Clinical Policy Title:	ozanimod
Policy Number:	RxA.649
Drug(s) Applied:	Zeposia®
Original Policy Date:	09/14/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Zeposia is a sphingosine 1-phosphate receptor modulator 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Zeposia® (ozanimod)	Multiple sclerosis, relapsing	Initial: 0.23 mg once daily on days 1 through 4; then 0.46 mg once daily on days 5 through 7; maintenance dose: 0.92 mg once daily starting on day 8.	0.92 mg/day

Dosage Forms

- Capsule: 0.23 mg, 0.46 mg, 0.92 mg

Clinical Policy

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

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all):

1. Diagnosis of relapsing multiple sclerosis (RMS),including clinically isolated syndrome, or relapsing remitting disease, or active secondary progressive disease.
2. Prescribed by or in consultation with a neurologist
3. Age $\geq$ 18 years
4. Dose does not exceed the following 0.92 mg orally once daily
5. Zeposia is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix B*)

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Multiple Sclerosis (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Zeposia is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix B*);
4. If request is for a dose increase, new dose does not exceed 0.92 mg daily.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MS: multiple sclerosis

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.
Disease-modifying therapies for MS include:

- Infusion therapies
  - natalizumab (Tysabri®)
  - mitoxantrone
  - ocrelizumab (Ocrevus™)
  - alemtuzumab (Lemtrada®)
- Injectable therapies
  - glatiramer (Copaxone®, Glatopa®)
  - interferon beta-1a (Avonex®, Rebif®)
  - interferon beta-1b (Betaseron®, Extavia®)
  - peginterferon beta-1a (Plegridy®)
- Oral therapies
  - dimethyl fumarate (Tecfidera®)
  - monomethyl fumarate (Bafiertam™)
  - diroximel fumarate (Vumerity®)
  - teriflunomide (Aubagio®)
  - fingolimod (Gilenya™)
  - siponimod (Mayzent®)
  - ozanimod (Zeposia®)
  - cladribine (Mavenclad®)
  - dalfampridine (Ampyra®)

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - In the last 6 months, experienced 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.

APPENDIX D: General Information

- Although many disease-modifying therapies for MS 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.

References

1. Zeposia (ozanimod) [prescribing information]. Summit, NJ: Celgene Corporation; March 2020. Accessed on May 27, 2021.
2. 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 [published correction appears in Neurology. 2019 Jan 8;92(2):112]. Neurology. 2018;90(17):777-788. Accessed on May 27, 2021.
3. U.S. Food and Drug Administration Approves Bristol Myers Squibb's ZEPOSIA® (ozanimod), a New Oral Treatment for Relapsing Forms of Multiple Sclerosis. Bristol Myers Squibb. 2020. Available at https://news.bms.com/press-release
4. 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; 18:1009.
5. 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; 18:1021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	08/11/2020	09/14/2020
Policy was reviewed: 1. Clinical policy title was updated. 2. Continued therapy approval criteria II.A.3 indicating ," Trial and failure of at…….or Zeposia" was removed. 3. References were reviewed and updated.	5/27/21	6/10/21