

## Clinical Policy: Ozanimod (Zeposia)

Reference Number: ERX.SPA.363

Effective Date: 03.25.20

Last Review Date: 08.21

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

### Description

Ozanimod (Zeposia®) is a sphingosine 1-phosphate receptor modulator.

### FDA Approved Indication(s)

Zeposia is indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Moderately to severely active ulcerative colitis (UC) in adults

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Zeposia is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Multiple Sclerosis (must meet all):

1. Diagnosis of one of the following (a, b, or c):
  - a. Clinically isolated syndrome;
  - b. Relapsing-remitting MS;
  - c. Secondary progressive MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Zeposia is not prescribed concurrently with other disease modifying therapies for MS (see *Appendix D*);
5. Documentation of baseline number of relapses per year and expanded disability status scale (EDSS) score;
6. Dose does not exceed 0.92 mg (1 capsule) per day.

**Approval duration: 6 months**

##### B. Ulcerative Colitis (must meet all):

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Documentation of a Mayo Score ≥ 6 (see *Appendix E*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Humira®, Stelara®, Xeljanz®/Xeljanz® XR;
7. Dose does not exceed 0.92 mg (1 capsule) per day.

**Approval duration: 6 months**

**B. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

**A. Multiple Sclerosis (must meet all):**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
  - a. If member has received < 1 year of total treatment: Member is responding positively to therapy;
  - b. If member has received ≥ 1 year of total treatment: Member meets one of the following (i, ii, iii, or iv):
    - i. Member has not had an increase in the number of relapses per year compared to baseline;
    - ii. Member has not had ≥ 2 new MRI-detected lesions;
    - iii. Member has not had an increase in EDSS score from baseline;
    - iv. Medical justification supports that member is responding positively to therapy;
3. Zeposia is not prescribed concurrently with other disease modifying therapies for MS (see *Appendix D*);
4. If request is for a dose increase, new dose does not exceed 0.92 mg (1 capsule) per day.

**Approval duration: first re-authorization: 6 months; second and subsequent re-authorizations: 12 months**

**B. Ulcerative Colitis (must meet all):**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Dose does not exceed 0.92 mg (1 capsule) per day.

**Approval duration: 12 months**

**C. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.  
**Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;
- B. Primary progressive MS.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration

MS: multiple sclerosis

UC: ulcerative colitis

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria.*

*The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
corticosteroids	<b>UC</b> budesonide (Uceris®) 9 mg PO QD	budesonide 9 mg/day
Humira® (adalimumab)	<b>UC</b> Initial dose: 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: 40 mg SC every other week starting on Day 29	40 mg every other week
Stelara® (ustekinumab)	<b>UC</b> Weight based dosing IV at initial dose, followed by 90 mg SC every 8 weeks  Weight ≤ 55 kg: 260 mg Weight 55 kg to 85 kg: 390 mg Weight > 85 kg: 520 mg	90 mg every 8 weeks
Xeljanz® (tofacitinib immediate-release)	<b>UC</b> <u>Induction:</u> 10 mg PO BID for 8 weeks, up to 16 weeks <u>Maintenance:</u> 5 mg PO BID	Induction: 20 mg/day  Maintenance: 10 mg/day
Xeljanz® XR (tofacitinib extended-release)	<b>UC</b> <u>Induction:</u> 22 mg PO QD for 8 weeks, up to 16 weeks <u>Maintenance:</u> 11 mg PO QD	Induction: 22 mg/day  Maintenance: 11 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

#### Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of any of the following in the last 6 months: myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III or IV heart failure; presence of Mobitz type II second-degree or third degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker; severe untreated sleep apnea; concomitant use of a monoamine oxidase inhibitor
- Boxed warning(s): none reported

#### Appendix D: General Information

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), diroximel fumarate (Vumerity®), monomethyl fumarate (Bafiertam™), fingolimod (Gilenya®), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus®), siponimod (Mayzent®), cladribine (Mavenclad®), ozanimod (Zeposia®), and ofatumumab (Kesimpta®).
- The American Academy of Neurology 2018 MS guidelines recommend the use of Gilenya, Tysabri, and Lemtrada for patients with highly active MS. Definitions of highly active MS vary and can include measures of relapsing activity and MRI markers of disease activity, such as numbers of gadolinium-enhanced lesions.
- Of the disease-modifying therapies for MS that are FDA-labeled for CIS, only the interferon products, glatiramer, and Aubagio have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the AAN 2018 MS guidelines.

#### Appendix E: Mayo Score

- Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician's global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0 – 2	Remission
3 – 5	Mild activity
6 – 10	Moderate activity
>10	Severe activity

- The following may be considered for medical justification supporting inability to use an immunomodulator for ulcerative colitis:
  - Documentation of Mayo Score 6 – 12 indicative of moderate to severe ulcerative colitis.

#### V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MS, UC	Days 1-4: 0.23 mg PO QD Days 5-7: 0.46 mg PO QD Day 8 and thereafter: 0.92 mg PO QD  If a dose of Zeposia is missed during the first 2 weeks of treatment, reinstate treatment using the titration regimen. If a dose of Zeposia is missed after the first 2 weeks of treatment, continue with the treatment as planned.	0.92 mg/day

#### VI. Product Availability

Capsules: 0.23 mg, 0.46 mg, 0.92 mg

#### VII. References

- Zeposia Prescribing Information. Summit, NJ: Celgene Corporation; May 2021. Available at: <https://www.zeposia.com>. Accessed June 14, 2021.
- Cohen JA, Comi G, Selmaj KW, et al. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (RADIANCE): a multicentre, randomised, 24-month, phase 3 trial. *Lancet Neurol.* 2019; 18 (11): 1021-1033. <https://www.ncbi.nlm.nih.gov/pubmed/31492652>. doi:10.1016/S1474-4422(19)30238-8.
- Comi G, Kappos L, Selmaj KW, et al. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (SUNBEAM): a multicentre, randomised, minimum 12-month, phase 3 trial. *Lancet Neurol.* 2019; 18 (11): 1009-1020. <https://www.ncbi.nlm.nih.gov/pubmed/31492651>. doi:10.1016/S1474-4422(19)30239-X.
- 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. Full guideline available at: <https://www.aan.com/Guidelines/home/GetGuidelineContent/904>.
- Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384-413.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.21.20	02.20
Drug is now FDA approved - criteria updated per FDA labeling; updated re-directions per current formulary status; added requirements for documentation of baseline relapses/EDSS and objective measures of positive response upon re-authorization; modified continued approval duration to 6 months for the first re-authorization and 12 months for second/subsequent re-authorizations; added primary progressive MS as a diagnosis not covered; references reviewed and updated.	05.12.20	08.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; references reviewed and updated.	10.09.20	02.21
2Q 2021 annual review: no significant changes; removed re-directions per preferred formulary status; reference reviewed and updated.	02.08.21	05.21
RT4: added criteria for newly FDA-approved indication for ulcerative colitis based on previously P&T-approved clinical guidance and rebate contract; references reviewed and updated.	08.12.21	08.21

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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