VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 08/05/2020; selected revision 09/09/2020 and 06/04/2021

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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zeposia is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Multiple Sclerosis.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** 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.
   - **B)** The 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 3 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 a biologic also counts as a trial of one systemic agent for ulcerative colitis. Refer to the Appendix 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 has had a response, as determined by the prescriber.
     Note: Examples of a response include decreased stool frequency or rectal bleeding. The patient may not have a full response, but there should have been a recent or past response to Zeposia.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zeposia is not recommended in the following situations:

1. **Concurrent Use with Other Disease-Modifying Agents Used for Multiple Sclerosis**.
   Note: Examples of disease-modifying agents used for multiple sclerosis include Avonex® (interferon beta 1a injection [intramuscular]), Betaseron®/Extavia® (interferon beta-1b injection), Rebif® (interferon beta-1a injection [subcutaneous {SC}]), Copaxone®/Glatopa® (glatiramer acetate injection), Plegridy® (peginterferon beta-1a injection), Aubagio® (teriflunomide tablets), Gilenya® (fingolimod tablets), Mavenclad® (cladribine tablets), Mayzent® (siponimod tablets), Tecfidera® (dimethyl fumarate delayed-release capsules), Vumerity® (diroximel fumarate delayed-release capsules), Bafiertam® (monomethyl fumarate delayed-release capsules), Ocrevus® (ocrelizumab injection for intravenous [IV] use), Tysabri® (natalizumab injection for IV infusion), Lemtrada® (alemtuzumab injection for IV use), and Kesimpta® (ofatumumab injection for SC use).[2] These agents are not indicated for use in combination. 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.**
   Note: An example of a non-relapsing form of multiple sclerosis is primary progressive multiple sclerosis. The efficacy of Zeposia has not been established in patients with multiple sclerosis with non-relapsing forms of the disease.[1]

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 (e.g., a tumor necrosis factor inhibitor [e.g., an adalimumab product {Humira, biosimilars}, an infliximab product {Remicade, biosimilars}, Simponi {golimumab subcutaneous injection}], Entyvio [vedolizumab intravenous {IV} infusion], Stelara [ustekinumab SC injection, ustekinumab IV infusion],) used for the treatment of ulcerative colitis.[1] Concomitant use of Zeposia with any of these therapies would be expected to increase the risk of immunosuppression. 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/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]. Summit, NJ: Celgene; May 2021.
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 May 28, 2021.
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
New Policy	--	04/15/2020
Early Annual Revision	**Conditions Not Recommended for Approval:** Bafiertam was added to the Note that provides examples of disease-modifying MS agents in which Zeposia should not be used with concurrently.	08/05/2020
Selected Revision	**Multiple Sclerosis:** Examples of relapsing forms of MS were added in a Note. **Conditions Not Recommended for Approval:** Regarding Use with Other Disease-Modifying Agents for MS, Kesimpta was added to the list of examples provided in the Note.	09/09/2020
Selected Revision	**Ulcerative Colitis:** This new condition of approval was added to the policy. . **Concurrent Use with a Biologic or with a Targeted Synthetic DMARD for Ulcerative Colitis:** This condition was added to the policy as a Conditions Not Recommended for Approval.	06/04/2021

APPENDIX

Product	Mechanism of Action	Examples of Inflammatory Indications for Products*
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, PsA, RA
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, 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-rzza SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO, PsA
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indication (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; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; 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; ^ Off-label use of Kineret in JIA supported in guidelines.