WellMed Doctors helping patients for more than 25 years	**Effective Date:** 08/18/2022	**Revision Date(s):** 9/03/19, 12/10/20, 06/16/22
Department: PHARMACY	**MMC Review/ Approval Date(s):** 9/26/2019, 1/13/2021, 08/09/22	**Total Page(s): 9**

Policy Number: 054.003
Title: Coverage Determination Policy for Vedolizumab (Entyvio®)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:
WellMed Coverage Determination Policies are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support WellMed coverage decision making. WellMed may modify these Policy Guidelines at any time. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the WellMed Coverage Determination Policies is believed to be accurate and current as of the date of publication, and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

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Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

For all vedolizumab (Entyvio®) PA requests, there must be documentation to support member has been screened and negative for TB, active and/or any other serious infections.

Coverage Determination (Initial/New Requests)

WellMed Medical Management will cover vedolizumab (Entyvio®) as medically necessary when **ALL** of the following are met:

1. Crohn's disease

a) Member has diagnosis of moderately to severely active Crohn's disease
b) History of failure, contraindication or intolerance to at least one of the following conventional therapies:
   - Tumor necrosis factor inhibitor (e.g. Humira (adalimumab), Cimzia (certolizumab)
   - Immunomodulator (e.g. azathioprine, 6-mercaptopurine)
   - Corticosteroids (e.g. prednisone) or is corticosteroid dependent (unable to successfully taper without a return of symptoms)
c) Member is not receiving vedolizumab in combination with either of the following:
   - Biologic DMARD: infliximab (Remicade), adalimumab (Humira), golimumab (Simponi), ustekinumab (Stelara)
   - Janus kinase inhibitor: tofacitinib (Xeljanz/Xeljanz XR)
   - Natalizumab (Tysabri)
d) Initial authorization will be for no more than 14 weeks

2. Ulcerative colitis

a) Member has diagnosis of moderate to severe active ulcerative colitis
b) Member has documented history of inadequate response, intolerance, or contraindication to corticosteroids or immunomodulators for at least 3 months at maximum tolerated doses (azathioprine, methotrexate, prednisone or other steroids, 6-mercaptopurine)
c) Member has documented history of inadequate response, intolerance, or contraindication to one or more Tumor Necrosis Factor (TNF) inhibitors for at least 3 months at maximum tolerated doses (e.g. adalimumab, infliximab, golimumab)
d) Member is not receiving vedolizumab in combination with either of the following:
   - Biologic DMARD: infliximab (Remicade), adalimumab (Humira), golimumab (Simponi), ustekinumab (Stelara)
   - Janus kinase inhibitor: tofacitinib (Xeljanz/Xeljanz XR)
   - Natalizumab (Tysabri)
e) Initial authorization will be for no more than 14 weeks

3. **Immune Checkpoint Inhibitor-Related Toxicities (Non-FDA Indication)**
   a) Member has diagnosis of severe (G3-4) immunotherapy-related diarrhea or colitis
   b) Member has been receiving immune checkpoint inhibitor therapy (e.g. atezolizumab, durvalumab, nivolumab, pembrolizumab etc.)
   c) Member has documented history of inadequate response, intolerance, or contraindication to infliximab or has immune-related hepatitis
   d) Maximum of up to 3 doses will be authorized. (No Renewal)

Coverage Determination (Renewal/Continuation of Therapy Requests)

1. For all renewal requests, there must be clear documentation that there is positive clinical response (e.g. improvement from baseline in CDAI, Mayo clinic score, rectal bleeding etc.)
2. For patients who show no evidence of therapeutic benefit (refractory disease) by week 14, Entyvio® will no longer be approved for continuation per FDA-approved product labeling.
3. Member is receiving ongoing monitoring for presence of TB and active infections
4. The requested dosing is within the FDA recommended (refer to FDA Approved Indications and Dosing)

FDA Approved Dose and Indication:

Indication	Approved Dosing
Crohn's disease, Active: Moderate to severe	300 mg intravenous weeks 0, 2 and 6 then every 8 weeks thereafter
Ulcerative colitis, Active: Moderate to severe	300 mg intravenous weeks 0, 2 and 6 then every 8 weeks thereafter
Immune Checkpoint Inhibitor-Related Toxicities	300 mg intravenously, weeks 0, 2 and 6

FDA Approved Indications	Drug
Moderate to Severe Active Crohn's disease	**Vedolizumab (Entyvio®)**
Moderate to Severe Active Ulcerative colitis	**Vedolizumab (Entyvio®)**

General Background:

Vedolizumab is a recombinant humanized immunoglobulin G1 monoclonal antibody for the treatment of moderate to severe ulcerative colitis and Crohn's disease. It binds to alpha-4-beta-7- integrin receptor and blocks the interaction of alpha-4-beta-7- integrin with mucosal addressing cell adhesion molecule-1 (MAdCAM-1); thereby, inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue.

For patients who show no evidence of therapeutic benefit by week 14, Entyvio® package insert recommends discontinuing therapy. Vedolizumab use is associated with increased risk for developing infection. It is recommended for patient to be brought up to date with all immunizations before starting vedolizumab therapy. Vedolizumab is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to vedolizumab or any of its excipients (such as dyspnea, bronchospasm, urticaria, flushing, rash and increased heart rate). **Although rare, vedolizumab package insert recommends monitoring patients for any new or worsening neurological signs or symptoms associated with Progressive Multifocal Leukoencephalopathy (PML).**

Clinical Evidence:

Sandborn et al. evaluated efficacy of vedolizumab as induction and maintenance therapy for Crohn's disease. The trial was phase 3, randomized, parallel-group, double blind, placebo-controlled study. The two primary end points in the trial of induction therapy measured clinical remission of Crohn's Disease Activity Index (CDAI score of ≤ 150 points) and CDAI-100 response (≥100-point decrease in the CDAI score) at week 6. Patients enrolled in the study had CDI score of 220 to 450. The CDI scores range from 0 to approximately 600 and higher score indicates greater disease activities. The primary end point was clinical remission at week 52 in the maintenance therapy trial. In the double blind induction trial, a total of 368 patients were randomly assigned to receive intravenous vedolizumab 300 mg or placebo at weeks 0 and 2 and were followed through week 6. In cohort 1, 14.5% of patients who received vedolizumab and 6.8% who received the placebo achieved the primary end point CDAI ≤ 150 (p = 0.02); 31.4% and 25.7% of patients had ≥ 100 point decrease in their CDAI score (P = 0.23). Among patients in cohort 2, a total of 17.7% had a clinical remission and 34.4% had a CDAI-100 response at week 6. For the maintenance therapy, 36.4% of the patients receiving vedolizumab every 4 weeks and 39% of those receiving vedolizumab every 8 weeks were in clinical remission vs 21.6% of patients receiving placebo (P < 0.001 and P = 0.004). The study concluded that patients treated with vedolizumab induction therapy were more likely than those receiving placebo to have a remission at week 6; however, they were not more likely to have a CDAI-100.

Feagan et al. conducted two integrated randomized, double-blind, placebo-controlled trials. The efficacy and safety of vedolizumab in patients with active ulcerative colitis were evaluated. The study consists of induction and maintenance trials conducted in 211 medical centers in 34 countries. In cohort 1, 374 patients received intravenous vedolizumab 300 mg or placebo at weeks 0 and 2. A total of 521 patients were enrolled in cohort 2 to received open-label vedolizumab at weeks 0 and 2, with disease evaluation at week 6. The primary outcomes for induction therapy were reduction in the Mayo Clinic score of at least 3 points and a decrease of at least 30% from the baseline score. Also patient must achieve a decrease of at least 1 point on the rectal bleeding subscale or an absolute rectal bleeding score of 0 or 1. In both cohorts, patients who responded to vedolizumab therapy at week 6 were randomly assigned to continue vedolizumab as maintenance therapy or placebo. Maintenance drugs were administered every 4 or 8 weeks for up to 52 weeks. The primary outcome was clinical remission at week 52.

In cohort 1, 47.1% of patients receiving vedolizumab vs 25.5% of patients on placebo therapy achieved primary outcomes at week 6 (p < 0.001). At week 52, 44.8% of patients in the vedolizumab therapy every 4 weeks had clinical remission while 41.8% of those on vedolizumab every 8 weeks vs 15.9% on placebo were in clinical remission (P < 0.001). The study concluded that vedolizumab is more effective than placebo as induction and maintenance therapy for ulcerative colitis.

HCPCS Code:

HCPCS Code	Description
J3380	Injection, vedolizumab (Entyvio®), 1 mg

Acronyms:

UC = Ulcerative colitis
CD = Crohn's Disease
MAdCAM-1 = Mucosal addressin cell adhesion molecule-1
TNF = Tumor Necrosis Factor
TB Tuberculosis
FDA = Food and Drug Administration
CDAI = Crohn's Disease Activity Index
DMARD = Disease-Modifying Anti-Rheumatic Drug
PML Progressive Multifocal Leukoencephalopathy

References:

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2. Entyvio [package insert]. Deerfield, IL; Takeda Pharmaceuticals America, Inc; March 2020. Accessed May 9, 2022.
3. Feagan BG, Rutgeerts P, Sands BE, et al, " Vedolizumab as Induction and Maintenance Therapy for Ulcerative Colitis" *N Engl J Med* 2013;369:699-710.
4. NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®). Management of Immunotherapy-Related Toxicities. Version 2.2019. Available at www.nccn.org. Accessed on September 11, 2020.
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