

## Entyvio™ (vedolizumab) (Intravenous)

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**Effective Date:** 01/01/2020

**Review date:** 09/18/2019, 12/18/2019, 4/29/2020, 8/3/2020, 5/06/2021, 3/3/2022, 8/10/23, 12/14/2023, 01/10/2024, 3/13/2024, 7/17/2024

**Scope:** Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

### I. Length of Authorization

- Coverage will be provided for 4 months initially and may be renewed every 6 months thereafter.
- Immune Checkpoint Inhibitor related diarrhea/colitis: 3 doses and may not be renewed
- Therapy for Ulcerative Colitis in patients who will be receiving subcutaneous maintenance doses: Coverage will be provided for 2 intravenous doses and 4 subcutaneous doses

### II. Dosing Limits

#### A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

**Loading Dose:**

- Entyvio 300 mg single use vial: 1 vial at weeks 0, 2, & 6 (3 vials total per 42 days)

**Maintenance Dose:**

- Entyvio 300 mg single use vial: 1 vial every 8 weeks (56 days)

#### B. Max Units (per dose and over time) [Medical Benefit]:

**Crohn's Disease and Ulcerative Colitis:**

- **Loading Dose:** 300 billable units at weeks 0, 2, & 6
- **Maintenance Dose:** 300 billable units every 8 weeks

**Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis**

- 300 billable units (300 mg) at weeks 0, 2, & 6

### III. Summary of Evidence

Clinical trials evaluating the efficacy and safety of Entyvio have demonstrated its effectiveness in the treatment of moderate to severe Crohn's disease (CD) and ulcerative colitis (UC). In patients with CD, Entyvio has shown significant improvements in clinical response, clinical remission, and mucosal healing

compared to placebo or other biologic agents. Similarly, in patients with UC, Entyvio has demonstrated efficacy in inducing and maintaining clinical remission, improving endoscopic and histologic outcomes, and reducing the need for corticosteroids and hospitalizations. Entyvio has a favorable safety profile, with common adverse events including headache, nasopharyngitis, and abdominal pain.

#### IV. Initial Approval Criteria

Coverage is provided in the following conditions:

- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements
- Must be prescribed by, or in consultation with, a specialist in gastroenterology; **AND**
- Patient aged 18 years or older; **AND**
- Patient is free of any active, severe infections; **AND**
- Patient has been screened for tuberculosis according to local practice (if applicable); **AND**
- Entyvio will not be used concomitantly with an injectable biologic response modifier including TNF-inhibitors (e.g., Humira (adalimumab), Enbrel (etanercept), Remicade (infliximab), etc.) and IL-inhibitors (e.g., Cosentyx (secukinumab), Tremfya (guselkumab), Ilumya (tildrakizumab), Skyrizi (risankizumab), Bimzelx (bimekizumab), Omvoh (mirikizumab), etc.) or other oral non-biologic agent (e.g., Otezla (apremilast), Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Velsipity (etrasimod), etc.)
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**

#### Crohn's disease †

- Documented moderate to severe disease; **AND**
- Medicaid and MMP members must have a documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of corticosteroids or immunomodulators (e.g., azathioprine, 6-mercaptopurine, or methotrexate, etc.); **AND**
- Medicaid and MMP members must have a documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of adalimumab; **OR**
- Commercial members must have a documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of corticosteroids or immunomodulators (e.g., azathioprine, 6-mercaptopurine, or methotrexate, etc.); **OR**
- Commercial members must have a documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of on previous therapy with a TNF modifier such as adalimumab, certolizumab, or infliximab

### Ulcerative colitis †

- Documented moderate to severe disease; **AND**
- Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of corticosteroids or immunomodulators (e.g., azathioprine, 6-mercaptopurine, or methotrexate)

### Management of Immune Checkpoint Inhibitor related diarrhea/colitis ‡

- Patient has been receiving therapy with an immune checkpoint inhibitor (e.g., nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, cemiplimab, ipilimumab, tremelimumab, dostarlimab, retifanlimab, etc.); **AND**
  - Patient has mild (G1) diarrhea or colitis related to their immunotherapy with persistent or progressive symptoms and a positive lactoferrin/calprotectin; **OR**
  - Patient has moderate (G2) to severe (G3-4) diarrhea or colitis related to their immunotherapy

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s)

## V. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet criteria identified in section IV; **AND**
- Patient is receiving ongoing monitoring for presence of TB or other active infections; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: anaphylaxis or other serious allergic reactions, severe infections, progressive multifocal leukoencephalopathy (PML), jaundice or other evidence of significant liver injury, etc.; **AND**

### Crohn's Disease

- Disease response as indicated by improvement in signs and symptoms compared to baseline such as endoscopic activity, number of liquid stools, presence and severity of abdominal pain, presence of abdominal mass, body weight compared to IBW, hematocrit, presence of extra intestinal complications, use of anti-diarrheal drugs, tapering or discontinuation of corticosteroid therapy, and/or an improvement on a disease activity scoring tool [e.g., an improvement on the Crohn's Disease Activity Index (CDAI) score or the Harvey-Bradshaw Index score].

### Ulcerative Colitis

- Disease response as indicated by improvement in signs and symptoms compared to baseline such as stool frequency, rectal bleeding, and/or endoscopic activity, tapering or discontinuation of corticosteroid therapy, normalization of C-reactive protein (CRP) or fecal calprotectin (FC), and/or an improvement on a disease activity scoring tool [e.g., an improvement on the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) score or the Mayo Score].

### Management of Immune Checkpoint Inhibitor related diarrhea/colitis ‡

- May not be renewed

## VI. Dosage/Administration

Indication	Dose
Crohn's Disease	<u>Loading dose:</u> 300 mg, intravenously, at weeks 0, 2, & 6 <u>Maintenance dose:</u> 300 mg, intravenously, every 8 weeks thereafter
Ulcerative Colitis	<u>Loading dose:</u> <ul style="list-style-type: none"> <li>• Patients who will be receiving <u>intravenous</u> maintenance doses: Administer 300 mg intravenously at weeks 0, 2, &amp; 6 (<i>see maintenance dosing below</i>)</li> <li>• Patients who will be receiving <u>subcutaneous</u> maintenance doses: Administer 300 mg intravenously at weeks 0 and 2, (<i>see Entyvio SC maintenance dosing starting at week 6</i>).</li> </ul> <u>Maintenance dose:</u> <ul style="list-style-type: none"> <li>• 300 mg, intravenously, every 8 weeks thereafter; <u>OR</u></li> <li>• 108 mg, subcutaneously, starting week 6 and every 2 weeks thereafter</li> </ul>
Immune Checkpoint Inhibitor related diarrhea/colitis	300 mg, intravenously, at weeks 0, 2, & 6

## VII. Other

- Note: Entyvio 108 mg subcutaneous dose is only available through the pharmacy benefit for all lines of business.

## VIII. Billing Code/Availability Information

### Jcode:

- J3380 - Injection, vedolizumab, 1 mg; 1 billable unit = 1 mg

### NDC:

- Entyvio 300 mg single use vial: 67464-0300-xx

## IX. References

1. Entyvio [package insert]. Deerfield, IL; Takeda Pharmaceuticals America, Inc; August 2021. Accessed March 2024.
2. Lichtenstein GR, Loftus EV, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113: 481-517. doi: 10.1038/ajg.2018.27; published online 27 March 2018
3. Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol*. 2010 Mar;105(3):501-23.
4. Dignass A, Lindsay JO, Sturm A, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 2: current management. *J Crohns Colitis*. 2012 Dec;6(10):991-1030.
5. Terdiman JP, Gruss CB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti-TNF- $\alpha$  biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. *Gastroenterology*. 2013 Dec;145(6):1459-63. doi: 10.1053/j.gastro.2013.10.047.
6. Gomollón F, Dignass A, Annese V, et al. EUROPEAN Evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 1: Diagnosis and medical management. *J Crohns Colitis*. 2016 Sep 22. pii: jjw168.
7. Harbord M, Eliakim R, Bettenworth D, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. *J Crohns Colitis*. 2017 Jan 28. doi: 10.1093/ecco-jcc/jjx009.
8. National Institute for Health and Care Excellence. NICE 2012. Crohn's Disease: Management. Published 10 October 2012. Clinical Guideline [CG152]. <https://www.nice.org.uk/guidance/cg152/resources/crohns-disease-management-pdf-35109627942085>.
9. Lewis JD, Chuai S, Nessel L, et al. Use of the Non-invasive Components of the Mayo Score to Assess Clinical Response in Ulcerative Colitis. *Inflamm Bowel Dis*. 2008 Dec; 14(12): 1660–1666. doi: 10.1002/ibd.20520

10. Paine ER. Colonoscopic evaluation in ulcerative colitis. *Gastroenterol Rep (Oxf)*. 2014 Aug; 2(3): 161–168.
11. Walsh AJ, Bryant RV, Travis SPL. Current best practice for disease activity assessment in IBD. *Nature Reviews Gastroenterology & Hepatology* 13, 567–579 (2016) doi:10.1038/nrgastro.2016.128
12. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019 Mar;114(3):384-413.
13. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) vedolizumab. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc.” To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2019.
14. Bergqvist, V, Hertervig E, Gedeon P, et al. Vedolizumab treatment for immune checkpoint inhibitor-induced enterocolitis. *Cancer Immunology Immunotherapy* 66: 581-592, No. 5, May 2017.

### Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications



ICD-10	ICD-10 Description
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding

ICD-10	ICD-10 Description
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications
K52.1	Toxic gastroenteritis and colitis
R19.7	Diarrhea, unspecified



## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC