Oscar Clinical Guideline: Zeposia (ozanimod) (PG234, Ver. 4)

Zeposia (ozanimod)

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

Zeposia (ozanimod) is a sphingosine 1-phosphate (S1P) receptor modulator approved for the treatment of relapsing forms of multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease; and, moderately to severely active ulcerative colitis (UC) in adults. It works by reducing the migration of lymphocytes to sites of inflammation, potentially reducing disease activity in both conditions. In those prescribed Zeposia (ozanimod), anti-neoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies should co-administered with caution due to the additive immunosuppressive effects.

1. 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 (DMTs) 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).
2. Ulcerative Colitis (UC) is a chronic inflammatory bowel disease that affects the colon and rectum. It is characterized by periods of active disease and remission, with symptoms including bloody diarrhea, abdominal pain, and urgency. For UC, treatment goals include inducing and maintaining remission, with options ranging from anti-inflammatory drugs to biologics.

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.

"Severe obstructive sleep apnea" is defined as an Apnea-hypopnea index (AHI) greater than 30 events per hour.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

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

1. The member meets ALL of the following:

a. No evidence of experiencing myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure in the last 6 months*; and*
b. No evidence of a presence of Mobitz type II second-degree or third-degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial block, unless the member has a functioning pacemaker*; and*
c. No evidence of severe untreated sleep apnea*; and*
d. No evidence of concomitant use of a monoamine oxidase (MAO) inhibitor; *AND*

2. Zeposia (ozanimod) is being prescribed at 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. *The requested medication is being used within the Plan's Quantity Limit of; AND*
    - *The recommended maintenance dose is 0.92 mg orally once daily.*
        i. *30 capsules per 30 days for maintenance dose (0.92 mg capsules).*
    - *Dosage must be titrated over 7 days according to the following schedule:*
        ii. *Days 1-4: 0.23 mg once daily.*
        iii. *Days 5-7: 0.46 mg once daily.*
        iv. *Day 8 and thereafter: 0.92 mg once daily.*
3. The member meets ALL the criteria for the applicable indication listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Multiple Sclerosis

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

4. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of multiple sclerosis; *AND*
5. The member is 18 years of age or older; *AND*
6. The member 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).

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

Ulcerative Colitis

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

4. Prescribed by or in consultation with a gastroenterologist; *AND*
5. The member is 18 years of age or older; *AND*

6. Has a diagnosis of moderately to severely active ulcerative colitis.

If the above prior authorization criteria are met, the requested medication will be approved for up to 12-months.[5]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Multiple Sclerosis

The Plan considers Zeposia (ozanimod) medically necessary when recent (within the last 6-months) clinical chart documentation provided indicates the member meets ONE (1) of the following:

1. Improvement in at least ONE (1) objective measure, such as:
    a. Reduced disease activity on MRI*; and/or*
    b. Improved or stable disability scores*; and/or*
    c. Reduced relapse rate*; and/or*
    d. Improved fatigue or walking assessments; *AND/OR*
2. The member has shown stabilization or improvement in at least ONE (1) MS symptom, such as:
    a. Motor function*; and/or*
    b. Fatigue*; and/or*
    c. Vision*; and/or*
    d. Bowel/bladder function*; and/or*
    e. Spasticity*; and/or*
    f. Walking/gait*; and/or*
    g. Pain/numbness/tingling.

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

Ulcerative Colitis

The Plan considers Zeposia (ozanimod) medically necessary when recent (within the last 6-months) clinical chart documentation provided indicates the member meets ONE (1) of the following:

1. Improvement in at least ONE (1) objective measure, such as:
    a. Reduced inflammatory markers (e.g., fecal calprotectin, C-reactive protein)*; and/or*
    b. Improved appearance of mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE) or intestinal ultrasound;*; and/or*
    c. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo Score); *and/or*

   d. Reduced corticosteroid dose; *AND/OR*
2. Improvement in at least ONE (1) symptom, such as:
   a. Decreased pain*; and/or*
   b. Reduced fatigue*; and/or*
   c. Decreased stool frequency*; and/or*
   d. Reduced rectal bleeding; *and/or*
   e. Reduced urgency of defecation.

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]

Zeposia (ozanimod) 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 in combination with other disease-modifying therapies for MS or UC. The safety and efficacy of combining Zeposia with other DMTs or biologics have not been established.
- Treatment of mild UC or use as first-line therapy for UC before trial of conventional treatments. Current evidence and guidelines support its use in moderate to severe UC after failure of other therapies.
- Use for the treatment of non-relapsing forms of multiple sclerosis, such as primary progressive MS (PPMS). Treatment of other autoimmune or inflammatory conditions not specifically approved by the FDA. While Zeposia's mechanism of action may suggest potential benefits in other conditions, clinical evidence is currently insufficient to support its use outside of approved indications.
- Use individuals under the age of 18 for either MS or UC. The safety and efficacy in pediatric populations has not been established.
- Treatment of Alzheimer's disease. There are no studies to support the use of Zeposia (ozanimod) for the management of Alzheimer's disease.

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