

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Inflammatory Conditions – Entyvio Intravenous Utilization Management Medical Policy

- Entyvio® (vedolizumab intravenous infusion – Takeda)

REVIEW DATE: 04/22/2026

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 Weeks 0, 2, and 6, followed by every 8 weeks thereafter.¹ Alternatively, at Week 6, or at any scheduled Entyvio IV infusion in patients with a clinical response or remission, therapy can be switched to Entyvio subcutaneous (SC). The recommended maintenance dose of Entyvio SC is 108 mg SC once every 2 weeks. Additionally, data from the pivotal trial extension studies provide evidence that shortening the dosing interval in patients who lose clinical response to standard Entyvio dosing can help recapture therapeutic benefit.^{8,9}

Guidelines

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

- **Crohn's Disease (CD):** The American College of Gastroenterology (ACG) [2025] and the American Gastroenterological Association (AGA) [2025] have guidelines for the management of CD in adults.^{2,3} Both guidelines recommend upfront use of advanced therapies, rather than step-up therapy after failure of corticosteroids and/or immunomodulators. Advanced therapies recommended include tumor necrosis factor (TNF) inhibitors, Entyvio, interleukin (IL)-23 inhibitors, IL-12/23 inhibitors, and Rinvoq® (upadacitinib extended-release tablets).
- **Ulcerative Colitis (UC):** The AGA (2024) and the ACG (2025) have clinical practice guidelines on the management of moderate to severe UC.^{4,5} In moderate to severe disease, systemic corticosteroids or advanced therapies may be utilized for induction of remission. Advanced therapies recommended include TNF inhibitors, Entyvio, IL-23 inhibitors, IL-12/23 inhibitors, sphingosine-1-phosphate (S1P) receptor modulators, and Janus kinase (JAK) inhibitors. If steroids are utilized for induction, efforts should be made to introduce steroid-sparing agents for maintenance therapy. Of note, guidelines state that corticosteroids may be avoided entirely when other effective induction strategies are planned.⁵ Both guidelines also recommend that any drug that effectively treats induction should be continued for maintenance.^{4,5}

Other Uses with Supportive Evidence

There are guidelines and/or published data supporting the use of Entyvio in the following conditions:

- **Gastrointestinal Toxicity Associated with Checkpoint Inhibitor Therapy:** The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for Management of Immunotherapy-Related Toxicities (version 1.2026 – October 23, 2025) recommend Entyvio intravenous as an option, following corticosteroids, for esophagitis, gastritis, duodenitis, or colitis associated with immune checkpoint inhibitor therapy.⁶
- **Graft-Versus-Host Disease:** Guidelines for hematopoietic cell transplantation from the National Comprehensive Cancer network (NCCN) [version 2.2026 – April 3, 2026] list Entyvio intravenous among the agents used for steroid-refractory acute GVHD.⁷ For patients with steroid-refractory acute GVHD, Jakafi® (ruxolitinib tablets) is the only category 1 recommended agent. Other

alternative agents recommended by NCCN for acute GVHD (category 2A) include the following: alemtuzumab IV infusion, alpha-1 antitrypsin, anti-thymocyte globulin, Simulect® (basiliximab intravenous injection), calcineurin inhibitors (e.g., tacrolimus, cyclosporine), Enbrel® (etanercept subcutaneous injection), extracorporeal photopheresis, infliximab, mammalian target of rapamycin inhibitors (e.g., sirolimus), mycophenolate mofetil, Nipent™ (pentostatin intravenous injection), tocilizumab, urinary-derived human chorionic gonadotropin/epidermal growth factor, and Entyvio.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Entyvio intravenous. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Entyvio intravenous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Entyvio intravenous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Entyvio intravenous is recommended in those who meet one of the following:

FDA-Approved Indications

1. Crohn's Disease. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):

- i. Patient is ≥ 18 years of age; AND
- ii. The medication is prescribed by or in consultation with a gastroenterologist; OR

B) Patient is Currently Receiving Entyvio Intravenous or Subcutaneous. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- i. Patient has been established on the requested drug for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with the requested drug is reviewed under criterion A (Initial Therapy).
- ii. Patient meets at least ONE of the following (a or b):
 - a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include 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.
 - b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or blood in stool.

Dosing. Approve ONE of the following dosage regimens (A or B):

A) Initial Therapy. Approve ONE of the following (i or ii):

- i. The dose is 300 mg as an intravenous infusion at Week 0, 2, and 6, and then no more frequently than once every 8 weeks thereafter; OR

- ii. The dose is 300 mg as an intravenous infusion administered at Week 0 and 2; OR
- B) Patient is Currently Receiving Entyvio Intravenous or Subcutaneous. Approve up to a maximum dose of 300 mg administered intravenously no more frequently than once every 4 weeks.

2. Ulcerative Colitis. Approve for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i and ii):
 - i. Patient is ≥ 18 years of age; AND
 - ii. The medication is prescribed by or in consultation with a gastroenterologist; OR
- B) Patient is Currently Receiving Entyvio Intravenous or Subcutaneous. Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i. Patient has been established on Entyvio intravenous or subcutaneous for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Entyvio intravenous or subcutaneous is reviewed under criterion A (Initial Therapy).
 - ii. Patient meets at least ONE of the following (a or b):
 - a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of assessment for inflammatory response include fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.
 - b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or decreased rectal bleeding.

Dosing. Approve ONE of the following dosage regimens (A or B):

- A) Initial Therapy. Approve ONE of the following (i or ii):
 - i. The dose is 300 mg as an intravenous infusion at Week 0, 2, and 6, and then no more frequently than once every 8 weeks thereafter; OR
 - ii. The dose is 300 mg as an intravenous infusion administered at Week 0 and 2; OR
- B) Patient is Currently Receiving Entyvio Intravenous or Subcutaneous. Approve up to a maximum dose of 300 mg administered intravenously no more frequently than once every 4 weeks.

Other Uses with Supportive Evidence

3. Gastrointestinal Toxicity Associated with Checkpoint Inhibitor Therapy. Approve for the duration noted if the patient meets ONE of the following (A or B):

Note: Examples of checkpoint inhibitors are Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Yervoy (ipilimumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion), Bavencio (avelumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), and Libtayo (cemiplimab-rwlc intravenous infusion).

- A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
 - i. Patient is ≥ 18 years of age; AND
 - ii. According to the prescriber, patient developed gastrointestinal toxicity while receiving a checkpoint inhibitor; AND
 - iii. Patient is symptomatic despite a trial of at least ONE systemic corticosteroid; AND
Note: Examples of a corticosteroid include methylprednisolone and prednisone.
 - iv. The medication is prescribed by or in consultation with a gastroenterologist or an oncologist; OR

B) Patient is Currently Receiving Entyvio Intravenous. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of objective measures may include clinically significant improvement or normalization of serum markers (e.g., C-reactive protein), fecal markers (e.g., fecal calprotectin), endoscopic assessment, and/or reduced dosage of corticosteroids).

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or decreased rectal bleeding.

Dosing. Approve if dosage regimen meets BOTH of the following (A and B):

A) The dose is 300 mg as an intravenous infusion administered at Week 0, 2, and 6; AND

B) Subsequent doses are separated by at least 8 weeks.

4. Graft-Versus-Host Disease. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 month if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is $\geq$ 18 years of age ; AND

ii. Patient has acute graft-versus-host disease; AND

iii. Patient has tried at least one systemic medication for graft-versus-host disease; AND

Note: Examples of systemic medications include corticosteroids (e.g., methylprednisolone), antithymocyte globulin, cyclosporine, tacrolimus, mycophenolate mofetil, Jakafi (ruxolitinib tablets), Simulect (basiliximab intravenous injection), an etanercept product, an infliximab product, sirolimus, Nipent (pentostatin intravenous injection), and a tocilizumab product.

iv. The medication is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center; OR

B) Patient is Currently Receiving Entyvio Intravenous. Approve for 3 months if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 1 month; AND

Note: A patient who has received < 1 month of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Entyvio); OR

Note: Examples of objective measures include improvement on endoscopic assessment, normalization of liver function tests, red blood cell count, or platelet count; or resolution of fever or rash.

b) Compared with baseline (prior to initiating Entyvio), patient experienced an improvement in at least one symptom, such as improvement in oral mucosal or gastrointestinal symptoms (e.g., diarrhea, nausea, vomiting, anorexia) or decreased fatigue.

Dosing. Approve if dosage regimen meets BOTH of the following (A and B):

A) The dose is 300 mg as an intravenous infusion administered at Week 0, 2, and 6; AND

B) Subsequent doses are separated by at least 8 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Entyvio intravenous is not recommended in the following situations:

- 1. Concurrent Use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug.** This medication should not be administered in combination with another biologic or with a targeted synthetic oral small molecule drug used for an inflammatory condition (see [Appendix](#) for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.
Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine) in combination with this medication.
- 2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria.** Criteria will be updated as new published data are available.

REFERENCES

1. Entyvio intravenous infusion, subcutaneous injection [prescribing information]. Deerfield, IL: Takeda; February 2026.
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3. 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.
4. Singh S, Loftus EV Jr, Limketkai BN, et al. AGA Living Clinical Practice Guideline on Pharmacological Management of Moderate-to-Severe Ulcerative Colitis. *Gastroenterology*. 2024 Dec;167(7):1307-1343.
5. Rubin D, Ananthakrishnan A, Siegel C. ACG Clinical Guideline Update: Ulcerative Colitis in Adults. *Am J of Gastroenterol*. 2025 June;120(6):1187-1224.
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7. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 2.2026 – April 3, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on April 7, 2026.
8. Loftus EV Jr, Colombel JF, Feagan BG, et al. Long-term Efficacy of Vedolizumab for Ulcerative Colitis. *J Crohns Colitis*. 2017 Apr 1;11(4):400-411.
9. Vermeire S, Loftus EV Jr, Colombel JF et al. Long-term Efficacy of Vedolizumab for Crohn's Disease. *J Crohns Colitis*. 2017 Apr 1;11(4):412-424.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	Crohn's Disease: For a patient currently taking, it was clarified this applies to the intravenous or subcutaneous formulation.	04/24/2024
Selected Revision	Conditions Not Recommended for Approval: Concurrent use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug was changed to as listed (previously oral small molecule drug was listed as Disease-Modifying Antirheumatic Drug).	09/11/2024
Annual Revision	Crohn's Disease: Updated dosing to add option of approval for 300 mg intravenous infusion administered at Week 0 and 2. Ulcerative Colitis: Updated dosing to add option of approval for 300 mg intravenous infusion administered at Week 0 and 2.	04/09/2025
Selected Revision	Ulcerative Colitis: For initial therapy, removed the following options of approval: (1) the patient has tried one systemic therapy; (2) the patient has pouchitis and tried an antibiotic, probiotic, corticosteroid enema, or mesalamine enema.	07/23/2025
Selected Revision	Gastrointestinal Toxicity Associated with Checkpoint Inhibitor Therapy: This was added as a new condition of approval. Graft-Versus-Host Disease: This was added as a new condition of approval.	08/13/2025
Selected Revision	Crohn's Disease: Dosing was divided into an initial therapy and continuation of therapy regimen. Added an option of approval for 300 mg intravenous infusion	08/27/2025

	administered every 4 weeks for a patient currently receiving Entyvio intravenous or subcutaneous. Ulcerative Colitis: Dosing was divided into an initial therapy and continuation of therapy regimen. Added an option of approval for 300 mg intravenous infusion administered every 4 weeks for a patient currently receiving Entyvio intravenous or subcutaneous.	
Selected Revision	Crohn's Disease: For initial therapy, the following options of approval were removed: The patient has tried or is currently taking systemic corticosteroids, or corticosteroids are contraindicated; patient has tried one conventional systemic therapy for Crohn's disease along with the associated Note; patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence). Appendix: Otezla XR (apremilast extended-release tablets) was added.	02/11/2026
Annual Revision	No criteria changes.	04/22/2026

APPENDIX

	Mechanism of Action	Examples of Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, HS, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, JIA, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, 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
Kineret® (anakinra SC injection)	Inhibition of IL-1	RA
Tocilizumab Products (Actemra® IV, biosimilars; Actemra SC, biosimilars)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	PJIA, RA
Siliq® (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, HS, nr-axSpA, PsO, PsA IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	AS, HS, nr-axSpA, PsO, PsA
Ustekinumab Products (Stelara® IV, biosimilars; Stelara SC, biosimilars)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC IV formulation: CD, UC
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Omvo® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PsO, PsA, UC IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: CD, PsO, PsA, UC IV formulation: CD, UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
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 antibody	RA
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Otezla® XR (apremilast extended-release tablets)	Inhibition of PDE4	PsO, PsA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	AA, RA
Litfulo® (ritlecitinib capsules)	Inhibition of JAK pathways	AA
Leqselvi® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, CD, nr-axSpA, PJIA, PsA, RA, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	Tablets: AS, PsA, RA, UC Oral solution: PJIA, PsA
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	AS, PsA, RA, UC
Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	UC

* Not an all-inclusive list of indications. 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; HS – Hidradenitis Suppurativa; 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; ERA – Enthesitis-related arthritis; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.