BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ENTYVIO® (vedolizumab) IV or SQ

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Entyvio (vedolizumab) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
   a. Moderately to severely active Crohn's disease (CD)
   b. Moderate to severe active ulcerative colitis (UC)

4. **For Crohn's disease:** Individual meets **ALL** of the following:

a. Diagnosis of moderate to severe active Crohn disease is confirmed with **ONE** of the following:
    i. **At least 5** of the following signs and symptoms:
        1. Crampy abdominal pain
        2. Chronic intermittent diarrhea (with or without blood)
        3. Fatigue
        4. Weight loss
        5. Anemia
        6. Perianal disease (e.g., anal fissures, anorectal abscess)
        7. Fistulas
        8. Elevated serum C-reactive protein and/or fecal calprotectin
        9. Extraintestinal manifestations such as arthritis or arthropathy, eye and skin disorders, biliary tract involvement, and kidney stones
    ii. Crohn's disease activity index > 220
b. Individual has documented failure (used for ≥ 3 consecutive months), contraindication or intolerance to the **ONE** of the following: [Note: This criterion is waived if the individual already has tried an FDA-approved Crohn's disease biologic]:
    i. Azathioprine
    ii. 6-mercaptopurine
    iii. Methotrexate
    iv. Oral corticosteroids
c. Individual has documented failure (used for ≥ 3 consecutive months), contraindication, intolerance, or is not a candidate for **TWO** of the following preferred agents:
    i. Adalimumab product
    ii. Cimzia
    iii. Rinvoq
    iv. Skyrizi
    v. Tremfya
    vi. Ustekinumab product
d. Individual is switching to Entyvio SQ injections after **ONE** of the following:
    i. Currently established on Entyvio IV infusions
    ii. Has received two doses of Entyvio IV infusions for induction

5. **For ulcerative colitis:** Individual meets **ALL** of the following:
    a. Diagnosis of moderate to severe ulcerative colitis is confirmed with **ONE** of the following:
        i. **At least 5** of the following signs and symptoms
            1. Bloody diarrhea
            2. Bowel movements 4-6 or more times per day
            3. Colicky abdominal pain
            4. Urgency
            5. Tenesmus
            6. Fever
            7. Fatigue
            8. Weight loss
            9. Anemia
            10. Elevated serum C-reactive protein or erythrocyte sedimentation rate
            11. Elevated fecal calprotectin
        ii. American College of Gastroenterology Ulcerative Colitis activity index rating of moderate to severe disease

b. Individual has documented failure (used for ≥ 3 consecutive months), contraindication, intolerance, or is not a candidate for the following **ONE** of the following [Note: This criterion is waived if the individual already has tried an FDA-approved Ulcerative Colitis biologic]:
    i. Azathioprine
    ii. 6-mercaptopurine
    iii. Oral corticosteroids
c. Individual has documented failure (used for ≥ 3 consecutive months), contraindication, intolerance, or is not a candidate for **TWO** of the following preferred agents:
    i. Adalimumab product
    ii. Rinvoq
    iii. Simponi
    iv. Skyrizi
    v. Tremfya
    vi. Ustekinumab product
    vii. Xeljanz or Xeljanz XR
d. Individual is switching to Entyvio SQ injections after **ONE** of the following:
    i. Currently established on Entyvio IV infusions
    ii. Has received two doses of Entyvio IV infusions for induction

6. Individual has **NONE** of the following:
    a. Active serious infections, including clinically important localized infections or sepsis when initiating or continuing therapy
    b. Untreated latent or active tuberculosis [Note any treatment for latent infection has been initiated prior to Entyvio (vedolizumab) therapy]
    c. Progressive multifocal leukoencephalopathy
    d. Concurrent use of live vaccines

7. Individual has evidence of up-to-date immunizations according to current immunization guidelines prior to initiation of Entyvio (vedolizumab)

8. Agent will not be used in combination with another biological immunomodulators or other potent immunosuppressants (e.g., adalimumab, Adbry, azathioprine, cyclosporine, Dupixent, infliximab, rituximab, Enbrel, Otezla, Vtama, Sotyktu, Xolair, or JAK inhibitors (Cibinqo, Olumiant, Opzelura, Rinvoq, Rinvoq LQ, Xeljanz IR, XR, solution), etc.)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Entyvio (vedolizumab) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist

2. Individual has documentation of positive clinical response to therapy defined as the following:
    a. For Crohn's Disease, **ONE** of the following:
        i. **AT LEAST** a 20% improvement in signs and symptoms of Crohn's disease

   ii. Decrease in Crohn's disease activity index of more than 70 from baseline or a Crohn's disease activity index of < 150 (in remission)
b. For Ulcerative Colitis, **ONE** of the following:
   i. **AT LEAST** a 20% improvement in signs and symptoms of Ulcerative Colitis
   ii. American College of Gastroenterology Ulcerative Colitis activity index rating of mild disease or disease in remission

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
   a. Progressive multifocal leukoencephalopathy (PML)
   b. Anaphylaxis or serious infusion-related reaction
   c. Jaundice or other evidence of liver injury

5. Individual has **NONE** of the following:
   a. Active serious infections, including clinically important localized infections or sepsis when initiating or continuing therapy
   b. Untreated latent or active tuberculosis [Note any treatment for latent infection has been initiated prior to Entyvio (vedolizumab) therapy]
   c. Concurrent use of live vaccines

6. Agent will not be used in combination with another biological immunomodulators or other potent immunosuppressants (e.g., Cimzia, adalimumab, Infliximab, Omvoh, Rinvoq, rituximab, Simponi, Skyrizi, Stelara, Tysabri, Velsipity, Zeposia, etc.)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Benefit Type:

Pharmacy Benefit:
ENTYVIO SQ

Medical Benefit:
ENTYVIO IV

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ENTYVIO® (vedolizumab) IV or SQ

Coding:

HCPCS: J3380

Description:

Entyvio (vedolizumab) is a monoclonal antibody that binds to integrin $\alpha_4\beta_7$ for the treatment of ulcerative colitis and Crohn's disease. Blocking integrin $\alpha_4\beta_7$ results in gut-selective anti-inflammatory activity.

Measurements of serum concentrations of vedolizumab and antibodies to vedolizumab have been investigated as a method to determine if an individual has developed antibodies to vedolizumab. Prometheus® Laboratories Inc. Anser™ VDZ test is one test that measures serum concentrations of vedolizumab and antibodies to vedolizumab.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Crohn's Disease Activity Index:

Sum each factor after adjustment with a weighting factor

Clinical or laboratory variable	Weighting factor	Factor Sum
Number of liquid or soft stools each day for seven days	x 2	
Abdominal pain (graded 0 = none, 1 = mild, 2 = moderate, 3 = severe) each day for 7 days	x 5	
General well-being (assessed from 0 = well, 1 = slightly under par, 2 = poor, 3 = very poor, 4 = terrible) each day for 7 days	x 7	
Presence of complications†	x 20	
Taking Lomotil (diphenoxylate/atropine) or opiates for diarrhea (0 = No, 1 = Yes)	x 30	
Presence of an abdominal mass (0 = none, 2 = questionable, 5 = definite)	x 10	
Hematocrit of < 0.47 in men and < 0.42 in women	x 6	
Percentage deviation from standard weight [1 – (ideal/observed)] x 100	x 1	
† **Complications**: one point each is added for each: • the presence of joint pains (arthralgia) or frank arthritis • inflammation of the iris or uveitis • presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers • anal fissures, fistulae or abscesses • other fistulae • fever during the previous week		
Total CDAI		

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Remission of CD: CDAI < 150
Moderate CD: CDAI 220-450
Severe CD: CDAI > 450
CD response: decrease in CDAI of > 70

Ulcerative Colitis Activity:

American College of Gastroenterology Ulcerative Colitis Activity Index				
	Remission	Mild	Moderate-severe	Fulminant
Stools (no./d)	Formed	< 4	> 6	> 10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	< 75% of normal	Transfusion needed
ESR	< 30	< 30	> 30	> 30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
Fecal calprotectin (mg/g)	< 150-200	> 150-200	> 150-200	> 150-200
Endoscopy (Mayo sub-score)	0-1	1	2-3	3
UCEIS	0-1	2-4	5-8	7-8
The above factors are general guides for disease activity. With the exception of remission, a patient does not need to have all the factors to be considered in a specific category. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.				

Endoscopic Assessment of Disease Activity		
Endoscopic Features	UCEIS Score	Mayo Score
Normal	0	0
Erythema, decreased vascular pattern, mild friability	1-3	1
Marked erythema, absent vascular pattern, friability, erosions	4-6	2
Spontaneous bleeding, ulceration	7-8	3

Immunomodulator therapies:

- Azathioprine
- 6-mercaptopurine
- Methotrexate

Resources:

Entyvio (vedolizumab). Prescribing information. Takeda Pharmaceuticals America, Inc.; 05/2024, at DailyMed https://dailymed.nlm.nih.gov/dailymed/. Accessed June 27, 2025.

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