

Clinical Policy: Ozanimod (Zeposia)

Reference Number: MDN.CP.PHAR.462

Effective Date: 04.01.22

Last Review Date: 04.22

Line of Business: Meridian IL 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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 \geq 18 years;
4. Failure of TWO of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c):*
 - a. Gilenya[®];
 - b. Tecfidera[®];
 - c. An interferon-beta agent (Betaseron[®], Rebif[®]) or Copaxone[®];

**Prior authorization is required for Gilenya*
5. Zeposia is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
6. Documentation of baseline number of relapses per year and expanded disability status scale (EDSS) score;
7. 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 \geq 18 years;
4. Documentation of a Mayo Score \geq 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 Humira[®] and Xeljanz/Xeljanz XR[®], each used for \geq 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated;
7. Dose does not exceed 0.92 mg (1 capsule) per day.

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Sclerosis (must meet all):

1. Currently receiving medication via Centene benefit 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 \geq 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 \geq 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: 12 months

B. Ulcerative Colitis (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new 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 Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

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 policies – CP.PMN.53 for Medicaid 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 |
|--|---|--|
| Aubagio [®] (teriflunomide) | MS 7 mg or 14 mg PO QD | 14 mg/day |
| Avonex [®] , Rebif [®] (interferon beta-1a) | MS Avonex: 30 mcg IM Q week Rebif: 22 mcg or 44 mcg SC TIW | Avonex: 30 mcg/week Rebif: 44 mcg TIW |
| Betaseron [®] (interferon beta-1b) | MS 250 mcg SC QOD | 250 mg QOD |
| Plegridy [®] (peginterferon beta-1a) | MS 125 mcg SC Q2 weeks | 125 mcg/2 weeks |
| glatiramer acetate (Copaxone [®] , Glatopa [®]) | MS 20 mg SC QD or 40 mg SC TIW | 20 mg/day or 40 mg TIW |
| Gilenya [®] (fingolimod) | MS 0.5 mg PO QD | 0.5 mg/day |
| dimethyl fumarate (Tecfidera [®]) | MS 120 mg PO BID for 7 days, followed by 240 mg PO BID | 480 mg/day |
| corticosteroids | UC budesonide (Uceris [®]) 9 mg PO QD | budesonide 9 mg/day |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose | | | | | | | | | | | | |
|----------------------------------|--|--|-------------------|--------------------------|---|-------------------|---|--------|---------------------|--------------------------|--|-------------------|--|--|
| Humira [®] (adalimumab) | <p>UC</p> <p><u>Initial dose:</u> <i>Adults:</i> 160 mg SC on Day 1, then 80 mg SC on Day 15</p> <p><i>Pediatrics:</i></p> <table border="1" data-bbox="670 495 1107 903"> <thead> <tr> <th data-bbox="670 495 834 569">Weight</th> <th data-bbox="834 495 1107 569">Days 1 through 15</th> </tr> </thead> <tbody> <tr> <td data-bbox="670 569 834 682">20 kg to less than 40 kg</td> <td data-bbox="834 569 1107 682">Day 1: 80 mg Day 8: 40 mg Day 15: 40 mg</td> </tr> <tr> <td data-bbox="670 682 834 903">40 kg and greater</td> <td data-bbox="834 682 1107 903">Day 1: 160 mg (single dose or split over tw consecutive days Day 8: 80 mg Day 15: 80 mg</td> </tr> </tbody> </table> <p><u>Maintenance dose:</u> <i>Adults:</i> 40 mg SC every other week starting on Day 29</p> <p><i>Pediatrics:</i></p> <table border="1" data-bbox="670 1121 1107 1419"> <thead> <tr> <th data-bbox="670 1121 834 1194">Weight</th> <th data-bbox="834 1121 1107 1194">Starting on Day 29*</th> </tr> </thead> <tbody> <tr> <td data-bbox="670 1194 834 1308">20 kg to less than 40 kg</td> <td data-bbox="834 1194 1107 1308">40 mg every other week or 20 mg every week</td> </tr> <tr> <td data-bbox="670 1308 834 1419">40 kg and greater</td> <td data-bbox="834 1308 1107 1419">80 mg every other week or 40 mg every week</td> </tr> </tbody> </table> <p><i>*Continue the recommended pediatric dosage in patients who turn 18 years of age and who are well-controlled on Humira regimen.</i></p> | Weight | Days 1 through 15 | 20 kg to less than 40 kg | Day 1: 80 mg Day 8: 40 mg Day 15: 40 mg | 40 kg and greater | Day 1: 160 mg (single dose or split over tw consecutive days Day 8: 80 mg Day 15: 80 mg | Weight | Starting on Day 29* | 20 kg to less than 40 kg | 40 mg every other week or 20 mg every week | 40 kg and greater | 80 mg every other week or 40 mg every week | <p>UC</p> <p>40 mg every week</p> |
| Weight | Days 1 through 15 | | | | | | | | | | | | | |
| 20 kg to less than 40 kg | Day 1: 80 mg Day 8: 40 mg Day 15: 40 mg | | | | | | | | | | | | | |
| 40 kg and greater | Day 1: 160 mg (single dose or split over tw consecutive days Day 8: 80 mg Day 15: 80 mg | | | | | | | | | | | | | |
| Weight | Starting on Day 29* | | | | | | | | | | | | | |
| 20 kg to less than 40 kg | 40 mg every other week or 20 mg every week | | | | | | | | | | | | | |
| 40 kg and greater | 80 mg every other week or 40 mg every week | | | | | | | | | | | | | |
| Simponi [®] (golimumab) | <p>UC</p> <p>Initial dose: 200 mg SC at week 0, then 100 mg SC at week 2</p> <p>Maintenance dose: 100 mg SC every 4 weeks</p> | <p>UC</p> <p>100 mg every 4 weeks</p> | | | | | | | | | | | | |

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 sinoatrial 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 | 0.92 mg/day |

| Indication | Dosing Regimen | Maximum Dose |
|------------|---|--------------|
| | Day 8 and thereafter: 0.92 mg PO QD If a dose of Zeposia is missed during the first 2 weeks of treatment, reinitiate 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. | |

VI. Product Availability

Capsules: 0.23 mg, 0.46 mg, 0.92 mg

VII. References

1. Zeposia Prescribing Information. Summit, NJ: Celgene Corporation; May 2021. Available at: <https://www.zeposia.com>. Accessed June 14, 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>.
5. 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, adapted from CP.PHAR.462 | 04.01.22 | 04.22 |

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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