CARECONTINUUM™

# UTILIZATION MANAGEMENT MEDICAL POLICY

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

**REVIEW DATE:** 04/24/2024; selected revision 09/11/2024

## 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]

## 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**

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**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 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 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.

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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, 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 mesalamine product does not count as a systemic therapy for ulcerative colitis. 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 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 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 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.
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 |
|---|---|---|
| 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 |

## 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 | UC |
| **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; 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 |
| **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: PsA, PsO, UC |
| | | IV formulation: 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, 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.