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| **Section:** | Prescription Drugs | **Effective Date:** | January 1, 2025 |
| **Subsection:** | Central Nervous System Drugs | **Original Policy Date:** | April 30, 2021 |
| **Subject:** | Ponvory | **Page:** | 1 of 8 |

***Last Review Date:*** December 13, 2024

# Ponvory

## Description

## Ponvory (ponesimod)

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

**Regulatory Status**
FDA-approved 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 (1).

Before initiating treatment with Ponvory, the following should be assessed: (1)

- a recent (i.e., within the last 6 months or after discontinuation of prior MS therapy) complete blood count (CBC), including lymphocyte count
- electrocardiogram (ECG) to determine whether preexisting conduction abnormalities are present
- recent (i.e., within the last 6 months) transaminase and bilirubin levels
- evaluation of the fundus, including the macula

- if patients are taking anti-neoplastic, immunosuppressive, or immune-modulating therapies, or if there is a history of prior use of these drugs, consider possible unintended additive immunosuppressive effects before initiating treatment with Ponvory
- test patients for antibodies to varicella zoster virus (VZV) before initiating Ponvory; VZV vaccination of antibody-negative patients is recommended prior to commencing treatment with Ponvory. If live attenuated vaccine immunizations are required, administer at least 1 month prior to initiation of Ponvory

Before initiation of Ponvory treatment results in a decrease in heart rate (HR), first-dose 4-hour monitoring is recommended for patients with sinus bradycardia [HR less than 55 beats per minute (bpm)], first- or second-degree AV block, or a history of myocardial infarction or heart failure occurring more than 6 months prior to treatment initiation and in stable condition. The first dose of Ponvory should be administered in a setting where resources to appropriately manage symptomatic bradycardia are available. Patients should be monitored for 4 hours after the first dose for signs and symptoms of bradycardia with a minimum of hourly pulse and blood pressure measurements. An ECG should be obtained in these patients prior to dosing and at the end of the 4-hour observation period (1).

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/IV heart failure (1).

Ponvory is also contraindicated in patients with Mobitz Type II 2nd degree or 3rd degree AV block, or sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker (1).

If 4 or more consecutive daily doses are missed during treatment initiation or maintenance treatment, reinitiate Day 1 of the dose titration (new starter pack) and follow first-dose monitoring recommendations (1).

Live, attenuated vaccines are generally not recommended for a person with MS because their ability to cause disease has been weakened but not totally inactivated (2).

Based on animal studies, Ponvory may cause fetal harm. Female patients of reproductive potential should be advised to use effective contraception during treatment and for 1 week after stopping Ponvory (1).

Safety and effectiveness of Ponvory in pediatric patients less than 18 years of age have not been established (1).

**Related policies**
Acthar Gel, Ampyra, Aubagio, Gilenya, Kesimpta, Lemtrada, Mavenclad, Mayzent, MS Injectables, Ocrevus, Tecfidera, Tysabri, Zeposia

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Ponvory may be considered **medically necessary** if the conditions indicated below are met.

Ponvory may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 18 years of age or older

**Diagnosis**

Patient must have the following:

Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

**AND ALL** of the following:

1. Baseline evaluations of **ALL** of the following have been done or will be done prior to starting therapy with Ponvory:
   a. Complete blood count (CBC), including lymphocyte count
   b. Electrocardiogram (ECG)
   c. Liver function tests (LFTs)
2. Heart rate ≥ 50 bpm
3. Patients with sinus bradycardia (heart rate <55 bpm), first- or second-degree (Mobitz type I) AV block, or a history of myocardial infarction or heart failure occurring more than 6 months prior to treatment initiation and in stable

condition **ONLY**: will be observed for 4 hours after the first dose for signs and symptoms of bradycardia with hourly pulse and blood pressure measurements and an ECG prior to dosing and at the end of the observation period

4. Patients with a history of uveitis and/or diabetes **ONLY**: will have an ophthalmic evaluation of the fundus, including the macula, prior to initiation of therapy
5. Female patients of reproductive potential **ONLY**: will be advised to use effective contraception during treatment with Ponvory and for 1 week after the last dose
6. **NO** history (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure
7. **NO** presence of Mobitz Type II 2nd degree or 3rd degree AV block, sick sinus syndrome, or sino-atrial block, unless patient has a pacemaker
8. **NO** significant QTc prolongation (QTcF >450 msec in males, >470 msec in females)
9. **NO** severe untreated sleep apnea
10. **NO** concurrent use with other MS disease modifying agents
11. **NOT** given concurrently with live vaccines
12. Patient **MUST** have tried **TWO** of the preferred MS medications (see Appendix 1) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

## Prior – Approval *Renewal* Requirements

**Age** 18 years of age or older

**Diagnosis**

Patient must have the following:

Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

**AND ALL** of the following:

1. Heart rate ≥ 50 bpm

2. Female patients of reproductive potential **ONLY**: will be advised to use effective contraception during treatment with Ponvory and for 1 week after the last dose
3. **NO** history (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure.
4. **NO** presence of Mobitz Type II 2nd degree or 3rd degree AV block, sick sinus syndrome, or sino-atrial block, unless patient has a pacemaker
5. **NO** significant QTc prolongation (QTcF >450 msec in males, >470 msec in females)
6. **NO** severe untreated sleep apnea
7. **NO** concurrent use with other MS disease modifying agents
8. **NOT** given concurrently with live vaccines
9. Patient **MUST** have tried **TWO** of the preferred MS medications (see Appendix 1) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Quantity** 1 fourteen-day starter pack (14 tablet titration pack)
**AND**
90 tablets per 90 days

**Duration** 12 months

### Prior – Approval *Renewal* Limits

**Quantity** 90 tablets per 90 days

**Duration** 12 months

## Rationale

**Summary**
Ponvory (ponesimod) is a sphingosine 1-phosphate (S1P) receptor 1 modulator that binds with high affinity to S1P receptor 1. Ponvory blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which Ponvory exerts therapeutic effects in multiple sclerosis is unknown but may involve reduction of lymphocyte migration into the central nervous system. Ponvory is contraindicated in patients who in the last 6 months experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure or Class III/IV heart failure. Ponvory is also contraindicated in patients with Mobitz Type II 2nd degree or 3rd degree AV block. Ponvory may cause fetal harm, and female patients of reproductive potential should be advised to use effective contraception during treatment and for 1 week after the last dose. Safety and effectiveness of Ponvory in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Ponvory while maintaining optimal therapeutic outcomes.

**References**

1. Ponvory [package insert. Titusville, NJ: Janssen Pharmaceuticals, Inc.; June 2024.
2. Cahill JF, Izzo A, Garg N. Immunization in patients with multiple sclerosis. Neurological Bulletin. 2010;2(1):17-21.

## Policy History

| Date | Action |
|---|---|
| April 2021 | Addition to PA |
| June 2021 | Annual review |
| September 2022 | Annual review and reference update |
| December 2022 | Annual review. |
| January 2023 | Per FEP, revised Medex requirement to t/f two preferred MS medications |
| March 2023 | Annual review and reference update |
| June 2023 | Annual review |
| December 2023 | Annual review and reference update |
| September 2024 | Annual review |
| December 2024 | Annual review and reference update |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.**

## Appendix 1 - List of Preferred Multiple Sclerosis (MS) Medications

| Medication Name | Route of Administration |
|---|---|
| dimethyl fumarate (generic Tecfidera) | Oral** |
| fingolimod (generic Gilenya) | Oral** |
| Mayzent | Oral** |
| teriflunomide (generic Aubagio) | Oral** |
| Zeposia | Oral** |

****** indicates separate criteria will need to be met

| Medication Name | Route of Administration |
|---|---|
| Avonex | Injectable |
| Betaseron | Injectable |
| glatiramer acetate (generic Copaxone) | Injectable |
| Glatopa | Injectable |
| Plegridy | Injectable |
| Rebif | Injectable |