MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Pharmacy Medical Policy

Entyvio (vedolizumab) Policy

Table of Contents

Policy Number: 162

BCBSA Reference Number: N/A

Related Policies

- Formulary Exception Form #434

Prior Authorization Information

Policy	☒ **Prior Authorization** ☐ Step Therapy ☐ Quantity Limit ☐ Administrative	Reviewing Department	**Pharmacy Operations:** Tel: 1-800-366-7778 Fax: 1-800-583-6289
		Policy Effective Date	**3/2024**
Pharmacy (Rx) or Medical (MED) benefit coverage	☒ Rx (Specialty Network); **OR** ☒ MED	**To request for coverage:** Providers may call, fax, or mail the attached form (Formulary Exception/Prior Authorization form) to the address below. **Blue Cross Blue Shield of Massachusetts** **Pharmacy Operations Department** 25 Technology Place Hingham, MA 02043 Tel: 1-800-366-7778 Fax: 1-800-583-6289 **Individual Consideration for the atypical patient:** Policy for requests that do not meet clinical criteria of this policy, see section labeled Individual Consideration	
Policy applies to Commercial Members: • Managed Care (HMO and POS), • PPO and Indemnity • MEDEX with Rx plan • Managed Major Medical with Custom BCBSMA Formulary • Comprehensive Managed Major Medical with Custom BCBSMA Formulary • Managed Blue for Seniors with Custom BCBSMA Formulary **Policy does NOT apply to**: • Medicare Advantage			

Summary

This is a comprehensive policy covering prior authorization, requirements for Entyvio (vedolizumab) for the treatment of moderate to severe Ulcerative Colitis (UC) and Crohn's Disease (CD).

Pathogenesis

Inflammatory Bowel Disease (IBD) is a condition characterized by chronic inflammation of the gastrointestinal (GI) tract. While the cause of IBD is unknown, it is however the result of the immune

system gone awry, triggered by either environmental factors or a genetic component. There are two main types of IBD conditions – UC and CD:

	Ulcerative Colitis	Chron's Disease
Location	Large intestine and rectum	Any part of GI tract from the mouth to the anus
Damage	Continuous damage usually starting at the rectum spreading into the colon	Patchy – damaged areas next to areas of health tissue
Inflammation	Present only in the innermost layer of the colon	May reach multiple layers of the walls of the GI tract

Entyvio (vedolizumab) is an integrin receptor antagonist approved for the use of moderate to severe Ulcerative Colitis and Crohn's Disease. It's FDA approved dosing is 300mg at week zero, two and six, then every 8 weeks thereafter. Entyvio (vedolizumab) should be discontinued in patients who do not show evidence of therapeutic benefit by week 14.

Formulary status of Integrin inhibitor agents:

Drug	Formulary Status (BCBSMA Commercial Plan)	FDA-approved Indication
Entyvio (vedolizumab), Intravenous	Covered, QCD, PA required	Moderate to severely active Ulcerative Colitis; moderate to severely active Crohn's disease
Entyvio (vedolizumab), Pen Injector	Covered, QCD, PA required	Moderate to severely active Ulcerative Colitis

PA – Prior Authorization; QCD – Quality Care Dosing/Quantity limit

Policy

No Coverage Requirements

For mild Crohn's Disease in low-risk patients, the recommended treatment approach is step up therapy up therapy with less potent drugs. These drugs have extensive evidence with good safety profiles such as:

- Oral 5-aminosalicylates (e.g., sulfasalazine, mesalamine)
- Glucocorticoids—topical or systemic (e.g., prednisone, budesonide)
- Immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate)

Please note that quantity limits may apply – please see limits found in Medical Policy #**621B**)

Entyvio ® (vedolizumab)

Length of Approval	Initial: 16 weeks; continuation of therapy: 12 months or 6 months for escalated dosing
Formulary status	Prior Authorization is required as per this medical policy. See section on individual consideration if an exception is required for the atypical patient.
Dosage considerations	Dosage considerations Standard Dosing Initiation: 3 single use vials (300 mg/vial) in the first 6 weeks or 42 days

	Continuation: 1 single use vial every 8 weeks or 56 days OR 1 pen injector every 2 weeks beginning at Week 6 post initiation. Note: We may approve an escalated dosing frequency of 1 single use vial (300 mg) every 4 weeks if additional criteria is met.

Initial Approval Criteria

APPROVAL duration – 16 weeks

Entyvio ® (vedolizumab) may be **MEDICALLY NECESSARY** when **ALL** of the following criteria are met:

Moderate to Severe Ulcerative Colitis

1. A documented diagnosis of moderate to severe Ulcerative Colitis; **AND**
2. Age is equal to or greater than 18 years; **AND**
3. The drug is prescribed by a board-certified or eligible gastroenterologist; **AND**
4. Documented history of failure, contraindication, or intolerance to at least one of the following conventional therapies:
    a. Tumor necrosis factor (TNF) blocker (e.g., infliximab, adalimumab, or golimumab); **OR**
    b. Immunomodulator (e.g., azathioprine, 6-mercaptopurine); **OR**
    c. Corticosteroid; **AND**
5. Not receiving in combination with any of the following:
    a. Biologic DMARD (e.g., JAK inhibitors, TNF inhibitors, IL-1 inhibitor, IL-6 inhibitor, etc.); **OR**
    b. Other Integrin Inhibitors (e.g., natalizumab); **AND**
6. For Subcutaneous Entyvio ONLY, there is clinical response or remission beyond week 6 following the first two Entyvio intravenous doses administered at Week 0 and Week 2; **AND**
7. Documented Dose and Frequency must be submitted and must be within the FDA approved Dosing and Frequency.

The recommended titration dosage of ENTYVIO in adults with Ulcerative Colitis:
Intravenous Entyvio - 300 mg administered by intravenous infusion at Week 0, Week 2 and Week 6 and then every 8 weeks thereafter; OR
Subcutaneous Pen Injector: 300 mg administered by intravenous infusion at Week 0 and Week 2 and then 108 mg subcutaneously at Week 6 and every 2 weeks thereafter

Moderate to Severe Crohn's Disease

1. A documented diagnosis of moderate to severe Crohn's Disease; **AND**
2. Age is equal to or greater than 18 years; **AND**
3. The drug is prescribed by a board-certified or eligible gastroenterologist; **AND**
4. Not receiving in combination with either of the following:

a. Potent Immunosuppressives (e.g., JAK inhibitors, TNF inhibitors, IL-1 inhibitor, IL-6 inhibitor, etc.); **OR**

b. Natalizumab; **AND**

5. Documented Dose and Frequency must be submitted and must be within the FDA approved Dosing and Frequency.

FDA-labeled dosing - The recommended titration dosage of ENTYVIO in adults with Crohn's disease is 300 mg administered by intravenous infusion at Week 0, Week 2 and Week 6 and then every 8 weeks thereafter

Renewal Criteria

RE-AUTHORIZATION duration – 12 months

We may renew coverage of Entyvio® if **ALL** the following criteria are met:

1. Individual continues to meet initial approval criteria; **AND**
2. Absence of unacceptable toxicity from the medication or serious allergic reactions, or severe infections; **AND**
3. Continued diagnosis and documentation of positive clinical response to Entyvio where a response to treatment as indicated by improvement in signs and symptoms compared to baseline including but not limited to:
    a. Reduction in stool frequency/bloody stools; **OR**
    b. Improvement abdominal pain; **OR**
    c. Endoscopic and laboratory response (e.g., C-reactive Protein); **AND**
4. Documented Dose and Frequency must be submitted and must be within the FDA approved Dosing and Frequency.

FDA-labeled dosing - The recommended dosage of ENTYVIO in adults with ulcerative colitis or Crohn's disease is 300 mg administered by intravenous infusion at zero, two and six weeks and then every eight weeks thereafter

Dose Escalation Criteria

INITIAL APPROVAL duration – 16 weeks

An escalated dosing regimen for Entyvio ® (vedolizumab) may be approved for one vial (300 mg) every 4 weeks if the following criteria are met:

1. Individual has been treated with standard maintenance dosing (i.e., every 8 weeks) for at least 2 doses or 16 weeks; **AND**
2. The increased dosing is being prescribed by or in consultation with a gastroenterologist; **AND**

3. Individual is not requesting dose escalation based solely on therapeutic drug levels or antibody testing alone in the absence of signs and symptoms of disease; **AND**
4. Partial or inadequate response to standard dosing characterized by:
    a. Individual initially achieved an adequate response to standard maintenance dosing but has subsequently lost response, as determined by the prescriber; **OR**
    b. Individual partially responded but had an inadequate response to standard maintenance dosing as determined by the prescriber; **AND**
5. Absence of unacceptable toxicity from the medication or serious allergic reactions, or severe infections; **AND**
6. Dose escalation does not exceed one vial (300 mg) every 4 weeks.
7. Documented Dose and Frequency must be submitted with dose escalation.

Dose Escalation Renewal Criteria

RE-AUTHORIZATION duration – 6 months

We may renew coverage of escalated dosing of Entyvio ® (vedolizumab) if **ALL** the following criteria are met:

1. Escalated dosage does not exceed one vial (300 mg) every 4 weeks; **AND**
2. Individual subsequently regained response or documentation of positive clinical response following increased dosing, as indicated by improvement in signs and symptoms of the disease including but not limited to:
    a. Reduction in stool frequency/bloody stools; **OR**
    b. Improvement abdominal pain; **OR**
    c. Endoscopic and laboratory response (e.g., C-reactive Protein); **AND**
3. Individual is not experiencing unacceptable adverse effects or serious allergic reactions, or severe infections; **AND**
4. Individual is being assessed regularly (at least annually) for dose de-escalation.
5. Documented Dose and Frequency must be submitted with dose escalation.

Use of Entyvio ® (vedolizumab) may be considered **INVESTIGATIONAL** for all other indications not specifically mentioned above.

Individual Consideration

Our medical policies are written for most people with a given condition. Each policy is based on peer reviewed clinical evidence. We also take into consideration the needs of atypical patient populations and diagnoses.

If the coverage criteria outlined is unlikely to be clinically effective for the prescribed purpose, the health care provider may request an exception to cover the requested medication based on an individual's unique clinical circumstances. This is also referred to as "individual consideration" or an "exception request."

Some reasons why you may need us to make an exception include: therapeutic contraindications; history of adverse effects; expected to be ineffective or likely to cause harm (physical, mental, or adverse reaction).

To facilitate a thorough and prompt review of an exception request, we encourage the provider to include additional supporting clinical documentation with their request. This may include:

- Clinical notes or supporting clinical statements;
- The name and strength of formulary alternatives tried and failed (if alternatives were tried) and specifics regarding the treatment failure, if applicable;
- Clinical literature from reputable peer reviewed journals;
- References from nationally recognized and approved drug compendia such as American Hospital Formulary Service® Drug Information (AHFS-DI), Lexi-Drug, Clinical Pharmacology, Micromedex or Drugdex®; and
- References from consensus documents and/or nationally sanctioned guidelines.

Providers may call, fax or mail relevant clinical information, including clinical references for individual patient consideration, to:

Blue Cross Blue Shield of Massachusetts
Pharmacy Operations Department
25 Technology Place
Hingham, MA 02043
Phone: 1-800-366-7778
Fax: 1-800-583-6289

We may also use prescription claims records to establish prior use of formulary alternatives or to show if step therapy criteria has been met. We will require the provider to share additional information when prescription claims data is either not available or the medication fill history fails to establish use of preferred formulary medications or that step therapy criteria has been met.

CPT Codes / HCPCS Codes / ICD Codes

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

HCPCS Codes

HCPCS Code	Code Description
J3380	Injection, vedolizumab, 1 mg
J3590	Unclassified drugs or biologics, Vedolizumab (SC)

ICD-10 Diagnosis Codes

ICD10 Diagnosis Code	Code Description

K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications

K51.40	Inflammatory polyps of colon without complications
K51.411	Inflammatory polyps of colon with rectal bleeding
K51.412	Inflammatory polyps of colon with intestinal obstruction
K51.413	Inflammatory polyps of colon with fistula
K51.414	Inflammatory polyps of colon with abscess
K51.418	Inflammatory polyps of colon with other complication
K51.419	Inflammatory polyps of colon with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela

Policy History

Date	Action
3/2024	Updated to require dose and frequency for Prior Authorization.
7/2023	Updated to align with 118E MGL § 51A
6/2023	Updated to new format, updated criteria for UC & CD coverage, references.
8/2022	Updated Criteria for both Crohn's and UC.
4/2021	Implement new standalone policy for Entyvio ® J3380 or J3380.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use ref

Managed Care Guidelines

Indemnity/PPO Guidelines

Clinical Exception Process

Medical Technology Assessment Guidelines

Forms

To request prior authorization using the Massachusetts Standard Form for Medication Prior Authorization Requests (eForm), click the link below:
Formulary Exception Form #434

Endnotes

1. FDA-approved indications
2. From National Blue Cross Blue Shield Association policy 5.01.05
3. Local Medicare policy http://www.medicarenhic.com/ and CMS guidelines http://www.hcfa.gov/pubforms/14%5Fcar/3b2049.htm#_1_7.

References

1. Entyvio ® [Product Information]. Lexington, MA. Takeda Pharmaceuticals U.S.A., Inc.; June 2022.
2. Medical Management of Low-Risk Adult Patients with Mild to Moderate Ulcerative Colitis. UptoDate Accessed: 6/1/2023
3. Management of Moderate to Severe Ulcerative Colitis in Adults. UptoDate Accessed: 6/1/2023
4. Overview of Drug Dosing and Monitoring of Biologic Agents and Small Molecule for Treatment of Ulcerative Colitis in Adults. UptoDate Accessed: 6/1/2023
5. Overview of Medical Management of High-risk, Adult Patients with Moderate to Severe Chron's Disease. UptoDate Accessed: 6/6/2023
6. GR Lichtenstein et al. ACG Clinical Guideline: Management of Chron's Disease in Adults. Am J Gastroenterology 2018;113:481-517.
7. JD Feuerstein et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Chron's Disease. Gastroenterology 2021;160:2496–2508.