Ponvory (ponesimod)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Ponvory
- **Generic name:** Ponesimod
- **Pharmacologic class:** Sphingosine 1-phosphate receptor modulator
- **Strength and Formulation:** 2mg, 3mg, 4mg, 5mg, 6mg, 7mg, 8mg, 9mg, 10mg, 20mg; tablets.
- **Manufacturer:** Janssen Pharmaceuticals, Inc.
- **How supplied:** Starter Pack (2mg, 3mg, 4mg, 5mg, 6mg, 7mg, 8mg, 9mg, 10mg)—14; Bottle (20mg)—30
- **Legal Classification:** Rx

Indication

- Treatment of relapsing forms of **multiple sclerosis (MS)**, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

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Dosage and Administration

- **Prior to initiation**
  - Obtain recent (eg, within the last 6 months or after discontinuation of prior MS therapy) CBC, including lymphocyte count.
  - Obtain an electrocardiogram; if preexisting conduction abnormalities are present, refer to cardiologist and first-dose monitoring is recommended.
  - Obtain recent (eg, within the last 6 months) transaminase and bilirubin levels.
  - Obtain an ophthalmic evaluation of the fundus, including the macula.
  - Test for antibodies to varicella zoster virus (VZV); if negative, VZV vaccination is recommended at least 1 month prior to initiating Ponvory.

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Dosage and Administration

- Swallow whole.
- **Titration** using the 14-day starter pack is required for treatment initiation.
- Initially 2mg once daily on days 1 and 2; 3mg once daily on days 3 and 4; 4mg once daily on days 5 and 6; 5mg once daily on day 7; 6mg once daily on day 8; 7mg once daily on day 9; 8mg once daily on day 10; 9mg once daily on day 11; 10mg once daily on days 12, 13, and 14.
- **Maintenance**: 20mg once daily on day 15 and thereafter.

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Dosage and Administration

- **First-dose 4-hour monitoring** is recommended for patients with sinus bradycardia, first- or second-degree [Mobitz type I] AV block, or a history of MI or heart failure occurring more than 6 months prior to treatment initiation and in stable condition: see full labeling.
- If **4 or more consecutive doses are missed** during titration or maintenance, treatment should be reinitiated with day 1 of the titration regimen (new starter pack).
- If **fewer than 4 consecutive doses are missed**
  - During titration: may resume treatment with first missed titration dose and resume titration schedule.
  - During maintenance: resume treatment with maintenance dosage.

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Considerations for Specific Populations

- **Pregnancy:** No adequate and well-controlled studies in pregnant women; may cause fetal harm based on animal studies.
- **Nursing mothers:** No data on the presence of Ponvory in human milk, effects on breastfed infant, or effects on milk production; consider benefits of breastfeeding with potential adverse effects on infant.
- **Pediatric**: Not established.
- **Geriatrics**: Clinical studies did not include sufficient numbers to determine difference from younger patients; use caution.
- **Hepatic impairment**: Not recommended in patients with moderate or severe hepatic impairment (Child-Pugh class B and C, respectively).

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Contraindications

- Recent (within the last 6 months) occurrence of MI, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III or IV heart failure.
- Presence of Mobitz Type II 2nd- or 3rd degree AV block, sick sinus syndrome, or sino-atrial block, unless paced.

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Warnings and Precautions

- Increased risk of **infections** (may be fatal).
- Obtain recent CBC including lymphocyte count prior to initiation.
- Consider treatment interruption if serious infection develops.
- Delay treatment in patients with active infection until resolution.
- Withhold if progressive multifocal leukoencephalopathy (PML) is suspected; discontinue if PML is confirmed.
- Test for antibodies to VZV; if negative, VZV vaccination is recommended at least 1 month prior to initiation.

Warnings and Precautions

- Risk of bradyarrhythmia, AV conduction delays: titration is required for treatment initiation.
- Not recommended for use in patients with a history of cardiac arrest, cerebrovascular disease, uncontrolled hypertension, or severe untreated sleep apnea; refer to cardiologist if treatment is considered.
- Perform an overall benefit/risk assessment in patients with a history of recurrent syncope or symptomatic bradycardia; refer to cardiologist if treatment is considered.
- Monitor BP during treatment.

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Warnings and Precautions

- Use caution in patients with severe respiratory disease (eg, pulmonary fibrosis, asthma, COPD): perform spirometric evaluation during treatment if clinically indicated.
- Monitor for hepatic dysfunction; discontinue if significant liver injury is confirmed.
- Periodic skin exams are recommended esp. those with risk factors for skin cancer; monitor for suspicious skin lesions and evaluate promptly if observed.
- Advise to limit exposure to sunlight and UV light.
- Concomitant phototherapy with UV-B radiation or PUVA-photochemotherapy: not recommended.

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Warnings and Precautions

- Advise females of reproductive potential to use effective contraception during and for 1 week after stopping Ponvory treatment.
- Perform ophthalmic evaluation of the fundus, including the macula, prior to initiation, and if any change in vision occurs during therapy.
- Increased risk of macular edema in patients with a history of uveitis and diabetes mellitus.
- Discontinue if posterior reversible encephalopathy syndrome is suspected.
- Monitor for severe increase in disability after treatment discontinuation.

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Interactions

- Concomitant antineoplastic, immunosuppressant or immune-modulating therapies may increase risk of immunosuppression; use caution when switching from long-acting immunotherapies; caution for 1–2 weeks after discontinuing Ponvory.
- Initiation after treatment with alemtuzumab: not recommended.
- Concomitant QT prolonging drugs (eg, quinidine, procainamide, amiodarone, sotalol): risk of torsades de pointes; refer to cardiologist if treatment is considered.

Interactions

- Concomitant β-blockers, digoxin, diltiazem, verapamil during initiation may be associated with severe bradycardia or heart block; refer to cardiologist if treatment is considered.
- Avoid live attenuated vaccines during and for 1-2 weeks after discontinuing Ponvory; may have suboptimal response.
- Antagonized by strong CYP3A4 and UGT1A1 inducers (eg, rifampin, phenytoin, carbamazepine): concomitant use not recommended.

Adverse Reactions

- **Most common (≥10%)**: Upper respiratory tract infection, hepatic transaminase elevation, hypertension.
- **Others**: UTI, dyspnea, dizziness, cough, macular edema, basal cell carcinoma/melanoma, decreased pulmonary function.
- **Rare**: Posterior reversible encephalopathy syndrome.

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Mechanism of Action

- The mechanism by which **ponesimod** exerts therapeutic effects in multiple sclerosis is unknown, but may involve reduction of lymphocyte migration into the central nervous system.
- Ponesimod is a sphingosine 1-phosphate (S1P) receptor 1 modulator that binds with high affinity to S1P receptor 1.
- Ponesimod blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood.

Clinical Trials

- Approval was based on a randomized, double-blind, parallel group, active-controlled superiority phase 3 trial that compared the efficacy and safety of Ponvory to teriflunomide in 1133 patients with relapsing MS.
- Patients were randomly assigned 1:1 to receive either Ponvory 20mg once daily (n=567), beginning with a 14-day dose titration, or teriflunomide 14mg once daily (n=566) for 108 weeks.
- The **primary endpoint** was the annualized relapse rate (ARR) over 108 weeks.

Clinical Trials

- The ARR was statistically significantly lower in patients treated with Ponvory compared with teriflunomide (0.202 vs 0.290, respectively; relative reduction, 30.5%; *P* =.0003).
- The number of new or enlarging T2 hyperintense lesions per year was significantly lower in patients treated with Ponvory compared with teriflunomide (1.40 vs 3.16, respectively; relative reduction, 55.7%; *P* <.0001).
- The number of Gd-enhancing T1 lesions per MRI was also significantly lower in patients treated with Ponvory compared with teriflunomide (0.18 vs 0.43, respectively; relative reduction, 58.5%; *P* <.0001).

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/ponvory/