Effective Date **3/1/2024**
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Coverage Policy Number **IP0326**

Vedolizumab Intravenous

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for vedolizumab intravenous infusion (Entyvio®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Vedolizumab (Entyvio) is considered medically necessary when ONE of the following is met:

1. **Crohn's Disease.** Individual meets **ALL** of the following criteria:
    A. Age 18 years or older
    B. Documentation of **ONE** of the following:
        i. Failure, contraindication, or intolerance to a corticosteroid OR a corticosteroid will be taken concurrently with vedolizumab

ii. Failure, contraindication, or intolerance to **ONE** conventional systemic therapy OR conventional systemic therapy will be taken concurrently with vedolizumab (for example, azathioprine, 6-mercaptopurine, or methotrexate)
iii. Individual has already tried a biologic for Crohn's disease. Refer to Appendix for examples of biologics used for Crohn's disease.
iv. Meets **ONE** of the following:
    a. Severe disease needing hospitalization
    b. Involvement of the upper GI tract
    c. Smoker
    d. Less than 40 years of age
    e. Stricturing disease
    f. Perianal disease
    g. Other enterocutaneous fistula
    h. Extraintestinal manifestations (ankylosing spondylitis, pyoderma gangrenosum, erythema nodosum)
    i. Previous Crohn's disease-related surgery (for example, ileocolonic resection to reduce the chance of Crohn's disease recurrence)
    j. Bowel obstruction
    k. History of abscess or perforation (after healing)

C. The medication is prescribed by, or in consultation with, a gastroenterologist

Dosing for Crohn's Disease. The dose is 300 mg as an intravenous infusion at Weeks 0, 2, and 6, then every 8 weeks thereafter.

2. **Ulcerative Colitis.** Individual meets **ALL** of the following criteria:
    A. Age 18 years or older
    B. Documentation of **ONE** of the following:
        i. Failure, contraindication, or intolerance to **ONE** conventional systemic therapy (for example, 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone)
        ii. Individual has already tried a biologic or targeted synthetic DMARD (tsDMARD) for ulcerative colitis. Refer to Appendix for examples of biologics and tsDMARDs used for ulcerative colitis.
        iii. Individual has pouchitis AND has tried therapy with an antibiotic (for example, metronidazole, ciprofloxacin), corticosteroid enema or suppository, or mesalamine enema or suppository
    C. The medication is prescribed by, or in consultation with, a gastroenterologist

Dosing for Ulcerative Colitis. The dose is 300 mg as an intravenous infusion at Weeks 0, 2, and 6, then every 8 weeks thereafter.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of vedolizumab (Entyvio) is considered medically necessary for **ALL** covered diagnoses when the above medical necessity criteria have been met prior to the start of Entyvio therapy (intravenous or subcutaneous) **AND** there is documentation of beneficial response compared with baseline (prior to initiating Entyvio).

Examples of beneficial response include:

1. **Crohn's Disease:** decreased pain, fatigue, stool frequency, and/or blood in stool; or improvement via fecal markers (e.g., fecal lactoferrin, fecal calprotectin), serum markers (e.g., C-reactive protein), imaging studies (magnetic resonance enterography [MRE], computed tomography enterography [CTE]), endoscopic assessment, and/or reduced dose of corticosteroids.

2. **Ulcerative Colitis:** decreased pain, fatigue, stool frequency, and/or decreased rectal bleeding; or improvement via fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.

Authorization Duration

Initial approval duration: 12 months
Reauthorization approval duration: 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven including the following (this list may not be all inclusive):

1. **Concurrent Use with Other Biologics or with Targeted Synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) used for an Inflammatory Condition.**
   Entyvio should not be used in combination with tumor necrosis factor inhibitors or with Tysabri due to increased risk of infections.[1] There is also an increased risk of progressive multifocal leukoencephalopathy if used in combination with Tysabri. Combination therapy with other biologics or with targeted synthetic DMARDs used to treat inflammatory conditions (see Appendix for examples) is generally not recommended due to a potential for a higher rate of adverse effects with combinations and lack of data supportive of additive efficacy.

   Note: This does NOT exclude the use of conventional immunosuppressants (e.g., 6-mercaptopurine, azathioprine) in combination with Entyvio.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3380	Injection, vedolizumab, 1mg

Background

OVERVIEW
Entyvio intravenous (IV), an integrin receptor antagonist, is indicated for the following uses:[1]

- **Crohn's disease**, in adults with moderately to severely active disease.
- **Ulcerative colitis**, in adults with moderately to severely active disease.

Therapy begins with Entyvio 300 mg IV at Week 0 and Week 2. At Week 6, or at any scheduled Entyvio IV infusion in patients with a clinical response or remission, therapy can be switched to Entyvio SC. The recommended dose of Entyvio SC is 108 mg SC once every 2 weeks. In the pivotal studies evaluating Entyvio,

all patients had previously tried corticosteroids and/or conventional agents for Crohn's disease and ulcerative colitis.

Guidelines
Guidelines for the treatment of inflammatory conditions recommend use of Entyvio.

- **Crohn's Disease:** The American College of Gastroenterology (ACG) has updated guidelines (2018) for Crohn's disease.[2] Entyvio is among the recommendations for treatment of patients with moderate to severe disease or moderate to high risk disease (for induction of remission as well as maintenance of this remission). Guidelines from the American Gastroenterological Association (AGA) [2021] include Entyvio among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission.[5]
- **Ulcerative Colitis:** Updated ACG guidelines for ulcerative colitis (2019) note that the following agents can be used for induction of remission in moderately to severely active disease: Uceris® (budesonide extended-release tablets); oral or intravenous systemic corticosteroids, Entyvio, Xeljanz® (tofacitinib tablets), or tumor necrosis factor inhibitors.[3] Current guidelines for ulcerative colitis from the AGA (2020) include Entyvio among the therapies recommended for moderate to severe disease.[6]

References

1. Entyvio intravenous infusion [prescribing information]. Deerfield, IL: Takeda; September 2023.
2. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of Crohn's disease in adults. *Am J Gastroenterol.* 2018;113(4):481-517.
3. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
4. Bressler B, Marshall JK, Bernstein CN, et al. Clinical practice guidelines for the medical management of nonhospitalized ulcerative colitis: the Toronto consensus. *Gastroenterology*. 2015;148(5):1035-1058.
5. Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. *Gastroenterology*. 2021;160(7):2496-2508.
6. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158(5):1450-1461.

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA

Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO
		IV formulation: CD
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	SC: UC
		IV: CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Sotyktu™ (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indications (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; TYK2 – Tyrosine kinase 2.