vedolizumab (Entyvio®) intravenous

Medicare Advantage Medical Policy #MA-143
Original Effective Date: 01/01/2026
Current Effective Date: 01/01/2026

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Per the Self-Administered Drug list as defined by the Medicare Administrative Contractor for the Health Plan, subcutaneous vedolizumab (Entyvio®)‡ is eligible for coverage under Part D only and not targeted by this policy.

Based on review of available data, the Health Plan may consider the use of intravenous vedolizumab (Entyvio®)‡ for the treatment of adult ulcerative colitis (UC) or adult Crohn's disease (CD) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for intravenous vedolizumab (Entyvio) will be considered when ALL of the following criteria are met:

- Patient has a diagnosis of moderately to severely active UC OR moderately to severely active CD; AND
- Patient is 18 years of age or older; AND
- Patient had an inadequate response with, lost response to, or was intolerant to a tumor necrosis factor (TNF) blocker (e.g. Remicade®‡, Humira®‡) or immunomodulator (e.g., azathioprine or 6-mercaptopurine) OR patient had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids; AND
- Entyvio is NOT being used concurrently with other biologic products (e.g., Humira, Remicade) for the treatment of moderately to severely active UC OR moderately to severely active CD.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of intravenous vedolizumab (Entyvio) when the patient has not had an inadequate response to other therapies (e.g., corticosteroids, azathioprine, 6-mercaptopurine, tumor necrosis factor inhibitors [Remicade, Humira]) to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of intravenous vedolizumab (Entyvio) when patient selection criteria are not met (with the exception of the criteria denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Entyvio

Vedolizumab (Entyvio) is an integrin receptor antagonist, which ultimately inhibits the migration of memory T-lymphocytes across the endothelium into the inflamed gastrointestinal parenchymal tissue. Entyvio is available as an intravenous (IV) and subcutaneous (SC) formulation. Entyvio IV is approved for the treatment of adults with moderately to severely active ulcerative colitis (UC) or moderately to severely active Crohn's disease (CD). It is dosed at 300 mg and is infused intravenously over a 30 minute period at 0, 2, and 6 weeks, then every 8 weeks thereafter. Entyvio SC is approved for maintenance therapy for adults with moderately to severely active UC or moderately to severely active CD following the use of IV Entyvio as an induction therapy. The recommended dose of Entyvio SC is 108 mg once every 2 weeks after at least two IV induction doses (at Week 0 and Week 2), starting on Week 6. Patients in clinical response or remission beyond Week 6 may also be switched from Entyvio IV to Entyvio SC. Entyvio carries warnings for hypersensitivity reactions, infections, and progressive multifocal leukoencephalopathy (PML). No cases of PML have been observed in clinical trials for Entyvio, but PML has occurred with the use of another integrin receptor antagonist.

Crohn's Disease

Crohn's disease is a chronic autoimmune disease that can affect any part of the gastrointestinal tract but most commonly occurs in the ileum. As a result of the immune attack, the intestinal wall becomes thick, and deep ulcers may form. In addition to the bowel abnormalities, CD can also affect other organs in the body. Typically, first line treatments such as corticosteroids, 6-mercaptoprine and azathioprine are used to treat this condition.

Ulcerative Colitis

Ulcerative colitis is a chronic, episodic, inflammatory disease of the large intestine and rectum characterized by bloody diarrhea. This disease usually begins in the rectal area and may eventually extend through the entire large intestine. Repeated episodes of inflammation lead to thickening of the wall of the intestine and rectum with scar tissue. Death of colon tissue or sepsis may occur with severe disease. The goals of treatment are to control the acute attacks, prevent recurrent attacks and promote healing of the colon. Hospitalization is often required for severe attacks. Typically, first line treatments such as corticosteroids, 6-mercaptopurine and azathioprine are used to treat this condition.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Entyvio was approved by the FDA in May of 2014 for the treatment of adult patients with moderately to severely active UC or adult patients with CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids. In March of 2020, the package insert indication wording was changed to: the treatment of adults with moderately to severely active ulcerative colitis or moderately to severely active Crohn's disease. In September of 2023, the FDA approved a subcutaneous version of Entyvio for maintenance therapy for adults with moderately to severely active UC. In April of 2024, Entyvio's FDA label expanded to include approval for use of Entyvio SC as maintenance therapy in adults with moderately to severely active CD.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Entyvio IV were evaluated in two randomized, double-blind, placebo controlled trials (UC Trials I and II) in adult patients with moderately to severely active UC. The efficacy assessments for UC Trial I were at 6 weeks. Clinical response at week 6 was seen in 47% of Entyvio patients vs. 26% of placebo patients. Clinical remission at week 6 was 17% for Entyvio vs. 5% for placebo. Improvement of endoscopic appearance of the mucosa at week 6 was reached by 41% of Entyvio subjects vs. 25% of placebo subjects. All of the measures were statistically significant. UC Trial II included patients with clinical response at week 6. Patients were randomized to receive placebo or Entyvio every 8 weeks or Entyvio every 4 weeks. Efficacy was measured at week 52. 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). 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. 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. The Entyvio every four week dosing regimen did not demonstrate additional clinical benefit over the every eight dosing week regimen. The every four week dosing regimen is not the recommended dosing regimen.

The safety and efficacy of Entyvio IV were evaluated in three randomized, double-blind, placebo-controlled clinical trials (CD Trials I, II, and III) in adult patients with moderately to severely active

CD. The efficacy assessments for CD Trial 1 were at week 6. In CD Trial I, a statistically significantly higher percentage of patients treated with Entyvio achieved clinical remission as compared to placebo at week 6. The difference in the percentage of patients who demonstrated clinical response, was however, not statistically significant at week 6. Compared to CD Trial I, CD Trial II enrolled a higher number of patients who had over the previous five-year period had an inadequate response, loss of response, or intolerance to one or more TNF blockers. Efficacy assessments were at weeks 6 and 10. For the primary endpoint (clinical remission at week 6), treatment with Entyvio did not result in statistically significant improvement over placebo. In order to be randomized to treatment in CD Trial III, patients had to have received Entyvio and be in clinical response at week 6. Patients were randomized to receive placebo or Entyvio every 8 weeks or Entyvio every 4 weeks. Efficacy assessments were at week 52. In CD Trial III a greater percentage of patients in groups treated with Entyvio as compared to placebo were in clinical remission at week 52. A greater percentage of patients in groups treated with Entyvio as compared to placebo had a clinical response at week 52. In the subgroup of patients who were receiving corticosteroids at baseline and who were in clinical response at week 6, 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. The Entyvio every four week dosing regimen did not demonstrate additional clinical benefit over the every eight dosing week regimen. The every four week dosing regimen is not the recommended dosing regimen.

References

1. Entyvio [Package Insert]. Takeda Pharmaceuticals U.S.A., Inc. Lexington, MA. Revised April 2024.

Policy History

Original Effective Date: 01/01/2026
Current Effective Date: 01/01/2026
09/16/2025 UM Committee review and approval. New policy.
Next Scheduled Review Date: 09/2026

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3380
ICD-10 Diagnosis	All Related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;

B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.