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5.60.044

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	April 24, 2020
Subject:	Zeposia	**Page:**	1 of 7

Last Review Date: March 7, 2025

Zeposia

Description

Zeposia (ozanimod)

Preferred MS product: Zeposia
Zeposia is non-preferred for UC

Background
Zeposia (ozanimod) is a sphingosine-1-phosphate (S1P) receptor modulator that binds with high affinity to S1P receptors 1 and 5. Zeposia blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which Zeposia exerts therapeutic effects in multiple sclerosis and ulcerative colitis is unknown but may involve the reduction of lymphocyte migration into the central nervous system and intestine (1).

Regulatory Status
FDA-approved indications: Zeposia is a sphingosine 1-phosphate receptor modulator indicated for the treatment of: (1)

- 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

Before initiation of treatment with Zeposia, the following should be assessed: (1)

- Complete blood count (CBC) – Obtain a recent (i.e., within the last 6 months or after discontinuation of prior MS therapy) CBC including lymphocyte count

- Cardiac evaluation – Obtain an electrocardiogram (ECG) to determine whether preexisting conduction abnormalities are present
- Liver function tests – Obtain recent (i.e., within the last 6 months) transaminase and bilirubin levels
- Ophthalmic assessment – In patient with a history of uveitis or macular edema, obtain an evaluation of the fundus, including the macula
- Vaccination – Test patients for antibodies to varicella zoster virus (VZV) before initiating Zeposia; VZV vaccination of antibody-negative patients is recommended prior to commencing treatment with Zeposia. If live attenuated vaccine immunizations are required, administer at least 1 month prior to initiation of Zeposia.

Zeposia is contraindicated in patients who in the last 6 months experienced a myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure (1).

Zeposia is also contraindicated in patients with 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 (1).

The safety and effectiveness of Zeposia in pediatric patients less than 18 years of age have not been established (1).

Related policies
Acthar Gel, Ampyra, Aubagio, Gilenya, Kesimpta, Lemtrada, Mavenclad, Mayzent, MS Injectables, Ocrevus, Ponvory, Tecfidera, Tysabri

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zeposia may be considered **medically necessary** if the conditions indicated below are met.

Zeposia may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
    a. **NO** concurrent use with other MS disease modifying agents
2. Moderately to severely active Ulcerative Colitis (UC)
    a. Inadequate response, intolerance, or contraindication to at least **ONE** conventional therapy option (see Appendix 1)
    b. **NOT** to be used in combination with a biologic DMARD or targeted synthetic DMARD for UC (e.g., Entyvio, Humira, Simponi, Stelara, Xeljanz)
    c. Patient **MUST** have tried the preferred product(s) (see Appendix 2) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

AND ALL of the following:

1. Baseline evaluations of **ALL** of the following have been done or will be done prior to starting therapy with Zeposia:
    a. Complete blood count (CBC), including lymphocyte count
    b. Electrocardiogram (ECG)
    c. Liver function tests (LFTs)
2. Heart rate ≥ 55 bpm
3. **NO** history (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure
4. **NO** presence of Mobitz Type II second-degree or third degree AV block, sick sinus syndrome, or sino-atrial block, unless patient has a pacemaker
5. **NO** significant QTc prolongation (QTcF >450 msec in males, >470 msec in females)
6. **NO** severe untreated sleep apnea
7. Patients with a history of uveitis and/or diabetes **ONLY**: will have an ophthalmic evaluation of fundus, including the macula, prior to initiation of therapy
8. **NOT** given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
    a. **NO** concurrent use with other MS disease modifying agents
2. Ulcerative Colitis (UC)
    a. Condition has improved or stabilized
    b. **NOT** to be used in combination with a biologic DMARD or targeted synthetic DMARD for UC (e.g., Entyvio, Humira, Simponi, Stelara, Xeljanz)
    c. Patient **MUST** have tried the preferred product(s) (see Appendix 2) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

AND ALL of the following:

1. Heart rate ≥ 55 bpm
2. **NO** history (within the last 6 months) of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III/IV heart failure.
3. **NO** presence of Mobitz Type II second-degree or third degree AV block, sick sinus syndrome, or sino-atrial block, unless patient has a pacemaker
4. **NO** significant QTc prolongation (QTcF >450 msec in males, >470 msec in females)
5. **NO** severe untreated sleep apnea
6. **NOT** given concurrently with live vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 90 capsules per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Zeposia (ozanimod) is a sphingosine-1-phosphate (S1P) receptor modulator that binds with high affinity to S1P receptors 1 and 5. Zeposia blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The mechanism by which Zeposia exerts therapeutic effects in multiple sclerosis and ulcerative colitis is unknown but may involve the reduction of lymphocyte migration into the central nervous system and intestine. The safety and effectiveness of Zeposia in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Zeposia while maintaining optimal therapeutic outcomes.

References

1. Zeposia [package insert, Summit, NJ: Celgene Corporation; August 2024.

Policy History

Date	Action
April 2020	Addition to PA
June 2020	Annual review
September 2020	Annual review. Addition of requirements per SME: obtain lymphocyte count prior to initiation of therapy, heart rate ≥ 55 bpm; no significant QTc prolongation; no severe untreated sleep apnea; ophthalmic evaluation prior to therapy for patients with a history of uveitis and/or diabetes
December 2020	Annual review and reference update

June 2021	Annual review. Addition of indication: ulcerative colitis. Added Appendices 1 and 2
September 2021	Annual review
April 2022	Added Rinvoq as a preferred UC product to chart (Appendix 2)
June 2022	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.60.044
June 2023	Annual review and reference update
December 2023	Annual review and reference update
March 2024	Annual review
December 2024	Annual review and reference update
March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.

Appendix 1 – List of Conventional Therapies

Conventional Therapy Options
1. Mild to moderate disease – induction of remission: a. Oral budesonide, oral mesalamine b. Alternatives: metronidazole, ciprofloxacin
2. Mild to moderate disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission: a. Prednisone, methylprednisolone intravenously (IV) b. Alternatives: methotrexate IM
4. Moderate to severe disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission c. Metronidazole ± ciprofloxacin
6. Perianal and fistulizing disease – maintenance of remission d. Azathioprine, mercaptopurine e. Alternative: methotrexate IM

Appendix 2 - List of Preferred Products

Diagnosis	Standard Option/Basic Option Preferred Products	Blue Focus Preferred Products
Ulcerative colitis (UC)	*must try **TWO** preferred products: Humira Rinvoq Skyrizi Stelara (SC)	Humira