



## PRIOR AUTHORIZATION POLICY

**POLICY:** Inflammatory Conditions – Entyvio Subcutaneous Prior Authorization Policy

- Entyvio® (vedolizumab subcutaneous injection – Takeda)

**REVIEW DATE:** 04/09/2025

### INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

## CIGNA NATIONAL FORMULARY COVERAGE:

### OVERVIEW

Entyvio subcutaneous (SC), an integrin receptor antagonist, is indicated for treatment of the following uses:<sup>1</sup>

- **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 subcutaneous, all patients had previously tried corticosteroids, conventional agents, or biologics for 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.<sup>2</sup> 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.<sup>3</sup>
- **Ulcerative Colitis:** The AGA (2024) and ACG (2019) have clinical practice guidelines on the management of moderate to severe ulcerative colitis in adults.<sup>4,5</sup> AGA recognizes all of the FDA-approved advanced therapies as potential options for adults with moderate to severe UC.<sup>4</sup> Advanced therapies include the biologics and targeted synthetic small molecule drugs. In general, the AGA recommends starting with advanced therapies and/or immunomodulators. Immunomodulators are recommended in the setting of maintenance of clinical remission induced by corticosteroids. The ACG recommend TNF inhibitors, Entyvio® (vedolizumab IV infusion/subcutaneous injection), Stelara® (ustekinumab IV infusion/subcutaneous injection), or Xeljanz®/Xeljanz® XR (tofacitinib tablets, tofacitinib extended-release tablets) for induction treatment of moderate to severe disease.<sup>5</sup> The guidelines also recommend that any drug that effectively treats induction should be continued for maintenance.

## **POLICY STATEMENT**

Prior Authorization is recommended for prescription benefit coverage of Entyvio subcutaneous. All approvals are provided for the duration listed below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Entyvio subcutaneous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Entyvio subcutaneous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

• **Entyvio® (vedolizumab subcutaneous injection – Takeda)**  
**is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

## **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, iii, and iv):
    - i. Patient is  $\geq 18$  years of age; AND

ii. According to the prescriber, the patient is currently receiving Entyvio intravenous or will receive induction dosing with Entyvio intravenous within 2 months of initiating therapy with Entyvio subcutaneous; AND

iii. 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

iv. 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 subcutaneous or intravenous 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.

**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  $\geq 18$  years of age; AND
  - ii. According to the prescriber, the patient is currently receiving Entyvio intravenous or will receive induction dosing with Entyvio intravenous within 2 months of initiating therapy with Entyvio subcutaneous; AND
  - iii. 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.
  - iv. The medication is prescribed by or in consultation with a gastroenterologist; OR
- B) Patient is Currently Receiving Entyvio Subcutaneous or Intravenous.** Approve for 1 year if the patient meets BOTH of the following (i and ii):
- i. Patient has been established on Entyvio subcutaneous or intravenous for at least 6 months; AND
 

Note: A patient who has received < 6 months of therapy or who is restarting therapy with Entyvio subcutaneous or intravenous 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.

## CONDITIONS NOT COVERED

- **Entyvio® (vedolizumab subcutaneous injection – Takeda)** is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 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.

## REFERENCES

1. Entyvio [prescribing information]. Deerfield, IL: Takeda; May 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. 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 DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.

## HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	10/11/2023
Early Annual Revision	Crohn's Disease: This newly approved indication was added to the policy. Ulcerative Colitis: A requirement was added that the patient is ≥ 18 years of age.	04/24/2024
Selected Revision	<b>Conditions Not Covered:</b> 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	No criteria changes.	04/09/2025

## APPENDIX

	Mechanism of Action	Examples of Indications*
<b>Biologics</b>		
<b>Adalimumab SC Products</b> (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
<b>Cimzia®</b> (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
<b>Etanercept SC Products</b> (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
<b>Infliximab IV Products</b> (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
<b>Zymfentra®</b> (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
<b>Simponi®, Simponi Aria®</b> (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
<b>Tocilizumab Products</b> (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
<b>Kevzara®</b> (sarilumab SC injection)	Inhibition of IL-6	RA
<b>Orencia®</b> (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
<b>Rituximab IV Products</b> (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
<b>Kineret®</b> (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
<b>Omvoh®</b> (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	CD, UC
<b>Ustekinumab Products</b> (Stelara® IV, biosimilar; Stelara SC, biosimilar)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
<b>Siliq®</b> (brodalumab SC injection)	Inhibition of IL-17	PsO
<b>Cosentyx®</b> (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
<b>Taltz®</b> (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
<b>Bimzelx®</b> (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO, AS, nr-axSpA, PsA
<b>Ilumya®</b> (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
<b>Skyrizi®</b> (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
<b>Tremfya®</b> (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: CD, PsA, PsO, UC
		IV formulation: CD, UC
<b>Entyvio®</b> (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
<b>Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs</b>		
<b>Otezla®</b> (apremilast tablets)	Inhibition of PDE4	PsO, PsA
<b>Cibinqo™</b> (abrocitinib tablets)	Inhibition of JAK pathways	AD
<b>Olumiant®</b> (baricitinib tablets)	Inhibition of JAK pathways	RA, AA

<b>Litfulo</b> ® (ritlecitinib capsules)	Inhibition of JAK pathways	AA
<b>Leqselvi</b> ® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
<b>Rinvoq</b> ® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
<b>Rinvoq</b> ® <b>LQ</b> (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
<b>Sotyktu</b> ® (deucravacitinib tablets)	Inhibition of TYK2	PsO
<b>Xeljanz</b> ® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
<b>Xeljanz</b> ® <b>XR</b> (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
<b>Zeposia</b> ® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
<b>Velsipity</b> ® (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.

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