Oscar Clinical Guideline: Ponvory (ponesimod) (PG230, Ver. 3)

Ponvory (ponesimod)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. It typically presents in young adults (generally diagnosed before 50 years of age) with symptoms such as vision problems, muscle weakness, numbness, and difficulty with balance and coordination. The most common form is relapsing-remitting MS (occurring in about 85% of patients), characterized by acute attacks followed by periods of remission. Treatment goals include reducing relapses, slowing disability

progression, and managing symptoms. Disease-modifying therapies are the primary treatment approach and include injectable medications (e.g., interferons, glatiramer acetate), oral medications (e.g., dimethyl fumarate, fingolimod, teriflunomide, etc.), and infusion therapies (e.g., natalizumab, ocrelizumab).

MS is a progressive disease, meaning that symptoms tend to worsen over time, and it can be classified into several types, including relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).

Currently, there is no cure for MS, but various treatment options are available to manage symptoms, slow the progression of the disease, and improve quality of life.

- Disease-modifying therapies (DMTs) are a class of medications that target the immune system to reduce inflammation and slow down the progression of the disease. The type of DMT prescribed will depend on the type and severity of MS, as well as the individual's medical history and preferences. Some common DMTs include interferon beta, glatiramer acetate, dimethyl fumarate, and fingolimod.
- High dose corticosteroids, such as high dose intravenous methylprednisolone or oral prednisone can be prescribed to reduce inflammation during acute MS relapses.
- Symptomatic treatments are also available to manage specific symptoms of MS, such as muscle spasms, bladder problems, and depression. Physical therapy, occupational therapy, and speech therapy can help individuals with MS maintain mobility, independence, and communication skills.

Ponvory (ponesimod) is a disease-modifying therapy approved for treating relapsing forms of multiple sclerosis (MS) in adults, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. It selectively binds to the sphingosine 1-phosphate (S1P) receptor, preventing lymphocytes from leaving lymph nodes and reducing circulating lymphocytes. Ponesimod has demonstrated superiority to teriflunomide (Aubagio) in reducing annualized relapse rates and MRI lesions in clinical trials. It requires dose titration to mitigate initial heart rate effects and is generally used after inadequate response to or intolerance of other MS therapies due to its safety profile. It is recommended that those with sinus bradycardia (heart rate less than 55 beats per minute), first- or second-degree [Mobitz type I] atrioventricular (AV) block, or a history of myocardial infarction or heart failure occurring more than 6 months prior to treatment initiation and in stable condition, be monitored for at least the first 4 hours after the initial dose of Ponvory (ponesimod) because it can lower heart rate. In those prescribed Ponvory (ponesimod), anti-neoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies should be co-administered with caution due to the additive immunosuppressive effects. Ponvory (ponesimod) may also increase the risk of pulmonary function decline, liver injury, increased blood pressure, and macular edema. Those who are pregnant or of childbearing potential should use effective contraception during and for one (1) week after stopping Ponvory (ponesimod).

Definitions

"Clinically isolated syndrome" refers to a first episode of neurologic symptoms lasting at least 24 hours caused by inflammation or demyelination in the central nervous system.

"Compendia" are summaries of drug information and medical evidence to support decision-making about the appropriate use of drugs and medical procedures. Examples include, but are not limited to:

1. American Hospital Formulary Service Drug Information
2. Clinical pharmacology
3. National Comprehensive Cancer Network Drugs and Biologics Compendium
4. Thomson Micromedex DrugDex
5. United States Pharmacopeia-National Formulary (USP-NF)

"Disease-modifying therapy" is a medication that modifies the course of MS by reducing relapses and slowing disability progression.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"MRI" or "Magnetic Resonance Imaging" refers to a medical imaging technique that creates detailed three-dimensional (3D) images of the organs and tissues in your body. A brain MRI can reveal areas of active MS disease called lesions within the central nervous system.

"Multiple sclerosis" is a chronic autoimmune disease of the central nervous system characterized by inflammation, demyelination, and neurodegeneration.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"Primary progressive MS" refers to worsening neurologic function from the onset of symptoms, without early relapses or remissions.

"Relapse" is defined as the appearance of new symptoms or the worsening of existing symptoms lasting at least 24 hours in the absence of fever or infection.

"Relapsing-remitting MS" refers to a disease course characterized by clearly defined attacks of new or increasing neurologic symptoms followed by periods of partial or complete recovery.

"[s]" indicates state mandates may apply.

"Secondary progressive MS" is a disease course following relapsing-remitting MS that is characterized by a progressive worsening of neurologic function over time with or without relapses.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Multiple Sclerosis

The Plan considers Ponvory (ponesimod) medically necessary when recent (within the last 3 months) clinical chart documentation provided indicates the member meets ALL of the following:

1. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of multiple sclerosis; *AND*
2. Is 18 years of age or older; *AND*
3. Has ONE (1) of the following forms of multiple sclerosis:
    a. Relapsing-remitting (RRMS)*; or*
    b. Active secondary progressive disease (SPMS)*; or*
    c. Clinically isolated syndrome (CIS); *AND*
4. The member Is unable to use, or has tried and failedTWO (2) of the following:[s]
    a. An interferon beta product (e.g., Avonex, Betaseron, Plegridy, or Rebif)*; and/or*
    b. Dimethyl Fumarate (generic Tecfidera)*; and/or*
    c. Fingolimod (generic Gilenya)*; and/or*
    d. Glatiramer acetate (Copaxone)*; and/or*
    e. Teriflunomide (generic Aubagio); *AND*
5. The member meets ALL of the following criteria:
    a. No evidence of recent (within the last 6 months) myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), or decompensated heart failure requiring hospitalization*; and/or*
    b. No evidence of Class III or IV heart failure*; and/or*
    c. No evidence of Mobitz type II second-degree, third-degree AV block, sick sinus syndrome, or sino-atrial block, unless the member has a functioning pacemaker; *AND*
6. Ponvory (ponesimod) will be used as monotherapy for multiple sclerosis (i.e., member is not using and will not use other disease-modifying MS therapies while on Ponvory [ponesimod]); *AND*
7. Ponvory (ponesimod) is being prescribed t a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.

- *Initial titration: Use the 14-day starter pack, titrating from 2 mg to 20 mg over 14 days*
    - *i. Initial fill: One 14-day starter pack*
    - *ii. Those with sinus bradycardia (heart rate less than 55 beats per minute), 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, should be monitored for at least the first 4 hours after the initial dose of Ponvory (ponesimod) in a health care setting.*
        1. *Monitoring should include at least hourly pulse and blood pressure measurements and an ECG should be obtained prior to initiation and at the end of the 4-hour observation period. Additional monitoring may be required, and consultation with a cardiologist may be required at the discretion of the treating provider.*
- *Maintenance: 20 mg orally once daily*
    - *i. Maintenance: 30 tablets per 30 days*

If the above prior authorization criteria are met, the requested medication will be authorized for up to 12-months.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Multiple Sclerosis

The Plan considers Ponvory (ponesimod) medically necessary when recent (within the last 6-months) clinical chart documentation provided indicates the member meets BOTH of the following:

1. The requested medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; *AND*
2. The member has experienced at least ONE (1) of the following:
    a. Improvement in at least ONE (1) objective measure, such as:
        i. Reduced disease activity on MRI*; and/or*
        ii. Improved or stable disability scores*; and/or*
        iii. Reduced relapse rate*; and/or*
        iv. Improved fatigue or walking assessments; *AND/OR*
    b. The member has shown stabilization or improvement in at least ONE (1) MS symptom, such as:
        i. Motor function*; and/or*
        ii. Fatigue*; and/or*
        iii. Vision*; and/or*

iv. Bowel/bladder function*; and/or*
v. Spasticity*; and/or*
vi. Walking/gait*; and/or*
vii. Pain/numbness/tingling.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[5]

Experimental or Investigational / Not Medically Necessary[5]

Ponvory (ponesimod) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, unproven, or not medically necessary. Non-covered indications include, but are not limited to, the following:

- Use for the treatment of non-relapsing forms of multiple sclerosis, such as primary progressive MS (PPMS). Current evidence and FDA approval are limited to relapsing forms of MS.
- Treatment of other autoimmune or inflammatory conditions not specifically approved by the FDA.
- Use in combination with other disease-modifying therapies for multiple sclerosis.
- Use in individuals under 18 years of age. There is not enough high quality evidence to support the safety and efficacy of Ponvory (ponesimod) in a pediatric population.
- Chronic graft versus host disease (GVHD). There are no high quality studies to support the safety and efficacy of Ponvory (ponesimod) for the management of chronic GVDH.

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