

## Clinical Policy: Ozanimod (Zeposia)

Reference Number: IL.ERX.SPA.363

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Line of Business: Illinois Medicaid

[Revision Log](#)

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

### Description

Ozanimod (Zeposia<sup>®</sup>) 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.

### 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<sup>™</sup> 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, and member is contraindicated to both, or has experienced clinically significant adverse effects to one, of the following at up to maximally indicated doses: an interferon-beta agent (*Betaseron<sup>®</sup> and Rebif<sup>®</sup> are preferred agents*), glatiramer (*Copaxone<sup>®</sup> 20 mg is preferred*);
  - b. Relapsing-remitting MS, and failure of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: dimethyl fumarate (*Tecfidera<sup>®</sup> brand is preferred*) and any of the following: an interferon-beta agent (*Betaseron and Rebif are preferred agents*) or glatiramer (*Copaxone 20 mg is preferred*);
- \*Prior authorization is required for all disease modifying therapies for 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. 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. 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

*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 and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Rebif® (interferon beta-1a)	22 mcg or 44 mcg SC TIW	44 mcg TIW
Betaseron® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
dimethyl fumarate (Tecfidera®)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 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<sup>®</sup>, Glatopa<sup>®</sup>), interferon beta-1a (Avonex<sup>®</sup>, Rebif<sup>®</sup>), interferon beta-1b (Betaseron<sup>®</sup>, Extavia<sup>®</sup>), peginterferon beta-1a (Plegridy<sup>®</sup>), dimethyl fumarate (Tecfidera<sup>®</sup>), diroximel fumarate (Vumerity<sup>®</sup>), monomethyl fumarate (Bafiertam<sup>™</sup>), fingolimod (Gilenya<sup>®</sup>), teriflunomide (Aubagio<sup>®</sup>), alemtuzumab (Lemtrada<sup>®</sup>), mitoxantrone (Novantrone<sup>®</sup>), natalizumab (Tysabri<sup>®</sup>), ocrelizumab (Ocrevus<sup>®</sup>), siponimod (Mayzent<sup>®</sup>), cladribine (Mavenclad<sup>®</sup>), ozanimod (Zeposia<sup>®</sup>), and ofatumumab (Kesimpta<sup>®</sup>).
- 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.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
MS	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**

1. Zeposia Prescribing Information. Summit, NJ: Celgene Corporation; September 2020. Available at: <https://www.zeposia.com>. Accessed February 8, 2021.
2. 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.
3. 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.
4. 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>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.19.21	05.21

**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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