

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Inflammatory Conditions – Entyvio Intravenous Utilization Management Medical Policy

- Entyvio® (vedolizumab intravenous infusion – Takeda)

REVIEW DATE: 06/28/2023

OVERVIEW

Entyvio, 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.

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 treatment 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

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Entyvio. 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 as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Entyvio 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 is recommended in those who meet one of the following:

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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.

B) Patient is Currently Receiving Entyvio. 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 the following dosage regimen (A and B):

- A) The dose is 300 mg as an intravenous infusion at Weeks 0, 2, and 6; AND
- B) Subsequent doses are separated by at least 8 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, ii, and iii):

- i. Patient is ≥ 18 years of age; AND
- ii. Patient meets ONE of the following (a or b):
 - a) Patient has had a trial of ONE systemic therapy; OR
Note: Examples include 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, or a corticosteroid such as prednisone or methylprednisolone. A trial of a biologic also counts

as a trial of one systemic agent for ulcerative colitis. Refer to [Appendix](#) for examples of biologics used for ulcerative colitis.

b) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has pouchitis; AND

(2) Patient has tried an antibiotic, probiotic, corticosteroid enema, or mesalamine enema; AND

Note: Examples of antibiotics include metronidazole and ciprofloxacin. Examples of corticosteroid enemas include hydrocortisone enema.

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

2. Patient is Currently Receiving Entyvio. 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 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 the following dosage regimen (A and B):

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

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Entyvio is not recommended in the following situations:

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.

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; June 2022.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	<p>Crohn’s Disease: Initial approval duration was changed to 6 months (previously was 14 weeks). Note was clarified to state that a previous trial of a biologic applies to one biologic other than the requested drug. For a patient currently receiving this drug, it was clarified that this applies to a patient who is taking for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber.</p> <p>Ulcerative Colitis: An exception was added for a patient who has pouchitis and has tried a listed therapy (i.e., an antibiotic, probiotic, corticosteroid enema, or mesalamine enema). A patient who meets this exception is not required to try another therapy prior to Entyvio. Initial approval duration was changed to 6 months (previously was 14 weeks). Note was clarified to state that a previous trial of a biologic applies to one biologic other than the requested drug. For a patient currently receiving this drug, it was clarified that this applies to a patient who is taking for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber.</p>	06/22/2022
Annual Revision	No criteria changes.	06/28/2023

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
Kezvara[®] (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-asmm 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)	Integrin receptor antagonist	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.