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

Last Review Date: March 7, 2025

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. Washington, DC: Vanda Pharmaceuticals, Inc.; October 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

March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 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