Oscar Clinical Guideline: Zeposia (ozanimod) (PG234, Ver. 2)

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 MS and moderately to severely active UC in adults. It works by reducing the migration of lymphocytes to sites of inflammation, potentially reducing disease activity in both conditions.

1. Multiple Sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. It typically affects young adults and is characterized by episodes of neurological dysfunction that can lead to substantial disability over time. The most common form is relapsing-remitting MS (RRMS), which can progress to secondary progressive MS (SPMS). Treatment options for MS include disease-modifying therapies (DMTs) that aim to reduce relapse rates and slow disease progression.
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.

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

"**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.

"**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.

"**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

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 does **NOT** have **ANY** of the following:
    - 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***; or***

- 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***; or***
- severe untreated sleep apnea***; or***
- is taking a monoamine oxidase (MAO) inhibitor; ***AND***

2. Zeposia (ozanimod) will **NOT** be used concurrently with any anti-neoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies used for the treatment of MS and/or UC***; AND***
3. Zeposia (ozanimod) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature***; 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:*
        i. *Days 1-4: 0.23 mg once daily.*
        ii. *Days 5-7: 0.46 mg once daily.*
        iii. *Day 8 and thereafter: 0.92 mg once daily.*
4. The member meets **ALL** the criteria for the applicable indication listed below:

Medical Necessity Criteria for Initial Authorization

Multiple Sclerosis:

5. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of multiple sclerosis; ***AND***
6. Is 18 years of age or older; ***AND***
7. Has **ONE** of the following forms of multiple sclerosis:
    a. relapsing-remitting (RRMS)***; or***
    b. active secondary progressive disease (SPMS)***; or***
    c. clinically isolated syndrome (CIS).

Ulcerative Colitis:

5. Prescribed by or in consultation with a gastroenterologist; ***AND***
6. Is 18 years of age or older; ***AND***
7. Has a diagnosis of moderately to severely active ulcerative colitis; ***AND***
8. Is unable to use, or has tried and failed **BOTH** of the following:
    a. At least **ONE** of the following conventional therapies:
        i. Corticosteroids (e.g., prednisone, methylprednisolone)***; and/or***
        ii. 5-aminosalicylates (e.g., mesalamine, sulfasalazine)***; and/or***

iii. Immunosuppressants (e.g., azathioprine, 6-mercaptopurine)***; and***

b. At least **ONE** tumor necrosis factor (TNF) inhibitor (e.g., adalimumab, infliximab).

If the above prior authorization criteria are met, the requested medication will be approved for 12-months.

Medical Necessity Criteria for Reauthorization

Multiple Sclerosis:

Reauthorization for 12 months will be granted if the member has recent (within the last 6-months) clinical documentation showing at least **ONE** of the following:

1. Improvement in at least one 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. Stabilization or improvement in at least one 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.

Ulcerative Colitis:

Reauthorization for 12 months will be granted if the member has recent (within the last 6-months) clinical documentation showing at least **ONE** of the following:

1. Improvement in at least one objective measure, such as:
    a. Reduced inflammatory markers (e.g., fecal calprotectin, C-reactive protein)***; and/or***
    b. Improved endoscopic findings***; and/or***
    c. Reduced corticosteroid dose; ***AND/OR***
2. Improvement in at least one symptom, such as:
    a. Decreased pain***; and/or***
    b. Reduced fatigue***; and/or***

c. Decreased stool frequency***; and/or***

d. Reduced rectal bleeding.

Experimental or Investigational / Not Medically Necessary

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

- Concurrent use 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.
- 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. 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 in pediatric patients (under 18 years of age) for either MS or UC. Clinical trials have not established safety and efficacy in this population.

References

1. Bainbridge JL, Miravalle A, Wong PS. Multiple Sclerosis. In DiPiro JT, Yee GC, Posey LM, et al, eds. Pharmacotherapy: A Pathophysiologic Approach. 11th ed. New York, NY: McGraw-Hill; 2019.
2. Feuerstein JD, Isaacs KL, Schneider Y et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020; 158:1450-1461. [PubMed 31945371]
3. Hauser, S., & Cree, B. (2020). Treatment of Multiple Sclerosis: A Review.. The American journal of medicine. https://doi.org/10.1016/j.amjmed.2020.05.049.
4. McGinley MP, Goldschmidt CH, Rae-Grant AD. Diagnosis and Treatment of Multiple Sclerosis: A Review. JAMA. 2021;325(8):765–779. doi:10.1001/jama.2020.26858
5. Montalban X, Gold R, Thompson AJ, et al. ECTRIMS/EAN guideline on the pharmacological treatment of people with multiple sclerosis. Eur J Neurol. 2018;25(2):215-237. doi:10.1111/ene.13536
6. Multiple Sclerosis Society of Canada. Disease-modifying therapies. https://mssociety.ca/managing-ms/treatments/medications/disease-modifying-therapies-dmts.
7. National MS Society. Disease-modifying therapies for MS (updated March 2022). Available from National MS Society website:

https://nms2cdn.azureedge.net/cmssite/nationalmssociety/media/msnationalfiles/brochures/brochure-the-ms-disease-modifying-medications.pdf.
8. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018;90(17):777-788.
9. Reich DS, Lucchinetti CF, Calabresi PA. 2018. Multiple sclerosis. New England Journal of Medicine 378(2):169-180
10. Rubin DT, Ananthakrishnan AN, Siegel CA et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019; 114:384-413. [PubMed 30840605]
11. Sriwastava S, Chaudhary D, Srivastava S, et al. Progressive multifocal leukoencephalopathy and sphingosine 1-phosphate receptor modulators used in multiple sclerosis: an updated review of literature. J Neurol. 2022;269(3):1678-1687. doi:10.1007/s00415-021-10910-1
12. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence summary. Multiple Sclerosis Coalition. Available from the National MS Society Website: https://www.nationalmssociety.org/.
13. Tramacere I, Del Giovane C, Salanti G, et al. Immunomodulators and immunosuppressants for relapsing-remitting multiple sclerosis: a network meta-analysis. Cochrane Database Syst Rev 2015;9:CD011381.
14. Yang, J., Rempe, T., Whitmire, N., Dunn-Pirio, A., & Graves, J. (2022). Therapeutic Advances in Multiple Sclerosis. Frontiers in Neurology, 13. https://doi.org/10.3389/fneur.2022.824926.
15. Zeposia (ozanimod) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; August 2023.

Clinical Guideline Revision / History Information

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