Policy Number	RX501.117
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Vedolizumab

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical

journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

NOTE 1: Vedolizumab (Entyvio®) may be self-administered. Refer to the applicable pharmacy benefit plan when self-administered.

NOTE 2: This medical policy does NOT address oncologic indications. This medical policy IS NOT TO BE USED for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications.

Intravenous administration of vedolizumab (Entyvio®) **may be considered medically necessary** for the following U.S. Food and Drug Administration (FDA) labeled indications:

- Adult individuals (18 years of age or older) with moderate to severely active ulcerative colitis;
- Adult individuals (18 years of age or older) with moderate to severely active Crohn's disease.

NOTE 3: See Description section for information on disease severity classification(s).

Intravenous administration of vedolizumab (Entyvio®) **is considered experimental, investigational and/or unproven** for all other non-FDA approved indications.

NOTE 4: Vedolizumab (Entyvio®) shall not be used concurrently with natalizumab or tumor necrosis factor (TNF) blockers.

Policy Guidelines

None.

Description

Inflammatory Bowel Disease
Inflammatory bowel disease (IBD) is a general term used to describe diseases that cause inflammation of the intestines. Crohn's disease (CD) and ulcerative colitis (UC) are the 2 major IBDs. (2)

In Crohn's disease, inflammation usually occurs in the lower part of the small intestine (distal ileum) but may affect any part of the digestive tract. The inflammation in CD extends deep into the affected tissue, in contrast to UC, which causes inflammation and ulcers in the inner lining of the colon and rectum. Inflammation in CD is asymmetrical and segmental, with areas of both healthy and diseased tissue, in contrast to UC where inflammation spreads upward from the rectum toward the large intestines, leaving no healthy tissue in its path. (3, 4)

Both CD and UC are chronic and affect men and women on an approximately equal basis and are seen primarily in northern Europe and North America. Over the past decade, several reports have noted an increase in the prevalence of CD in various geographic regions. Although there are many theories concerning the cause of CD and UC, none have been proven. Approximately 5 to 20 percent of individuals with CD have a blood relative with some form of IBD. Symptoms can occur at any age, although they often develop between the ages of 15 and 35. Since many of the symptoms of CD and UC are similar, diagnosis is often difficult, time consuming, and invasive. Once a diagnosis of CD or UC is made, determining the severity of disease becomes important in order to select the appropriate treatment algorithm. (3-6)

Treatment of CD is based on disease severity and the impact on the individual's quality of life. The gastroenterologist may use the Crohn's Disease Activity Index (CDAI, Table 1) in addition to other tests to determine disease severity. The CDAI range is divided into 4 categories (7):

- Remission (<150);
- Mild to moderate (150-220);
- Moderate to severe (220 to 450); and
- Severe (>450).

Moderate to severe Crohn's may also include diarrhea, abdominal pain and tenderness, intermittent nausea or vomiting, significant weight loss and moderate to severe active intestinal lining disease. (7)

Individuals with severe CD often exhibit more prominent symptoms of diarrhea, abdominal pain and tenderness, persistent vomiting, significant weight loss with marked muscle loss, fever, evidence of intestinal obstruction or abscesses and severe intestinal lining disease. (7)

Table 1. Crohn's Disease Activity Index and Weighting Factors (8)

Clinical or laboratory variable	Weighting factor
Number of liquid or soft stools each day for seven days- Total (1 week)	x 2
Abdominal pain (graded from 0-3 on severity) each day for seven days- add up each individual day or if the pain level was consistent, take the average level of abdominal pain and multiply by seven. 0=none, 1=mild, 2=moderate, 3=severe. Total (past week)	x 5
General well-being, subjectively assessed from 0 (generally well), 1= slightly under par, 2=poor, 3=very poor, 4 =terrible. Add up past 7 days prior to visit.	x 7

Presence of complications - One point each is added for each set of complications: • Presence of joint pains (arthralgia) or arthritis. • Inflammation of the iris or uveitis. • Presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers. • Anal fissures, fistulae or abscesses. • Other fistulae. • Fever during the previous week.	x 20
Taking Lomotil or opiates for diarrhea	x 30
Presence of an abdominal mass (0 as none, 2 as questionable, 5 as definite)	x 10
Hematocrit of <0.47 in men and <0.42 in women	x 6
Percentage deviation from standard weight	x 1

In their 2025 Clinical Guideline for UC in Adults (9), the ACG proposed definitions of mildly, moderately, and severely active disease, as outlined in Table 2 below.

Table 2. Proposed American College of Gastroenterology Ulcerative Colitis Activity Index (9)

	Remission	**Mild**	**Moderate-Severe**	**Fulminant**
Stools (no./d)	Formed stools	<4	>6	>10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	<75% of normal	Transfusion required
ESR	<30	<30	>30	>30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
FC (µg/g)	<150-200	>150-200	>150-200	>150-200
Endoscopy (Mayo subscore)	0-1	1	2-3	3
Endoscopy (UCEIS)	0-1	2-4	5-8	7-8

The above factors are general guides for disease activity. With the exception of remission, a patient does not need to have all the factors to be considered in a specific category.
CRP: C-reactive protein; d: day; ESR: erythrocyte sedimentation rate; FC: fecal calprotectin; no: number; UCEIS: Ulcerative Colitis Endoscopic Index of Severity.

The Mayo Score/Disease Activity Index (DAI) for Ulcerative Colitis is a scoring system used for individuals with known UC, and may be used when considering changing, adding, or stopping a UC medication. This tool is not used to diagnose UC. (10) The higher the score (maximum 12 points), the more severe the ulcerative colitis.

Vedolizumab (Entyvio®)

Vedolizumab is a humanized monoclonal antibody that specifically binds to the α4β7 integrin and blocks the interaction of α4β7 integrin with mucosal cell adhesion molecule-1 (MAdCAM-1) and inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. Vedolizumab does not bind to or inhibit function of the α4β1 and αEβ7 integrins and does not antagonize the interaction of α4 integrins with vascular cell adhesion molecule-1 (VCAM-1). (1)

The α4β7 integrin is expressed on the surface of a discrete subset of memory T-lymphocytes that preferentially migrate into the gastrointestinal tract. MAdCAM-1 is mainly expressed on gut endothelial cells and plays a critical role in the homing of T-lymphocytes to gut lymph tissue. The interaction of the α4β7 integrin with MAdCAM-1 has been implicated as an important contributor to the chronic inflammation that is a hallmark of UC and CD. (1)

Regulatory Status
The U.S. Food and Drug Administration (FDA) approved vedolizumab (Entyvio®) for intravenous (IV) injection on May 20, 2014, for the treatment of adults with (1, 11):

- Moderate to severe ulcerative colitis;
- Moderate to severe Crohn's disease.

On September 27, 2023, the FDA approved a subcutaneous administration of Entyvio® for maintenance therapy in adults with moderately to severely active ulcerative colitis after induction therapy with Entyvio IV. (1, 11)

Refer to the applicable pharmacy benefit plan when self-administered as this policy is specific to the use of IV administration of vedolizumab (Entyvio®).

Rationale

This policy was originally developed in 2020 and is based on the U.S. Food and Drug Administration (FDA) labeled indications for vedolizumab (Entyvio®).

Ulcerative Colitis
Intravenous Administration
The safety and efficacy of Entyvio were evaluated in two randomized, double-blind, placebo-controlled trials (UC Trials I and II) in adult patients with moderately to severely active ulcerative colitis (UC) defined as Mayo score of 6 to 12 with endoscopy subscore of 2 or 3.

The Mayo score ranges from 0 to 12 and has 4 subscales that are each scored from 0 (normal) to 3 (most severe): stool frequency, rectal bleeding, findings on endoscopy, and physician global assessment. An endoscopy subscore of 2 is defined by marked erythema, lack of vascular pattern, friability, and erosions; an endoscopy subscore of 3 is defined by spontaneous bleeding and ulceration.

Enrolled patients in the U.S. had over the previous 5-year period an inadequate response or intolerance to immunomodulator therapy (i.e., azathioprine or 6-mercaptopurine) and/or an inadequate response, loss of response, or intolerance to a tumor necrosis factor (TNF) blocker. Outside the U.S., prior treatment with corticosteroids was sufficient for entry if over the previous 5-year period the patients were corticosteroid dependent (i.e., unable to successfully taper corticosteroids without a return of the symptoms of UC) or had an inadequate response or intolerance to corticosteroids.

Patients that had received natalizumab ever in the past and patients that had received a TNF blocker in the past 60 days were excluded from enrollment. Concomitant use of natalizumab or a TNF blocker was not allowed. (1)

UC Trial I - Intravenous

In UC Trial I, 374 patients were randomized in a double-blind fashion (3:2) to receive Entyvio 300 mg or placebo by intravenous infusion at Week 0 and Week 2. Efficacy assessments were at Week 6. Concomitant stable dosages of aminosalicylates, corticosteroids (prednisone dosage ≤30 mg/day or equivalent), and immunomodulators (azathioprine or 6- mercaptopurine) were permitted through Week 6.

At baseline, patients received corticosteroids (54%), immunomodulators (azathioprine or 6-mercaptopurine) (30%), and/or aminosalicylates (74%). Thirty-nine percent of patients had an inadequate response, loss of response, or intolerance to TNF blocker therapy. Eighteen percent of patients had an inadequate response, inability to taper or intolerance to prior corticosteroid treatment only (i.e., had not received prior immunomodulators or TNF blockers). The median baseline Mayo score was 9 in the Entyvio group and 8 in the placebo group.

In UC Trial I, a greater percentage of patients treated with Entyvio compared to patients treated with placebo achieved clinical response at Week 6 (defined in Table 3). A greater percentage of patients treated with Entyvio compared to patients treated with placebo also achieved clinical remission at Week 6 (defined in Table 3). In addition, a greater percentage of patients treated with Entyvio had an improvement in endoscopic appearance of the mucosa at Week 6 (defined in Table 3. (1)

Table 3. Proportion of Patients Meeting Efficacy Endpoints at Week 6 (UC Trial I) (1)

Endpoint	**Placebo N=149**	**Entyvio N=225**	**p-value**	**Treatment Difference and 95% CI**
Clinical response* at Week 6	26%	47%	<0.001	22% (12%, 32%)
Clinical remission† at Week 6	5%	17%	0.001	12% (5%, 18%)
Improvement of endoscopic appearance of the mucosa‡ at Week 6	25%	41%	0.001	16% (6%, 26%)

* Clinical response: reduction in complete Mayo score of ³3 points and ³30% from baseline with an accompanying decrease in rectal bleeding subscore of ³1 point or absolute rectal bleeding subscore of ≤1 point.
† Clinical remission: complete Mayo score of ≤2 points and no individual subscore >1 point.
‡ Improvement of endoscopic appearance of the mucosa: Mayo endoscopy subscore of 0 (normal or inactive disease) or 1 (erythema, decreased vascular pattern, mild friability).

UC Trial II - Intravenous

In order to be randomized to treatment in UC Trial II, patients had to have received Entyvio and be in clinical response at Week 6. Patients could have come from either UC Trial I or from a group who received Entyvio open-label.

In UC Trial II, 373 patients were randomized in a double-blind fashion (1:1:1) to one of the following regimens beginning at Week 6: Entyvio 300 mg every 8 weeks, Entyvio 300 mg every 4 weeks or placebo every 4 weeks. Efficacy assessments were at Week 52. Concomitant aminosalicylates and corticosteroids were permitted through Week 52. Concomitant immunomodulators (azathioprine or 6-mercaptopurine) were permitted outside the U.S. but were not permitted beyond Week 6 in the U.S.

At Week 6, patients were receiving corticosteroids (61%), immunomodulators (azathioprine or 6-mercaptopurine) (32%), and aminosalicylates (75%). Thirty-two percent of patients had an inadequate response, loss of response, or intolerance to TNF blocker therapy. At Week 6, the median Mayo score was 8 in the Entyvio every 8-week group, the Entyvio every 4-week group, and the placebo group. Patients who had achieved clinical response at week 6 and were receiving corticosteroids were required to begin a corticosteroid-tapering regimen at Week 6.

In UC Trial II, a greater percentage of patients in groups treated with Entyvio as compared to placebo achieved clinical remission at Week 52 and maintained clinical response (clinical response at both Weeks 6 and 52) (Table 4). In addition, a greater percentage of patients in groups treated with Entyvio as compared to placebo were in clinical remission at both Weeks 6 and 52 and had improvement of endoscopic appearance of the mucosa at Week 52 (Table 4). In the subgroup of patients who achieved clinical response at Week 6 and were receiving corticosteroid medication at baseline, a greater proportion of patients in groups treated with Entyvio as compared to placebo discontinued corticosteroids and were in clinical remission at Week 52 (Table 4). The Entyvio every 4-week dosing regimen did not demonstrate additional clinical benefit over every 8-week dosing regimen. Every 4-week dosing regimen is not the recommended dosing regimen. (1)

Table 4. Proportion of Patients Meeting Efficacy Endpoints at Week 52* (UC Trial II) (1)

Endpoint	**Placebo† N=126**	**Entyvio Every 8 Weeks N=122**	**p-value**	**Treatment Difference and 95% CI**
Clinical remission at Week 52	16%	42%	<0.001	26%

				(15%, 37%)
Clinical response at both Weeks 6 and 52	24%	57%	<0.001	32% (20%, 44%)
Improvement of endoscopic appearance of the mucosa[‡] at Week 52	20%	52%	<0.001	18% (4%, 31%)
Clinical remission at Both Weeks 6 and 52	9%	21%	0.008	12% (3%, 21%)
Corticosteroid-free clinical remission[§]	14%[§]	31%[§]	0.012	18% (4%, 31%)

[*] Patients must have achieved clinical response at Week 6 to continue into UC Trial II. This group includes patients that were not in clinical remission at Week 6.
[†] The placebo group includes those patients who received Entyvio at Week 0 and Week 2 and were randomized to receive placebo from Week 6 through Week 52.
[‡] Improvement of endoscopic appearance of the mucosa: Mayo endoscopy subscore of 0 (normal or inactive disease) or 1 (erythema, decreased vascular pattern, mild friability) at Week 52.
[§] Corticosteroid-free clinical remission: Assessed in the subgroup of patients who were receiving corticosteroids at baseline and who were in clinical response at Week 6 (n=72 for placebo and n=70 for Entyvio every eight weeks). Corticosteroid-free clinical remission was defined as the proportion of patients in this subgroup that discontinued corticosteroids by Week 52 and were in clinical remission at Week 52.

Crohn's Disease
The safety and efficacy of Entyvio were evaluated in 3 randomized, double-blind, placebo-controlled clinical trials (CD Trials I, II, and III) in adult patients with moderately to severely active Crohn's disease (CD) (Crohn's Disease Activity Index [CDAI] score of 220 to 450). (1)

CD Trial I - Intravenous
In CD Trial I, 368 patients were randomized in a double-blind fashion (3:2) to receive Entyvio 300 mg or placebo by intravenous infusion at Week 0 and Week 2. Efficacy assessments were at Week 6. Concomitant stable dosages of aminosalicylates, corticosteroids (prednisone dosage ≤30 mg/day or equivalent), and immunomodulators (azathioprine, 6- mercaptopurine or methotrexate) were permitted through Week 6.

At baseline, patients were receiving corticosteroids (49%), immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate) (35%), and/or aminosalicylates (46%). Forty-eight percent of the patients had an inadequate response, loss of response, or intolerance to TNF blocker therapy. Seventeen percent of patients had inadequate response, inability to taper, or intolerance to prior corticosteroid treatment only (i.e., had not received prior immunomodulators or TNF blockers). The median baseline CDAI score was 324 in the intravenous ENTYVIO group and 319 in the placebo group.

In CD Trial I, a statistically significantly higher percentage of patients treated with Entyvio achieved clinical remission (defined as CDAI ≤150) as compared to placebo at Week 6 (Table 5). The difference in the percentage of patients who demonstrated clinical response (defined as a

≥100-point decrease in CDAI score from baseline), was however, not statistically significant at Week 6. (1)

CD Trial II - Intravenous

Compared to CD Trial I, CD Trial II enrolled a higher number of patients who had over the previous 5-year period had an inadequate response, loss of response, or intolerance to one or more TNF blockers (76%); this was the primary analysis population. In CD Trial II, 416 patients were randomized in a double-blind fashion (1:1) to receive either Entyvio 300 mg or placebo at Weeks 0, 2 and 6. Efficacy assessments were at Weeks 6 and 10. Concomitant aminosalicylates, corticosteroids, and immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate) were permitted through Week 10.

At baseline, patients were receiving corticosteroids (54%), immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate) (34%), and aminosalicylates (31%). The median baseline CDAI score was 317 in the ENTYVIO group and 301 in the placebo group.

For the primary endpoint (clinical remission at Week 6), treatment with Entyvio did not result in statistically significant improvement over placebo (Table 5). Secondary endpoints including assessments at Week 10 were not tested because the primary endpoint was not statistically significant. (1)

Table 5. Proportion of Patients in Clinical Remission at Week 6 (CD Trials I and II) (4)

	Placebo	**Entyvio**	**p-value**	**Treatment Difference and 95% CI**
CD Trial I: Clinical Remission* at Week 6	7% (10/148)	15% (32/220)	0.041‡	8% (1%, 14%)
CD Trial II†: Clinical Remission* at Week 6	12% (19/157)	15% (24/158)	NS§	3% (-5%, 11%)

* Clinical Remission: CDAI ≤150

† The primary analysis population for CD Trial II was patients that had an inadequate response, loss of response, or intolerance to one or more TNF blockers (76% of the overall population) ‡ Adjusted p-value for multiple comparisons of two primary endpoints

§ NS: Not significant (Secondary endpoints including assessments at Week 10 were not tested because the CD Trial II primary endpoint was not statistically significant)

CD Trial III - Intravenous

In order to be randomized to treatment in CD Trial III, patients had to have received Entyvio and be in clinical response (defined as a ≥70-point decrease in CDAI score from baseline) at Week 6. Patients could have come from either CD Trial I or from a group who received Entyvio open-label.

In CD Trial III, 461 patients were randomized in a double-blind fashion (1:1:1) to one of the following regimens beginning at Week 6: Entyvio 300 mg every 8 weeks, Entyvio 300 mg every 4 weeks or placebo every 4 weeks. Efficacy assessments were at Week 52. Concomitant aminosalicylates and corticosteroids were permitted through Week 52.

At Week 6, patients were receiving corticosteroids (59%), immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate) (31%) and aminosalicylates (41%). Fifty-one percent of patients had an inadequate response, loss of response, or intolerance to TNF blocker therapy. At Week 6, the median CDAI score was 322 in the Entyvio every 8-week group, 316 in the Entyvio every 4-week group, and 315 in the placebo group. Patients who had achieved clinical response (≥70 decrease in CDAI score from baseline) at Week 6 and were receiving corticosteroids were required to begin a corticosteroid-tapering regimen at Week 6.

In CD Trial III, a greater percentage of patients in groups treated with Entyvio as compared to placebo were in clinical remission (defined as CDAI score ≤150) at Week 52. A greater percentage of patients in groups treated with Entyvio as compared to placebo had a clinical response (defined as ≥100 decrease in CDAI score from baseline) at Week 52 (Table 6). In the subgroup of patients who were receiving corticosteroids at baseline and who were in clinical response at Week 6 (defined as ≥70 decrease in CDAI score from baseline), a greater proportion of patients in groups treated with Entyvio as compared to placebo discontinued corticosteroids by Week 52 and were in clinical remission at Week 52 (Table 6). The Entyvio every 4-week dosing regimen did not demonstrate additional clinical benefit over every 8-week dosing regimen. (1)

Table 6. Proportion of Patients Meeting Efficacy Endpoints at Week 52[*] (CD Trial III) (1)

	Placebo[†] N=153	**Entyvio Every 8 Weeks N=154**	**p-value**	**Treatment Difference and 95% CI**
Clinical remission[‡] at Week 52	22%	39%	0.001	17% (7%, 28%)
Clinical response[§] at Week 52	30%	44%	0.013	13% (3%, 24%)
Corticosteroid-free clinical remission[#]	16%	32%	0.015	16% (3%, 29%)

CI: Confidence interval.

[*] This group includes patients that were not in clinical remission at Week 6. Patients must have achieved clinical response (defined as ≥70 decrease in CDAI from baseline) at Week 6 to continue into CD Trial III.

[†] The placebo group includes those patients who received Entyvio at Week 0 and Week 2, and were randomized to receive placebo from Week 6 through Week 52

[‡] Clinical remission: CDAI ≤150

[§] Clinical response: ≥100 decrease in CDAI from baseline

[#] Corticosteroid-free clinical remission: Assessed in the subgroup of patients who were receiving corticosteroids at baseline and who were in clinical response (defined as ≥70 decrease in CDAI from baseline) at Week 6 (n=82 for placebo and n=82 for Entyvio every eight weeks). Corticosteroid-free clinical remission was defined as the proportion of patients in this subgroup that discontinued corticosteroids by Week 52 and were in clinical remission at Week 52.

Summary of Evidence

Based on the clinical studies provided to the U.S. Food and Drug Administration (FDA), Entyvio® may be considered medically necessary for the treatment of adult patients with moderate to severe ulcerative colitis (UC) or moderate to severe Crohn's disease (CD). Intravenous administration of vedolizumab (Entyvio®) is considered experimental, investigational and/or unproven for all other non-FDA approved indications. Per the FDA label, the safety and efficacy of Entyvio in the pediatric population has not been established. (1)

Professional Guidelines and Position Statements

American College of Gastroenterology (ACG)

The 2025 ACG guidelines made the following recommendations (12):

- Intravenous (IV) vedolizumab for induction and maintenance of symptomatic remission in individuals with moderately to severely active Crohn's disease (strong recommendation, moderate level of evidence).
- Subcutaneous vedolizumab as an option for maintenance of remission in patients with moderately to severely active CD who respond to 2 IV induction doses of vedolizumab (strong recommendation, moderate level of evidence).
- Vedolizumab use for induction of remission of perianal fistulizing CD (conditional recommendation, very low level of evidence).
- In patients with high-risk CD, ACG recommends vedolizumab therapy to prevent postoperative recurrence (conditional recommendation, low level of evidence).

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J3380

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
08/15/2025	Document updated with literature review. The following changes were made to Coverage: 1) Modified Note 4 to state: "Vedolizumab (Entyvio®) shall not be used concurrently with natalizumab or tumor necrosis factor (TNF) blockers. 2) Added "non-FDA approved" to the existing experimental, investigational and/or unproven statement. 3) renumbered all notes. Added references 2-7 and 10; others updated.
06/15/2024	Reviewed. No changes.
12/01/2023	Document updated with literature review. The following changes were made to Coverage: 1) Added NOTE 1 and renumbered all subsequent NOTEs; 2) Specified "intravenous administration" in Coverage statements; and 3) Changed "patients" to "individuals". No new references added; some updated.
06/01/2023	Document updated with literature review. The following change was made to Coverage: Added NOTE 2 and NOTE 3. No new references added but some updated; one removed.
07/01/2021	Reviewed. No changes.
10/01/2020	New medical document originating from RX501.051. Vedolizumab (Entyvio®) may be considered medically necessary for the following U.S. Food and Drug Administration (FDA) labeled indications: 1) Adult patients (18 years of age or older) with moderate to severely active ulcerative colitis; 2) Adult patients (18 years of age or older) with moderate to severely active Crohn's disease. NOTE 1: See Description section for information on disease severity classification(s). Vedolizumab (Entyvio®) is considered experimental, investigational and/or unproven for all other indications.