take PONVORY™ 1 time each day.
- Swallow PONVORY™ tablets whole.
- Take PONVORY™ with or without food.
- Do not stop taking PONVORY™ without talking with your healthcare provider first.
- Do not skip a dose.
- Start taking PONVORY™ with a 14-day starter pack.
- If you miss taking 1, 2, or 3 tablets in a row of PONVORY™ in the 14-day starter pack, continue treatment by taking the first dose you missed. Take 1 tablet as soon as you remember. Then, take 1 tablet a day to continue with the starter pack dose as planned.
- If you miss taking 1, 2, or 3 tablets in a row of PONVORY™ while taking the 20 mg maintenance dose, continue treatment with the 20 mg maintenance dose.
- If you miss taking 4 or more tablets in a row of PONVORY™, while taking the 14-day starter pack or the 20 mg maintenance dose, you need to restart treatment with a new 14-day starter pack. Call your healthcare provider if you miss 4 or more doses of PONVORY™. Do not restart PONVORY™ after stopping it for 4 or more days in a row without talking to your healthcare provider. If you have certain heart conditions, you may need to be monitored by your healthcare provider for at least 4 hours when you take your next dose.

What are the possible side effects of PONVORY™?

PONVORY™ may cause serious side effects, including:

- **breathing problems.** Some people who take PONVORY™ have shortness of breath. Call your healthcare provider right away if you have new or worsening breathing problems.
- **liver problems.** PONVORY™ may cause liver problems. Your healthcare provider should do blood tests to check your liver before you start taking PONVORY™. Call your healthcare provider right away if you have any of the following symptoms of liver problems:
 - unexplained nausea
 - vomiting
 - stomach (abdominal) pain
 - tiredness
 - loss of appetite
 - yellowing of the whites of your eyes or skin
 - dark urine
- **increased blood pressure.** Your healthcare provider should check your blood pressure during treatment.
- **types of skin cancer called basal cell carcinoma (BCC), melanoma, and squamous cell carcinoma.** Certain types of skin cancer have happened with drugs in the same class. Tell your healthcare provider if you have any changes in the appearance of your skin, including changes in a mole, a new darkened area on your skin, a sore that does not heal, or growths on your skin, such as a bump that may

be shiny, pearly white, skin-colored, or pink. Your doctor should check your skin for any changes during treatment with PONVORY™. Limit the amount of time you spend in sunlight and ultraviolet (UV) light. Wear protective clothing and use a sunscreen with a high sun protection factor.

· **a problem with your vision called macular edema.** Tell your healthcare provider about any changes in your vision. Your healthcare provider should test your vision before you start taking PONVORY™ and any time you notice vision changes during treatment with PONVORY™. Your risk of macular edema is higher if you have diabetes or have had an inflammation of your eye called uveitis.

Call your healthcare provider right away if you have any of the following symptoms:

- 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

· **swelling and narrowing of the blood vessels in your brain.** A condition called Posterior Reversible Encephalopathy Syndrome (PRES) has happened with drugs in the same class. Symptoms of PRES usually get better when you stop taking PONVORY™. However, if left untreated, it may lead to a stroke. Call your healthcare provider right away if you have any of the following symptoms:

- sudden severe headache
- sudden confusion
- sudden loss of vision or other changes in vision
- seizure

· **severe worsening of multiple sclerosis (MS) after stopping PONVORY™.**

When PONVORY™ is stopped, symptoms of MS may return and become worse compared to before or during treatment. Always talk to your healthcare provider before you stop taking PONVORY™ for any reason. Tell your healthcare provider if you have worsening symptoms of MS after stopping PONVORY™.

The most common side effects of PONVORY™ include:

- upper respiratory tract infections
- elevated liver enzymes (abnormal liver tests)
- high blood pressure (hypertension)

These are not all the possible side effects of PONVORY™. For more information, ask your healthcare provider or pharmacist. See "What is the most important information I should know about PONVORY™?"

Tell your doctor if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You are also encouraged to report side effects to the FDA: visit <http://www.fda.gov/medwatch> or call 1-800-FDA-1088. You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).

Please see full [Prescribing Information](#) and [Medication Guide](#).

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About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at [www.twitter.com/JanssenUS](https://twitter.com/JanssenUS). Janssen Pharmaceuticals, Inc. is one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding ponesimod. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Actelion Pharmaceuticals Ltd, Janssen Pharmaceuticals, Inc., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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