Medical Drug Clinical Criteria

Subject:	Entyvio (vedolizumab)		
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Table of Contents

Overview

This document addresses the use of Entyvio (vedolizumab), an integrin receptor antagonist which binds specifically to the α4β7 integrin and inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal tissue. Entyvio (vedolizumab) intravenous formulation is approved for the treatment of Crohn's disease and Ulcerative colitis. The subcutaneous formulation is approved for Ulcerative colitis and Crohn's disease and can be used for maintenance therapy in those who have completed induction doses with the IV formulation.

Crohn's Disease: According to the American Gastrointestinal Association clinical practice guidelines, evidence supports the use of methotrexate, corticosteroids, tumor necrosis factor inhibitors (TNFi) +/- immunomodulator, ustekinumab, or vedolizumab for induction of remission. Among the biologics, infliximab, adalimumab, ustekinumab, or vedolizumab are recommended or suggested over certolizumab for induction of remission. Evidence supports biologic agents, thiopurines, and methotrexate for maintenance of remission. Ustekinumab and vedolizumab are options for individuals with primary nonresponse to initial treatment with TNFi. Adalimumab, ustekinumab, or vedolizumab may be used in cases where an individual previously responded to infliximab and then lost response (secondary nonresponse).

Ulcerative Colitis: For those with moderately to severely active disease, the American College of Gastroenterology (ACG) guidelines strongly recommend induction of remission using oral budesonide MMX, oral systemic corticosteroids, TNFi, tofacitinib or vedolizumab (moderate to high quality evidence). The American Gastroenterological Association (AGA) guidelines define moderate to severe UC as those who are dependent on or refractory to corticosteroids, have severe endoscopic disease activity, or are at high risk of colectomy. AGA strongly recommends biologics (TNFi, vedolizumab, or ustekinumab) or tofacitinib over no treatment in induction and maintenance of remission (moderate quality of evidence). For biologic-naïve individuals, Infliximab or vedolizumab are conditionally recommended over adalimumab for induction of remission (moderate quality evidence).

Pediatric Use: Two publications (Conrad 2016, Singh 2016) describe the safety and efficacy of intravenous Entyvio (vedolizumab) in pediatric individuals with Crohn's disease or ulcerative colitis who had failed prior treatment with conventional therapy or one or more TNFi. Based on the available peer-reviewed literature and views of relevant medical specialists practicing in pediatrics and pediatric gastroenterology, the use of vedolizumab to induce or maintain remission may be considered a treatment option in a subset of the pediatric population 6 years of age or older with Crohn's disease or ulcerative colitis who are refractory to treatment with conventional drug therapy.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Entyvio (vedolizumab)

NOTE: Please see individual's pharmacy benefit for preferred products; Entyvio Subcutaneous is not a preferred product for CarelonRx pharmacy benefit.

Initial requests for intravenous Entyvio (vedolizumab) may be approved for the following:

I. Crohn's disease (CD) when the following criteria are met:
   A. Individual is 6 years of age or older (Conrad 2016, Singh 2016) with moderate to severe CD; **AND**
   B. Individual has had an inadequate response to or is intolerant of conventional therapy (such as systemic corticosteroids or immunosuppressants [such as thiopurines or methotrexate]); **OR**
   C. Individual has a contraindication to systemic corticosteroids or thiopurines or methotrexate;

OR

II. Ulcerative colitis (UC) when the following criteria are met:
   A. Individual is 6 years of age or older (Conrad 2016, Singh 2016) with moderate to severe UC; **AND**
   B. Individual has had an inadequate response to or is intolerant of conventional therapy (such as 5-Aminosalicylic acid products, systemic corticosteroids, or immunosuppressants [such as thiopurines]); **OR**
   C. Individual has a contraindication to 5-ASA products or systemic or corticosteroids or thiopurines;

OR

III. Immunotherapy-related toxicities when each of the following criteria are met (NCCN 2A):
   A. Individual is undergoing immune checkpoint inhibitor therapy for a cancer diagnosis; **AND**
   B. Individual is experiencing moderate to severe diarrhea or colitis as a result of immune checkpoint inhibitor treatment; **AND**
   C. Symptoms persist despite treatment with steroids;

OR

IV. Acute Graft-versus-host disease (GVHD) when each of the following criteria are met (NCCN 2A):
   A. Individual has a diagnosis of steroid-refractory acute GVHD; **AND**
   B. Individual is initiating vedolizumab in combination with systemic corticosteroids.

Continuation requests for intravenous Entyvio (vedolizumab) may be approved if the following criteria are met:

I. Individual has been receiving and is maintained on a stable dose of intravenous Entyvio (vedolizumab); **AND**
II. There is clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Initial requests for subcutaneous Entyvio (vedolizumab) may be approved for the following:

I. Ulcerative colitis (UC) when the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe UC; **AND**
   B. Individual has completed intravenous induction doses with Entyvio and is using subcutaneous Entyvio for maintenance therapy; **OR**
   C. Individual has been stabilized on intravenous Entyvio maintenance therapy and is switching to maintenance therapy with subcutaneous Entyvio;

OR

II. Crohn's disease (CD) when the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe CD; **AND**
   B. Individual has completed intravenous induction doses with Entyvio and is using subcutaneous Entyvio for maintenance therapy; **OR**
   C. Individual has been stabilized on intravenous Entyvio maintenance therapy and is switching to maintenance therapy with subcutaneous Entyvio.

Continuation requests for subcutaneous Entyvio (vedolizumab) may be approved if the following criteria are met:

I. Individual has been receiving and is maintained on a stable dose of subcutaneous Entyvio (vedolizumab); **AND**
II. There is clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Requests for Entyvio (vedolizumab) [intravenous and subcutaneous] may not be approved for the following:

I. In combination with oral or topical JAK inhibitors, ozanimod, etrasimod, deucravacitinib, or any of the following biologic immunomodulators: TNF antagonists, IL-23 inhibitors, IL-17 inhibitors, IL-6 inhibitors, IL-1 inhibitors, ustekinumab, abatacept, rituximab, or natalizumab; **OR**
II. Active, serious infection or a history of recurrent infections; **OR**
III. New or worsening neurological signs or symptoms of John Cunningham virus (JCV) infection or risk of progressive multifocal leukoencephalopathy (PML); **OR**
IV. When the above criteria are not met and for all other indications.

Quantity Limits

Entyvio (vedolizumab) Quantity Limit

Drug	Limit
Entyvio 300 mg/vial*^	1 vial per 56 days (8 weeks)
Entyvio (vedolizumab) 108 mg/ 0.68 mL prefilled syringe/pen	2 syringes/pens per 28 days
Override Criteria	

*Initiation of therapy: May approve up to 2 (two) additional single-use vials (300 mg/vial) in the first 6 weeks (42 days) of treatment.

^For Crohn's Disease (CD) or Ulcerative Colitis (UC), may approve increased dosing, up to 1 vial (300 mg) every 4 weeks if the following criteria are met:

I. Individual has been treated with standard maintenance dosing (i.e. every 8 weeks) for *at least* 2 doses or 16 weeks; **AND**
II. The increased dosing is being prescribed by or in consultation with a gastroenterologist; **AND**
III. Individual initially achieved an adequate response to standard maintenance dosing but has subsequently lost response, as determined by the prescriber; **OR**
IV. Individual partially responded but had an inadequate response to standard maintenance dosing as determined by the prescriber; **AND**
V. Symptoms, if present, are not due to active infections or any other gastrointestinal disorder other than the primary disease; **AND**
VI. Requested dosing does not exceed up to one vial (300 mg) every 4 weeks.

Initial approval duration for increased dosing for CD or UC: 16 weeks

^Requests for continued escalated dosing for CD or UC may be approved if the following criteria are met:

I. Requested dosing does not exceed up to one vial (300 mg) every 4 weeks; **AND**
II. Individual has subsequently regained response or achieved adequate response following increased dosing, as shown by improvement in signs and symptoms of the disease (including but not limited to reduction in stool frequency/bloody stools, improvement abdominal pain, or endoscopic response); **AND**
III. Individual is not experiencing unacceptable adverse effects from increased dosing; **AND**
IV. Individual will be assessed regularly for dose de-escalation.

Continued approval duration for increased dosing for CD or UC: 6 months

^For CD or UC, Increased dosing may not be approved for the following:

I. Individual has had no response to Entyvio at standard maintenance dosing (i.e. every 8 weeks); **OR**
II. Individual is requesting dose escalation in absence of signs and symptoms of the disease (for example, requesting based on results of therapeutic drug level or anti-drug antibody testing alone).

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3380	Injection, vedolizumab, 1 mg [Entyvio]
J3590	Unclassified biologics (when specified as injection, vedolizumab, 108 mg/0.68 mL prefilled syringe/pen [Entyvio SC].

ICD-10 Diagnosis

D89.810	Acute graft-versus-host disease
D89.812	Acute on chronic graft-versus-host disease
K50.00-K50.919	Crohn's disease (regional enteritis)
K51.00-K51.919	Ulcerative colitis
K52.1	Toxic gastroenteritis and colitis [when specified as Entyvio intravenous for immunotherapy-related toxicity]
R19.7	Diarrhea, unspecified [when specified as Entyvio intravenous for immunotherapy-related toxicity]

Document History

Revised: 11/15/2024
Document History:

- 11/15/2024 – Annual Review: Include use in graft versus host disease for IV formulation per NCCN; update subcutaneous quantity limit to monthly limit. Coding Reviewed: Added ICD-10-CM D89.810 and D89.812.

- 08/16/2024 – Select Review: Update quantity limit override. Coding Reviewed: Added ICD-10-CM K52.1, R19.7 to Entyvio intravenous. Effective 11/17/2023.
- 05/17/2024 – Select Review: Update clinical criteria for new Crohn's Disease indication for subcutaneous dosage form. Coding Reviewed: Added HCPCS code J3590 (when specified as Entyvio SC).
- 03/11/2024 – Select Review: No changes. Coding Reviewed: No changes.
- 02/23/2024 – Select Review: Separate continuation criteria for subcutaneous and intravenous formulations; wording and formatting updates. Coding Reviewed: No changes.
- 11/17/2023 – Annual Review: Update criteria and quantity limits to include new subcutaneous dosage form; include use in immunotherapy-related toxicities per NCCN; update contraindication to prior therapy language for clarity; include etrasimod in combination exclusion; add continuation of use language. Coding Reviewed: No changes.
- 11/18/2022 – Annual Review: Update combination exclusion use to include additional agents and specify biologic immunomodulators; include examples of conventional therapy per guidelines; add quantity limit override criteria for increased dosing; wording and formatting updates. Coding Reviewed: No changes.
- 11/19/2021 – Annual Review: Update prior trial requirements to remove TNF antagonists to align with other agents; update exclusion list for concomitant therapy with ozanimod. Coding reviewed: No changes.
- 11/20/2020 – Annual Review: Add continuation of use section; remove 5-ASA products as example of conventional therapy for Crohn's disease; add additional examples of combination use for clarity. Coding Reviewed: No changes.
- 09/23/2019 - Administrative update to add drug specific quantity limit.
- 11/16/2018 – Annual Review: Initial P&T review of Entyvio Clinical Guideline. Update clinical criteria to delete "active" disease wording. Update criteria to delete requirement agent is being used "to reduce signs and symptoms, maintain clinical response" etc. Wording and formatting changes to criteria for consistency. HCPCS and ICD-10 Coding Review: No changes.

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5. Feuerstein JD, Issacs KL, Schneider Y, et al. American Gastroenterological Association Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology 2020; 158:1450-1461.
6. Lichtenstein GR, Loftus EV, Isaacs KL et al. 2018 American College of Gastroenterology Guideline for the management of Crohn's disease in adults. *Am J Gastroenterol* 2018; 113:481–517.
7. Rubin DT, Ananthakrishnan AN, Siegel CA et al. American College of Gastroenterology Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol 2019; 114:384-413.
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10. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on September 25, 2024.
    a. Management of Immunotherapy-related Toxicities. V1.2024. Revised December 7, 2023.
    b. Hematopoietic Cell Transplantation (HCT). V2.2024. Revised August 30, 2024.