Entyvio® (vedolizumab)
(Intravenous)

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I. Length of Authorization

Coverage will be provided for 14 weeks initially and may be renewed every 6 months thereafter unless otherwise specified.

- Dose escalation requests for Crohn's Disease and Ulcerative Colitis: Coverage will be provided for 3 months and may be renewed every 6 months thereafter (*see Section V for therapy continuation details*).
- Therapy for the Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis: Coverage will be provided for 3 doses total 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 *[see Entyvio SQ policy – Document Number: IC-0733]*

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

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 4 weeks (28 days)

B. Max Units (per dose and over time) [HCPCS Unit]:

Crohn's Disease and Ulcerative Colitis:

- Loading Dose: 300 billable units (300 mg) at weeks 0, 2, & 6
- Maintenance Dose: 300 billable units (300 mg) every 4 weeks

Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis

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

III. Initial Approval Criteria [1]

Site of care specialty infusion program requirements are met (refer to EOCCO Site of Care policy).

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Patient is up to date with all vaccinations, in accordance with current immunization guidelines, prior to initiating therapy; **AND**

Universal Criteria [1]

- Patient does not have an active infection, including clinically important localized infections; **AND**
- Patient has been evaluated and screened for the presence of latent tuberculosis (TB) infection prior to initiating treatment and will receive ongoing monitoring for presence of TB during treatment; **AND**
- Patient is not on concurrent treatment with another integrin receptor antagonist, TNF-inhibitor, IL-inhibitor, biologic response modifier or other non-biologic agent (i.e., apremilast, tofacitinib, baricitinib, upadacitinib, abrocitinib, deucravacitinib, etc.); **AND**

Crohn's Disease † [1,2,15,16]

- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Documented moderate to severe active 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, etc.); **OR**
    - Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial on previous therapy with a Crohn's Disease indicated TNF modifier (i.e., adalimumab, certolizumab, or infliximab)

Ulcerative Colitis † [1,12,18-20]

- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Documented moderate to severe active disease; **AND**
    - Documented failure or ineffective response to a minimum 3-month trial of conventional therapy [aminosalicylates, corticosteroids, or immunomodulators (e.g.,

azathioprine, 6-mercaptopurine, methotrexate, etc.)] at maximum tolerated doses, unless there is a contraindication or intolerance to use; **OR**

- Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial on previous therapy with an Ulcerative Colitis indicated TNF modifier (i.e., adalimumab, golimumab, or infliximab)

Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis ‡ [13,14]

- 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); **Φ** Orphan Drug

IV. Renewal Criteria [1]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet universal and indication-specific criteria as identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: anaphylaxis or other serious allergic, severe infusion-related or hypersensitivity reactions, severe infections, progressive multifocal leukoencephalopathy (PML), jaundice or other evidence of significant liver injury, etc.; **AND**

Crohn's Disease [11,16]

- 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 [9-11,20]

- 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, 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 ‡ [13,14]

- May not be renewed.

V. Dosage/Administration [1,13,17]

Indication	Dose
Crohn's Disease	**Induction dose:** • Administer 300 mg intravenously at weeks 0, 2, & 6 **Maintenance dose:** • Administer 300 mg intravenously every 8 weeks thereafter ******NOTE:** Requests for higher dosing must be reviewed according to the dose escalation information below*
Ulcerative Colitis	**Induction dose:** • Patients who will be receiving intravenous maintenance doses: Administer 300 mg intravenously at weeks 0, 2, & 6 *(see maintenance dosing below)* • Patients who will be receiving subcutaneous maintenance doses: Administer 300 mg intravenously at weeks 0 and 2 *(see Entyvio SQ policy [Document Number: IC-0733] for maintenance dosing starting at week 6).* **Maintenance dose:** Administer 300 mg intravenously every 8 weeks thereafter ******NOTE:** Requests for higher intravenous dosing must be reviewed according to the dose escalation information below*
Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis	Administer 300 mg intravenously at weeks 0, 2, & 6
Dose escalation (up to the maximum dose and frequency specified below) may occur upon clinical review on a case-by-case basis provided that the patient has: ○ Shown an initial response to therapy; **AND** ○ Received the three loading doses at the dose AND interval specified above; **AND** ○ Received a minimum of one maintenance dose at the dose AND interval specified above; **AND** ○ Responded to therapy (by treatment week 14*) with subsequent loss of response; **AND** ○ Dose escalation must not exceed the following limits:	

Indication	Dose
	▪ 300 mg every 4 weeks ➢ Coverage will be provided for 3 months with continued approval (as specified in Sections I & IV) contingent upon demonstration of clinical improvement and vedolizumab levels (if available)** • Patients who do not regain response should discontinue therapy • Patients who are responding to therapy may continue with their current dosing**
*Note: • Request for dose escalation prior to week 14 will be evaluated considering the patient's clinical picture regarding severity of inflammation, factors which may result in subtherapeutic response to standard dosing (e.g., obesity, hypoalbuminemia, prior TNF-I exposure), timing of response and breakthrough/loss of response, AND one of the following: ○ vedolizumab trough (if available)** at week 14 is <14 micrograms/mL; **OR** ○ CRP elevation or calprotectin >150	
**vedolizumab trough levels must be obtained (if this is a covered test under the benefit). • Patients whose trough is 14-20 micrograms/mL may continue with 300 mg every 4 weeks. • Patients with a trough >20 micrograms/mL must increase the interval between administrations from 4 weeks to 6 weeks. Response should be assessed after receipt of 3 doses at this every 6-week interval. Those patients demonstrating loss of response may then decrease the interval back to 300 mg every 4 weeks. • Patients whose trough is <14 micrograms/mL are candidates to decrease the interval between administrations from 8 weeks to 4 weeks	

VI. Billing Code/Availability Information

HCPCS Code:

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

NDC:

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

VII. References

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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
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

ICD-10	ICD-10 Description
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
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

ICD-10	ICD-10 Description
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), Local Coverage Determinations (LCDs), and Local Coverage Article (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/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/LCA): 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