Utilization Review Policy 135

POLICY: Inflammatory Conditions – Entyvio Intravenous Utilization Management Medical Policy
- Entyvio® (vedolizumab intravenous infusion – Takeda)

EFFECTIVE DATE: 1/1/2020
LAST REVISED DATE: 04/09/2025; selected revision 07/23/2025, 08/13/2025, 08/27/2025

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

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

1. **Crohn's disease**, in adults with moderately to severely active disease.
2. **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. 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] has guidelines for the management of CD in adults.[2] In moderate to severe disease, systemic corticosteroids or advanced therapies may be utilized for induction of remission. Advanced therapies recommended include tumor necrosis factor (TNF) inhibitors, Entyvio, interleukin (IL)-23 inhibitors, IL-12/23 inhibitors, and Rinvoq® (upadacitinib). If steroids are utilized for induction, efforts should be made to introduce steroid-sparing agents for maintenance therapy. Guidelines from the American Gastroenterological Association (AGA) [2021] include various biologics among the therapies for moderate to severe CD, for induction and maintenance of remission.[3]
- **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 1.2025 – December 20, 2024) 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 2.2025 – June 5, 2025] 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), calcineurin inhibitors (e.g., tacrolimus, cyclosporine), Enbrel® (etanercept), extracorporeal photopheresis, infliximab, mammalian target of rapamycin inhibitors (e.g., sirolimus), mycophenolate mofetil, Nipent™ (pentostatin), tocilizumab, urinary-derived human chorionic gonadotropin/epidermal growth factor, and Entyvio® (vedolizumab).

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. 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 ALL of the following (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient meets ONE of the following (a, b, c, or d):

a) Patient has tried or is currently taking systemic corticosteroids, or corticosteroids are contraindicated in this patient; OR

b) Patient has tried one conventional systemic therapy for Crohn's disease; OR
Note: Examples of conventional systemic therapy for Crohn's disease include azathioprine, 6-mercaptopurine, or methotrexate. An exception to the requirement for a trial of or contraindication to steroids or a trial of one other conventional systemic agent can be made if the patient has already tried at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. Refer to Appendix for examples of biologics used for Crohn's disease. These patients who have already received a biologic are not required to "step back" and try another agent. A trial of mesalamine does not count as a systemic therapy for Crohn's disease.

c) Patient has enterocutaneous (perianal or abdominal) or rectovaginal fistulas; OR

d) Patient had ileocolonic resection (to reduce the chance of Crohn's disease recurrence); AND

iii. 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.

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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

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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.

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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 ≥ 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),

Simulect (basiliximab), an etanercept product, an infliximab product, sirolimus, Nipent (pentostatin), 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):

1. 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.
2. 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 [prescribing information]. Deerfield, IL: Takeda; April 2024.
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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.
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6. The NCCN Management of Immunotherapy-Related Toxicities Clinical Practice Guidelines in Oncology (version 1.2025 – December 20, 2024). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
7. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 2.2025 – June 5, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
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
Annual Revision	No criteria changes.	06/28/2023
Early Annual Revision	**Ulcerative Colitis:** For a patient currently taking, it was clarified this applies to the intravenous or subcutaneous formulation. A note was added to clarify that a mesalamine product does not count as a systemic therapy for ulcerative colitis.	10/11/2023
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
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
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 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.	08/27/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025

APPENDIX

	Mechanism of Action	Examples of 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, 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
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	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
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC
Ustekinumab Products (Stelara® IV, biosimilar; Stelara SC, biosimilar)	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; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, 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	PsO, AS, nr-axSpA, 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, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO, UC
		IV formulation: CD, UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA, AA
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, nr-axSpA, RA, PsA, CD, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, 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; 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; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.