Medical Policy:

Entyvio™ (vedolizumab) Intravenous and Subcutaneous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.78	April 4, 2025	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Length of Authorization

- Coverage will be provided for 14 weeks initially and may be renewed every 6 months thereafter
- Immune Checkpoint Inhibitor related diarrhea/colitis: 3 doses and may not be renewed

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

Crohn's Disease and Ulcerative Colitis:

Loading Dose:

- 300 billable units at weeks 0, 2, & 6

Maintenance Dose:

- 300 billable units every 8 weeks

Subcutaneous Dose

- 108mg Subcutaneously every 2 weeks

Management of Immune Checkpoint Inhibitor-Related Diarrhea/Colitis

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

Guideline

I. Initial Approval Criteria

Coverage is provided in the following conditions:

- 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**
- Patient is not on concurrent treatment with another TNF-inhibitor, biologic response modifier or other non-biologic agent (i.e., apremilast, tofacitinib, baricitinib); **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**

1. Crohn's disease † (IV)

A. Documented moderate to severe disease; **AND**
   i. 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**
   ii. Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial on previous therapy with a TNF modifier such as adalimumab, golimumab, or infliximab **OR**
   iii. Patient has evidence of high-risk disease for which corticosteroids or immunomodulators are inadequate and biologic therapy is necessary; **OR**
   iv. Patient is already established on a biologic or targeted synthetic therapy for the treatment of CD

2. Ulcerative colitis † (IV)

A. Documented moderate to severe disease; **AND**
   i. 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); **OR**
   ii. Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial on previous therapy with a TNF modifier such as adalimumab, golimumab, or infliximab **OR**
   iii. Patient has evidence of high-risk disease for which corticosteroids or immunomodulators are inadequate and biologic therapy is necessary; **OR**
   iv. Patient is already established on a biologic or targeted synthetic therapy for the treatment of CD

3. Ulcerative Colitis † (Subcutaneous)

A. According to the prescriber, the patient is currently receiving Entyvio intravenous or will receive induction dosing with Entyvio intravenous within 2 months of initiating therapy with Entyvio subcutaneous; **AND**
B. Patient meets **ONE** of the following (i **OR** ii):
    i. Patient has had a trial of **ONE** systemic therapy; **OR**
    Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a mesalamine product does not count as a systemic therapy for ulcerative colitis. A trial of a biologic also counts as a trial of one systemic agent for ulcerative colitis.
    ii. Patient meets **BOTH** of the following (a) **AND** (b):
        a. Patient has pouchitis; **AND**
        b. Patient has tried an antibiotic, probiotic, corticosteroid enema, or mesalamine enema; **AND**
        Note: Examples of antibiotics include metronidazole and ciprofloxacin. Examples of corticosteroid enemas include hydrocortisone enema.
    iii. Patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; **OR**
    iv. Patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence).

4. Management of Immune Checkpoint Inhibitor related diarrhea/colitis ‡ (IV)

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

5. Acute Graft Versus Host Disease ‡

A. Patient has received an allogeneic hematopoietic stem cell transplant; **AND**
B. Used for steroid-refractory acute GVHD; **AND**
C. Used in combination with systemic corticosteroids as additional therapy following no response to first-line therapies

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

II. Renewal Criteria

Coverage can be renewed based upon the following criteria:
1. Patient continues to meet criteria identified above; **AND**
2. Patient is receiving ongoing monitoring for presence of TB or other active infections; **AND**
3. 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

1. 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 regain, hematocrit, presence of extra intestinal complications, use of anti-diarrheal drugs,

tapering or discontinuation of corticosteroid therapy, improvement in biomarker levels [i.e., fecal calprotectin or serum C-reactive protein (CRP)] and/or an improvement on a disease activity scoring tool [e.g., an improvement on the Harvey-Bradshaw Index score, etc].

Ulcerative Colitis

1. Disease response as indicated by improvement in signs and symptoms compared to baseline such as stool frequency, rectal bleeding, 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.

Management of Immune Checkpoint Inhibitor related diarrhea/colitis ‡

1. May not be renewed

Acute Graft Versus Host Disease

1. Response to therapy with an improvement in one or more of the following:
    i. Clinician assessments (e.g., NIH Skin Score, Upper GI Response Score, NIH Lung Symptom Score, etc.)
    ii. Patient-reported symptoms (e.g., Lee Symptom Scale, etc.)

Limitations/Exclusions

Entyvio is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

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

Applicable NDCs

Code	Description
67464-0300-xx	Entyvio 300 mg single use vial
64764-0108-21	Entyvio 108 mg/0.68 ml Subcutaneous Pen

ICD-10 Diagnoses

Code	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
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
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

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	4/4/2025	Annual Review: Addition to CD and UC IV criteria. Patient has evidence of high-risk disease for which corticosteroids or immunomodulators are inadequate and biologic therapy is necessary; OR Patient is already established on a biologic or targeted synthetic therapy for the treatment of CD. Addition to UC SQ - Patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; OR Patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence). Updated criteria for Management of Immune checkpoint inhibitor-related diarrhea/colitis Addition of Acute Graft Versus Host Disease ‡ with initial and renewal criteria.
EmblemHealth & ConnectiCare	3/13/2024	Annual Review: Formatting, Updated dosing limits, no criteria changes
EmblemHealth & ConnectiCare	12/12/2023	Addition of IV after Crohn's and Ulcerative Colitis Indication Addition of; **Ulcerative Colitis † (Subcutaneous)** A. According to the prescriber, the patient is currently receiving Entyvio intravenous or will receive induction dosing with Entyvio intravenous within 2 months of initiating therapy with Entyvio subcutaneous; **AND** B. Patient meets ONE of the following (a **OR** b): i. Patient has had a trial of ONE systemic therapy; **OR**

		Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a mesalamine product does not count as a systemic therapy for ulcerative colitis. A trial of a biologic also counts as a trial of one systemic agent for ulcerative colitis. ii. Patient meets BOTH of the following (i) **AND** (ii): a. Patient has pouchitis; **AND** b. Patient has tried an antibiotic, probiotic, corticosteroid enema, or mesalamine enema; **AND** *Note: Examples of antibiotics include metronidazole and ciprofloxacin. Examples of corticosteroid enemas include hydrocortisone enema.* Addition of NDC 64764-0108-21 -Entyvio 108 mg/0.68 ml Subcutaneous Pen
EmblemHealth & ConnectiCare	7/5/2023	Annual Review: Updated Length of Authorization: Removed "Coverage is provided for 12 months and may be renewed." Added "Coverage will be provided for 14 weeks initially and may be renewed every 6 months thereafter" Management of Immune Checkpoint Inhibitor related diarrhea/colitis ‡ Initial Criteria: Removed "Patient has diarrhea or colitis related to their immunotherapy; **AND** Documented moderate or severe disease; **AND"** Added "Patient has moderate (grade 2) to severe (grade 3-4) diarrhea or colitis related to their immunotherapy"
EmblemHealth & ConnectiCare	4/21/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	6/23/2020	Updated clinical criteria for Crohn's disease and Ulcerative Colitis to include trials with corticosteroids, immunomodulators (e.g. azathioprine, 6-mercaptopurine, or methotrexate, etc.) OR a TNF modifier such as adalimumab, certolizumab, or infliximab.

References

1. Entyvio [package insert]. Deerfield, IL; Takeda Pharmaceuticals America, Inc; May 2019. Accessed December 2019.
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-α 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
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13. 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.