Washington State Health Care Authority

Cytokine and CAM Antagonists: Integrin Receptor Antagonists

Medical policy no. 66.27.00.AJ-6 Effective Date: 7/1/2025

Related medical policies:

Policy Number	Policy Name
66.27.00.AA	Cytokine and CAM Antagonists: Tumor Necrosis Factor (TNF) Inhibitors
66.27.00.AB	Cytokine and CAM Antagonists: IL-4/IL-13 Inhibitors
66.27.00.AC	Cytokine and CAM Antagonists: IL-6 Inhibitors
66.27.00.AD	Cytokine and CAM Antagonists: IL-12/IL-23 Inhibitors
66.27.00.AE	Cytokine and CAM Antagonists: IL-17 Inhibitors
66.27.00.AF	Cytokine and CAM Antagonists: Oral PDE-4 Inhibitors
66.27.00.AG	Cytokine and CAM Antagonists: T-Lymphocyte Inhibitors
66.27.00.AH	Cytokine and CAM Antagonists: Janus Associated Kinase (JAK) Inhibitors
66.27.00.AI	Cytokine and CAM Antagonists: IL-1 Inhibitors
66.27.00.AK	Cytokine and CAM Antagonists: S1-P Receptor Modulator

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 Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity:

Drug	Medical Necessity
vedolizumab (Entyvio, Entyvio Pen)	**Vedolizumab (Entyvio, Entyvio Pen)** 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	
Crohn's Disease vedolizumab (Entyvio, Entyvio Pen)	Vedolizumab (Entyvio, Entyvio Pen) 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 Crohn's disease (CD); **AND** a. Treatment with conventional therapy has been ineffective, unless all are contraindicated, or not tolerated. Conventional therapy is defined as: i. Oral corticosteroids (e.g., prednisone, methylprednisolone) used short-term to induce remission or alleviate signs/symptoms of disease flare; **AND** ii. At least one immunomodulatory agent (e.g., methotrexate, azathioprine, 6-mercaptopurine) [minimum trial of 12 weeks]; **OR** b. Documentation of high-risk disease (e.g., symptoms despite conventional therapy, obstruction, abscess, stricture, phlegmon, fistulas, resection, extensive bowel involvement, early age of onset, growth retardation, Crohn's Disease Activity Index (CDAI) > 450, Harvey-Bradshaw index > 7); **AND** 5. Treatment with two preferred Cytokine and CAM Apple Health Preferred Drug List (PDL) medications has each 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) Vedolizumab (Entyvio, Entyvio Pen) 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., improvement in endoscopic activity, taper or discontinuation of corticosteroids, reduction in number of liquid stools, decrease in presence and severity of abdominal pain, decrease in CDAI, decrease in Harvey-Bradshaw index). If ALL criteria are met, the request will be authorized for **12 months.**
Ulcerative Colitis vedolizumab (Entyvio, Entyvio Pen)	Vedolizumab (Entyvio, Entyvio Pen) 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; **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 two preferred Cytokine and CAM Apple Health Preferred Drug List (PDL) medications has each 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) Vedolizumab (Entyvio, Entyvio Pen) 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
Entyvio	Crohn's Disease	Induction: 300mg at weeks 0, 2, & 6 Maintenance: 300mg every 8 weeks	• 300mg/20mL vial: ○ Induction: 900 BU per 42 days ○ Maintenance: 300 BU per 56 days
	Ulcerative Colitis	Induction: • Patients who will be receiving IV maintenance doses: administer 300 mg intravenously at weeks 0, 2, & 6 • Patients who will be receiving SC maintenance doses: Administer 300 mg intravenously at weeks 0 and 2 Maintenance: 300mg every 8 weeks	• 300mg/20mL vial: ○ Induction for IV maintenance: 900 BU per 42 days ○ Induction for SC maintenance: 600 BU per 14 days ○ Maintenance: 300 BU per 56 days

Entyvio Pen	Crohn's Disease Ulcerative Colitis	After week 6 IV infusion and thereafter if switching, 108 mg subQ once every 2 weeks [	• 108mg/0.68mL solution: 2 PFP or PFS per 28 days

Coding:

HCPCS Code	Description
J3380	Injection, vedolizumab, 1 mg; 1 billable unit = 1 mg

Background:

Crohn's Disease

Therapeutic recommendations for patients with Crohn's disease (CD) are established based upon disease location, disease severity, disease associated complications, and future disease prognosis. The goals of therapy are to induce remission, prevent relapse, and prevent occurrence of disease complications, such as stricture and fistula. According to the 2018 American College of Gastroenterology (ACG) guidelines, for patients with moderate to severe disease and those with moderate to high-risk disease treatment with oral corticosteroids used short term to induce remission is recommended (strong recommendation, moderate level of evidence). However, it is noted that one in five patients will become steroid refractory which is thought to be the result of unreliable efficacy in healing of the mucosa associated with steroids (weak recommendation, low level of evidence). Corticosteroids are also implicated in the development of perforating complications (abscess and fistula) and are relatively contraindicated in those patients. The 2021 American Gastroenterological Association (AGA) clinical guidelines make similar recommendations and suggest the use of corticosteroids in adult outpatients with moderate to severe CD over no treatment for induction of remission (conditional recommendation, moderate level of evidence). In patients with moderate to severe CD who remain symptomatic despite current or prior corticosteroid therapy, 2018 ACG guidelines recommend immunomodulators such as azathioprine, 6-mercaptopurine (strong recommendation, moderate level of evidence), and methotrexate (conditional recommendation, low level of evidence) to be effective for maintenance of remission. Due to slow time to clinical response that may not be evident for as long as 12 weeks, these agents are not recommended for short-term induction. The 2021 AGA guidelines make similar suggestions and recommend use of thiopurines over no treatment for the maintenance of remission (conditional recommendation, low level of evidence). The timing of introduction of biologic agents is a matter of debate and more studies are needed to assess stepwise approach versus earlier administration of biologic agents in patients with moderate to severe disease. The 2019 British Society of Gastroenterology guidelines suggest that systemic corticosteroids are still an effective initial therapy for uncomplicated luminal moderate to severe disease, regardless of disease location; however, every effort should be made to limit exposure (strong recommendation, high-quality evidence). In patients with an aggressive disease course, or high risk, poor prognostic factors, early introduction of biologics may be considered (weak recommendation, moderate-quality evidence). High risk features include extensive disease, complex (stricturing or penetrating disease), perianal fistulizing disease, age under 40 years at diagnosis, and the need for steroids to control index flare; however, the predictive power of these features is limited.

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.

Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis
The primary facets of immune-related adverse event (irAE) management include recognition and grading of toxicity, immunosuppression, and individualized modification to ICI administration. Early recognition of symptoms and prompt intervention are key goals for the management of immunotherapy-related toxicity. Significant irAEs often necessitate holding immunotherapy, with permanent discontinuation of the class of agent associated with the toxicity in the setting of certain severe irAEs. Per NCCN guidelines for the Management of Immunotherapy Related Toxicities corticosteroids are the mainstay treatment for ICI-related toxicity; however, severe or steroid-refractory irAEs may require administration of additional immunosuppressive agents. Recommendation for use of specific immune-modulating agents to manage irAEs are typically extrapolated from evidence for treating autoimmune conditions of the relevant organ system. Case reports have described the use of vedolizumab for treating ICI-induced enterocolitis. Vedolizumab may provide more specific immune suppression for the inflamed GI mucosa, hence theoretically sparing systemic immune suppression and anti-tumor immune responses. Case series and reports have also documented successful treatment of ICI-mediated, steroid-dependent, or steroid-refractory enterocolitis with vedolizumab.

References:

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2. Tyruko [package Insert]. Princeton, NJ; Sandoz, Inc.; August 2023. Accessed February 2024.
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4. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022
5. 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
6. National Institute for Health and Care Excellence. NICE 2019. Ulcerative colitis: management. Published 03 May 2019. NICE guideline [NG130]. https://www.nice.org.uk/guidance/ng130
7. National Comprehensive Cancer Network. Management of Immunotherapy-Related Toxicities (Version 1.2024). NCCN. December 7, 2023. Accessed February 20, 2024. http://www.nccn.org/professionals/physician_gls/pdf/ immunotherapy.pdf

History:

Approved Date	Effective Date	Version	Action and Summary of Changes
08.14.2024	07.01.2025	66.27.00.AJ-6	- Split Tysabri from policy -Updated number of preferred products for Crohn's and UC indications
08.14.2024	04.01.2025	66.27.00.AJ-5	- Added language for preferred adalimumab biosimilars - Formatting updates
08.14.2024	03.01.2025	66.27.00.AJ-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
08.20.2020	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