Cytokine and CAM Antagonists: S1-P Receptor Modulators

WA.PHAR.49.AK Effective Date: 3/1/2025

Related medical policies:

Policy Number	Policy Name
WA.PHAR.49.AA	Cytokine and CAM Antagonists: Tumor Necrosis Factor (TNF) Inhibitors
WA.PHAR.49.AB	Cytokine and CAM Antagonists: IL-4/IL-13 Inhibitors
WA.PHAR.49.AC	Cytokine and CAM Antagonists: IL-6 Inhibitors
WA.PHAR.49.AD	Cytokine and CAM Antagonists: IL-12/IL-23 Inhibitors
WA.PHAR.49.AE	Cytokine and CAM Antagonists: IL-17 Inhibitors
WA.PHAR.49.AF	Cytokine and CAM Antagonists: Oral PDE-4 Inhibitors
WA.PHAR.49.AG	Cytokine and CAM Antagonists: T-Lymphocyte Inhibitors
WA.PHAR.49.AH	Cytokine and CAM Antagonists: Janus Associated Kinase (JAK) Inhibitors
WA.PHAR.49.AI	Cytokine and CAM Antagonists: IL-1 Inhibitors
WA.PHAR.49.AJ	Cytokine and CAM Antagonists: Integrin Receptor Antagonists

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit:
https://www.coordinatedcarehealth.com/content/dam/centene/centene-pharmacy/pdl/FORMULARY-CoordinatedCare_Washington.pdf

Medical necessity:

Drug	Medical Necessity
etrasimod (Velsipity) fingolimod HCl (Gilenya) fingolimod lauryl sulfate (Tascenso ODT) ozanimod (Zeposia) ponesimod (Ponvory) siponimod (Mayzent)	**Sphingosine 1-Phosphate (S1P) receptor modulators – etrasimod, fingolimod, ozanimod, ponesimod, siponimod** may be considered medically necessary in patients who meet the criteria described in the clinical policy below.

	If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Multiple sclerosis (MS) fingolimod HCl (Gilenya) fingolimod lauryl sulfate (Tascenso ODT) ozanimod (Zeposia) ponesimod (Ponvory) siponimod (Mayzent)	Fingolimod HCl (Gilenya), fingolimod lauryl sulfate (Tascenso ODT), ozanimod (Zeposia), ponesimod (Ponvory), or siponimod (Mayzent) may be approved when all the following documented criteria are met: 1. The patient meets the appropriate age limit for the requested product: a. For fingolimod hcl and fingolimod lauryl sulfate: 10 years of age or older; **OR** b. For ozanimod, ponesimod, or siponimod: 18 years of age or older; **AND** 2. Prescribed by, or in consultation with a neurologist; **AND** 3. Not used in combination with other disease modifying therapies (DMTs) for multiple sclerosis; **AND** 4. Diagnosis of one of the following: a. Relapsing remitting disease (RRMS) b. Active secondary progressive disease (SPMS) c. Clinically isolated syndrome (CIS); **AND** 5. Diagnosis is confirmed and documented by a laboratory report (e.g. MRI); **AND** 6. Documentation of baseline number of relapses per year or expanded disability status scale (EDSS score); **AND** 7. Treatment with two preferred multiple sclerosis Apple Health Preferred Drug List (PDL) medications has been ineffective unless all are contraindicated or not tolerated. If ALL criteria are met, the request will be authorized for **12 months.**
	Criteria (Reauthorization)
	Fingolimod (Gilenya), fingolimod lauryl sulfate (Tascenso ODT), ozanimod (Zeposia), ponesimod (Ponvory), or siponimod (Mayzent) may be approved when all the following documented criteria are met: 1. Not used in combination with other disease modifying therapies (DMTs) for multiple sclerosis; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g. decreased frequency of relapses, delayed progression, stable disease, etc.). If ALL criteria are met, the request will be authorized for **12 months.**

Ulcerative Colitis etrasimod (Velsipity) ozanimod (Zeposia)	Etrasimod (Velsipity) and ozanimod (Zeposia) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with a gastroenterologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Diagnosis of moderate-to-severe Ulcerative Colitis (UC); AND 5. Baseline assessments are included (e.g., stool frequency, endoscopy results, presence of rectal bleeding, disease activity scoring tool); AND 6. Treatment with conventional therapy (e.g., systemic corticosteroids, azathioprine, mesalamine, sulfasalazine) has been ineffective, unless all are contraindicated, or not tolerated [minimum trial of 12 weeks]; **AND** 7. Treatment with one preferred adalimumab biosimilar has been ineffective, unless all are contraindicated, or not tolerated [minimum trial of 12 weeks]. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Etrasimod (Velsipity) or ozanimod (Zeposia) may be approved when all the following documented criteria are met: 1. Not used in combination with another Cytokine and CAM medication; AND 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., decreased stool frequency, decreased rectal bleeding, improvement in endoscopic activity, tapering or discontinuation of corticosteroid therapy, or improvement on a disease activity scoring tool). If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits:

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
Fingolimod HCl	Multiple Sclerosis	0.5 mg once daily	• 0.25 mg capsules: 30 tablets per 30 days • 0.5 mg capsules: 30 tablets per 30 days
Gilenya	Multiple Sclerosis	0.5 mg once daily	• 0.25 mg capsules: 30 tablets per 30 days • 0.5 mg capsules: 30 tablets per 30 days
Mayzent	Multiple Sclerosis	Initiation: 4-5 day titration¥ Maintenance: 2 mg once daily	• 0.25 mg starter pack (Titrate to 2 mg dose): 12 tablets per 5 days

		Maintenance (with a CYP2C9*1/*3 or *2/*3 genotype): 1 mg once daily	• 0.25 mg tablets: 28 tablets per 28 days • 0.25 mg starter pack (Titrate to 1 mg dose): 7 tablets per 4 days • 1 mg tablets: 28 tablets per 28 days • 2 mg tablets: 30 tablets per 30 days
Ponvory	Multiple Sclerosis	Initiation: 14 day titration[#] Maintenance: 20 mg once daily	• 2-10 mg starter pack: 14 tablets per 14 days • 20 mg tablet: 30 tablets per 30 days
Tascenso ODT	Multiple Sclerosis	In adults and pediatric patients 10 years of age and older weighing more than 40 kg: 0.5 mg orally once daily. In pediatric patients 10 years of age and older weighing less than or equal to 40 kg: 0.25 mg orally once daily.	• 0.25 orally disintegrating tablet: 28 tablets per 28 days • 0.5 orally disintegrating tablet: 28 tablets per 28 days
Velsipity	Ulcerative Colitis	2 mg once daily	• 2 mg tablets: 30 tablets per 30 days
Zeposia	Multiple Sclerosis Ulcerative Colitis	Initial: 0.23 mg once daily (days 1 through 4) Titration: 0.46 mg once daily (days 5 through 7) Maintenance: 0.92 mg once daily starting day 8	• 7-Day Starter Pack (0.23 mg, 0.46 mg capsules): 7 capsules per 7 days • Starter Kit (7-day starter pack and 0.92 mg 30-count bottle): 37 capsules per 37 days • Starter Kit (7-day starter pack and 0.92 mg 21-count bottle): 28 capsules per 28 days • 0.92 mg capsules: 30 capsules per 30 days

[¥]Mayzent initiation:

CYP2C9 Genotype *1/*1, *1/*2, or *2/*2		
Titration Day	**Dose**	**Regimen**
Day 1	0.25 mg	1 x 0.25 mg
Day 2	0.25 mg	1 x 0.25 mg
Day 3	0.50 mg	2 x 0.25 mg
Day 4	0.75 mg	3 x 0.25 mg
Day 5	1.25 mg	5 x 0.25 mg

CYP2C9 Genotype *1/*3 or *2/*3		
Titration Day	**Dose**	**Regimen**
Day 1	0.25 mg	1 x 0.25 mg
Day 2	0.25 mg	1 x 0.25 mg
Day 3	0.50 mg	2 x 0.25 mg
Day 4	0.75 mg	3 x 0.25 mg

[#] Ponvory initiation:

Ponesimod Initial Dosage Titration	
Day of therapy	**Dose**
1 and 2	2 mg

3 and 4	3 mg
5 and 6	4 mg
7	5 mg
8	6 mg
9	7 mg
10	8 mg
11	9 mg
12, 13, and 14	10 mg
15 and thereafter	20 mg

Coding:

HCPCS Code	Description
N/A	N/A

Background:

Multiple Sclerosis

The American Academy of Neurology (AAN) 2019 practice guidelines note disease-modifying therapy (DMT) as the current standard of treatment for MS. Clinical evidence suggests DMT therapy is reasonably effective in managing MS, as data shows that on average, annualized relapse rates for MS patients in the United States drop from 0.46-1.8 to 0.18-0.49 relapses per year after management with DMT. Guidelines and consensus statements by the MS Coalition recommend clinicians should offer DMTs to people with relapsing forms of MS with recent clinical relapses or MRI activity. While both bodies advocate for a wide range of therapy options for patients, sequential treatment recommendations are not made. Per the MS Coalition consensus statement, clinicians should consider prescribing a high efficacy medication such as alemtuzumab, cladribine, fingolimod, ocrelizumab or natalizumab for newly diagnosed individuals with highly active MS.

Ulcerative Colitis

The 2019 American College of Gastroenterology (ACG) clinical guideline on the management of ulcerative colitis in adults recommend oral systemic corticosteroids for induction of remission in moderate to severe disease (strong recommendation, moderate quality of evidence). TNF inhibitors (adalimumab, golimumab, and infliximab), vedolizumab (Entyvio), and tofacitinib (Xeljanz) are also recommended for induction of remission (strong recommendation, moderate quality of evidence). For maintenance of remission, thiopurines are recommended if remission was achieved after corticosteroid induction (conditional recommendation, low quality of evidence). The guidelines note a systematic review of 1,632 patients with ulcerative colitis demonstrated that azathioprine and mercaptopurine had a 76% mean efficacy in maintaining remission. If remission was achieved with anti-TNF therapy, vedolizumab (Entyvio), or tofacitinib (Xeljanz), clinical guidelines support continuing with the same agent to maintain remission (strong recommendation, moderate quality of evidence). The 2020 American Gastroenterology Association (AGA) guidelines make similar recommendations. Additionally, AGA recommends early use of biologic agents, rather than gradual step up after failure of 5-ASA in moderate to severe disease at high risk for colectomy. However, overall quality of evidence supporting this recommendation was rated as very low. Guidelines also note that for patients with less severe disease, 5-ASA therapy may still be a reasonable choice of therapy to start with. For maintenance of remission, AGA makes no recommendation in favor of, or against, using biologic monotherapy, rather than thiopurine monotherapy due to absence of evidence.

References:

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3. Zeposia. Package insert. Bristol-Myers Squibb Company; 2023.
4. Ponvory. Package insert. Janssen Pharmaceuticals, Inc; 2023.
5. Mayzent. Package insert. Novartis Pharmaceuticals Corporation; 2023.
6. American Academy of Neurology. Practice Guideline: Disease-modifying Therapies for Adults with Multiple Sclerosis. 2018; https://www.aan.com/Guidelines/home/GetGuidelineContent/900.
7. Costello K and Kalb R. The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. Consensus Paper by the Multiple Sclerosis Coalition. 2019.
8. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019;114(3):384-413.
9. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006
10. Paschos P, Katsoula A, Salanti G, et al. Systematic review with network meta-analysis: the impact of medical interventions for moderate-to-severe ulcerative colitis on health-related quality of life. Aliment Pharmacol Ther. 2018 Dec;48(11-12):1174-1185. doi: 10.1111/apt.15005. Epub 2018 Oct 30. PMID: 30378141.
11. Trigo-Vicente C, Gimeno-Ballester V, García-López S, et al. Systematic review and network meta-analysis of treatment for moderate-to-severe ulcerative colitis. Int J Clin Pharm. 2018 Dec;40(6):1411-1419. doi: 10.1007/s11096-018-0743-4. Epub 2018 Nov 26. PMID: 30478492.
12. Turner et al. Management of Paediatric Ulcerative Colitis, Part 1: Ambulatory Care—An Evidence-based Guideline From European Crohn's and Colitis Organization and European Society of Paediatric Gastroenterology, Hepatology and Nutrition, Journal of Pediatric Gastroenterology and Nutrition: August 2018.

History:

Approved Date	Effective Date	Version	Action and Summary of Changes
08.14.2024	04.01.2025	66.27.00.AK-5	- Added language for preferred adalimumab biosimilars - Formatting updates
08.14.2024	03.01.2025	66.27.00.AK-4	Approved by DUR Board - Split 66.27.00 policy into different policies -Added new drug indications when applicable -Update language in medical necessity section

Previous policy changes (relevant from Cytokine & CAM Antagonists Policy)	
Date	**Action and Summary of Changes**
10.21.2021	Removed Hyrimoz from the policy and updated the initial dosing for infliximab.
11.30.2020	Removed Preferred/Non-Preferred listing and added link to AHPDL publication
11.12.2020	Added language in clinical policy section for cases which do not meet policy criteria
09.01.2020	Updated wording in clinical criteria for products with only one preferred option.
08.19.2020	Approved by DUR Board
8.20.2020	Update to dosing and limits section for all products and indications
08.12.2020	Updated policy clinical criteria and dosing & quantity limits to include nonradiographic axial spondyloarthritis

06.01.2020	Added new agents to class; updated age limit for Uveitis indication; updated dosing and quantity limits; updated HCPCS coding
07.31.2019	Updated criteria that trial of preferred biologics only applies to non-preferred biologics
06.07.2019	Updates to TB skin test requirements for apremalist; updates to initial authorization clinical criteria
11.02.2018	Addition of Hyrimoz (adalimumab-adaz)
09.07.2018	Addition of new medication
08.16.2017	New Policy

Appendix:

MS with a relapsing-remitting course (RRMS)

- Based upon two separate areas of damage (dissemination in space) in the CNS that have occurred at different points in time (dissemination in time). Unless contraindicated, MRI should be obtained.

Dissemination in time (Development/appearance of new CNS lesions over time)	Dissemination in space (Development of lesions in distinct anatomical locations within the CNS)

• ≥ 2 clinical attacks; OR
• 1 clinical attack AND one of the following:
  ○ MRI indicating simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time or by a new T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI compared to baseline scan
  ○ CSF-specific oligoclonal bands
	• ≥ 2 lesions; OR
	• 1 lesion AND one of the following:
	  ○ Clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location
	  ○ MRI indicating ≥ 1 T2-hyperintense lesions characteristic of MS in ≥ 2 of 4 areas of the CNS (periventricular, cortical or juxtacortical, infratentorial, or spinal cord)

Secondary progressive MS course

- MS course characterized by steadily increasing objectively documented neurological disability independent of relapses. Fluctuations, periods of stability, and superimposed relapses might occur. Secondary progressive multiple sclerosis is further distinguished as a progressive course following an initial relapsing-remitting course.
- Diagnosed retrospectively based on previous year's history.

Secondary Progressive MS (SPMS)

Active secondary progressive MS (SPMS) is defined as the following:

- Expanded Disability Status Scale (EDSS) score ≥ 3.0; AND
- Disease is progressive ≥ 3 months following an initial relapsing-remitting course (i.e., EDSS score increase by 1.0 in patients with EDSS ≤5.5 or increase by 0.5 in patients with EDSS ≥6); **AND**
  - ≥ 1 relapse within the previous 2 years; **OR**
  - Patient has gadolinium-enhancing activity OR new or unequivocally enlarging T2 contrast-enhancing lesions as evidenced by MRI

Clinically Isolated Syndrome (CIS)

Definitive diagnosis of Clinically Isolated Syndrome (CIS) is based upon ALL of the following

- A monophasic clinical episode with patient-reported symptoms and objective findings reflecting a focal or multifocal inflammatory demyelinating event in the CNS

- Neurologic symptom duration of at least 24 hours, with or without recovery
- Absence of fever or infection
- Patient is not known to have multiple sclerosis