PRIOR AUTHORIZATION POLICY

POLICY: Multiple Sclerosis and Ulcerative Colitis – Zeposia Prior Authorization Policy
- Zeposia® (ozanimod capsules – Celgene)

REVIEW DATE: 11/08/2023

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Zeposia, a sphingosine 1-phosphate receptor modulator, is indicated for the following uses:[1]
- Relapsing forms of **multiple sclerosis** (MS), in adults to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease.
- **Ulcerative colitis** (UC), in adults with moderately to severely active disease.

Guidelines/Clinical Efficacy

Published guidelines address recommended treatments for the following conditions:
- **Multiple sclerosis (MS):** Zeposia is not currently addressed in MS guidelines. In September 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.[2] Many options from various pharmacologic classes, involving different mechanisms of action and modes of administration, have shown benefits in patients with MS.
- **Ulcerative colitis (UC):** Zeposia is not currently addressed in UC guidelines. The American Gastroenterological Association (2020) and the American College of Gastroenterology (2019) have clinical practice guidelines on the management of moderate to severe UC and make recommendations for induction and maintenance of remission in adults.[3,4] Both endorse the use of

biologic agents and give specific patient circumstances in the selection for induction and maintenance therapies. The 10-week, induction pivotal trial for Zeposia included adult patients with moderately to severely active UC who had an inadequate response or were intolerant to any of the following agents: oral aminosalicylates, corticosteroids, immunomodulators (e.g., 6-mercaptopurine and azathioprine), or a biologic (e.g., tumor necrosis factor inhibitor, Entyvio [vedolizumab injection]).[1]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Zeposia. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Zeposia as well as the monitoring required for adverse events and long-term efficacy, approval requires Zeposia to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Zeposia® (ozanimod capsules – Celgene)** is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Multiple Sclerosis.** Approve for the duration noted below if the patient meets one of the following (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the patient meets the following (i and ii):
     - **i.** Patient has a relapsing form of multiple sclerosis; AND
       Note: Examples of relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease.
     - **ii.** Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; OR
   - **B)** Patient is Currently Receiving Zeposia for ≥ 1 Year. Approve for 1 year if the patient meets the following (i, ii, and iii):
     - **i.** Patient has a relapsing form of multiple sclerosis; AND
       Note: Examples of relapsing forms of multiple sclerosis include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease.
     - **ii.** Patient meets one of the following (a or b):
       - **a)** Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR
         Note: Examples include stabilization or reduced worsening in disease activity as evaluated by magnetic resonance imaging (MRI) [absence or a decrease in gadolinium enhancing lesions, decrease in the number of new or enlarging T2 lesions]; stabilization or reduced worsening on the Expanded Disability State Scale (EDSS) score; achievement in criteria for No Evidence of Disease Activity-3 (NEDA-3) or NEDA-4;

improvement on the fatigue symptom and impact questionnaire-relapsing multiple sclerosis (FSIQ-RMS) scale; reduction or absence of relapses; improvement or maintenance on the six-minute walk test or 12-Item MS Walking Scale; improvement on the Multiple Sclerosis Functional Composite (MSFC) score; and/or attenuation of brain volume loss.

b) Patient experienced stabilization, slowed progression, or improvement in at least one symptom such as motor function, fatigue, vision, bowel/bladder function, spasticity, walking/gait, or pain/numbness/tingling sensation; AND

iii. Medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis.

2. Ulcerative Colitis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient has had a trial of ONE systemic agent for ulcerative colitis; AND
Note: Examples of systemic agents for ulcerative colitis include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone, methylprednisolone. A trial of one biologic also counts as a trial of one systemic agent for ulcerative colitis. Refer to the Appendix A for examples of biologics used for ulcerative colitis.

iii. The medication is prescribed by or in consultation with a gastroenterologist.

B) Patient is Currently Receiving Zeposia. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of assessment for inflammatory response include fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or decreased rectal bleeding.

CONDITIONS

- **Zeposia® (ozanimod capsules – Celgene) is(are) considered experimental, investigational, or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

NOT RECOMMENDED FOR APPROVAL

1. **Concurrent Use with Other Disease-Modifying Agents Used for Multiple Sclerosis**. These agents are not indicated for use in combination (see Appendix B for examples). Additional data are required to determine if use of disease-modifying multiple sclerosis agents in combination is safe and provides added efficacy.

2. **Non-Relapsing Forms of Multiple Sclerosis.** The efficacy of Zeposia has not been established in patients with multiple sclerosis with non-relapsing forms of the disease.[1]
   Note: An example of a non-relapsing form of multiple sclerosis is primary progressive multiple sclerosis.

3. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-modifying Antirheumatic Drug (DMARD) for Ulcerative Colitis.** In the pivotal trials, patients who received Zeposia were not to receive concomitant treatment with non-corticosteroid immunosuppressive or immune-modulating therapies used for the treatment of ulcerative colitis (see Appendix A for examples).[1] Combination therapy is generally not recommended due to a potential for a higher rate of adverse effects with combinations and lack of evidence supporting additive efficacy. There are no data evaluating combination of Zeposia with a targeted synthetic DMARD (e.g., Xeljanz/Xeljanz XR (tofacitinib tablets, oral solution, and extended-release tablets); therefore, safety and efficacy of this combination is unknown.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Zeposia® capsules [prescribing information]. Princeton, NJ: Celgene/Bristol Myers Squibb; August 2023.
2. A Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis. September 2019. Available at: http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed on November 4, 2023.
3. Feuerstein JD, Isaac s KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158:1450-1461.
4. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. American College of Gastroenterology clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114:384-413.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	No criteria change.	10/26/2022
Update	08/10/2023: No criteria change. To Appendix B, Briumvi and Tascenso ODT were added. Also, it was noted that Aubagio is available as a generic.	NA

Annual Revision	No criteria change.	11/08/2023

APPENDIX A

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia□ (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel□, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Zymfentra™ (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO
		IV formulation: CD
Omvoh™ (mirikizumab-mrkz IV infusion and SC injection)	Inhibition of IL-23	UC
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion and SC injection)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, RA, PsA, UC
Sotyktu™ (deucravacitinib tablets)	Inhibition of TYK2	PsO

Velsipity™ (etrasimod tablets)	S1P receptor modulator	UC
Xeljanz® (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indications (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; TYK2 – Tyrosine kinase 2; S1P – Sphingosine 1-phospate receptor modulator.

APPENDIX B

Medication	Mode of Administration
Aubagio® (teriflunomide tablets, generic)	Oral
Avonex® (interferon beta-1a intramuscular injection)	Injection (self-administered)
Bafiertam® (monomethyl fumarate delayed-release capsules)	Oral
Betaseron® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Briumvi® (ublituximab-xiij intravenous infusion)	Intravenous infusion
Copaxone® (glatiramer acetate subcutaneous injection, generic)	Injection (self-administered)
Extavia® (interferon beta-1b subcutaneous injection)	Injection (self-administered)
Gilenya® (fingolimod capsules, generic)	Oral
Glatopa® (glatiramer acetate subcutaneous injection)	Injection (self-administered)
Kesimpta® (ofatumumab subcutaneous injection)	Injection (self-administered)
Lemtrada® (alemtuzumab intravenous infusion)	Intravenous infusion
Mavenclad® (cladribine tablets)	Oral
Mayzent® (siponimod tablets)	Oral
Ocrevus® (ocrelizumab intravenous infusion)	Intravenous infusion
Plegridy® (peginterferon beta-1a subcutaneous or intramuscular injection)	Injection (self-administered)
Ponvory® (ponesimod tablets)	Oral
Rebif® (interferon beta-1a subcutaneous injection)	Injection (self-administered)
Tascenso ODT® (fingolimod orally disintegrating tablets)	Oral
Tecfidera® (dimethyl fumarate delayed-release capsules, generic)	Oral
Tyruko® (natalizumab-sztn intravenous infusion)	Intravenous infusion
Tysabri® (natalizumab intravenous infusion)	Intravenous infusion
Vumerity® (diroximel fumarate delayed-release capsules)	Oral
Zeposia® (ozanimod capsules)	Oral