Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 10/03/2024

Entyvio® IV (vedolizumab)

HCPCS: J3380

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Diagnosis of Crohn's Disease (CD)
      i. Treatment with an adequate course of conventional therapy (such as steroids for 7 days, immunomodulators such as azathioprine for at least 2 months) has been ineffective or is contraindicated or not tolerated
   d. Diagnosis of Ulcerative Colitis (UC)
      i. Treatment with an adequate course of conventional therapy (such as steroids for 7 days, immunomodulators such as azathioprine for at least 2 months) has been ineffective or is contraindicated or not tolerated
   e. Not to be used in combination with other biologics or targeted disease modifying anti-rheumatic drugs (DMARDs) for the same indication
   f. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSM/BCN utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Entyvio is an integrin receptor antagonist indicated for:
  - Adults with moderately to severely active ulcerative colitis (IV/subcutaneous)
  - Adults with moderately to severely active Crohn's disease (IV only)
- Crohn's disease (CD)
  - The 2018 American College of Gastroenterology (ACG) guidelines establish therapeutic recommendations for patients with CD based upon disease location, disease severity, disease-associated complications, and future disease prognosis. Therapeutic approaches are individualized according to the symptomatic response and tolerance to medical intervention. Current therapeutic approaches should be considered a sequential continuum to treat acute disease or induce clinical remission and then to maintain response/remission. In general, clinical evidence of improvement should be evident within 2 – 4 weeks and the maximal improvement should occur within 12 – 16 weeks. Those with continued symptoms should be treated with an alternative therapy for mild to moderate disease, have their medication dose adjusted in order to attempt to optimize therapy, or advance to treatment for moderate to severe disease according to their clinical status.
  - Corticosteroids are used primarily for the treatment of flares of CD. Conventional corticosteroids are effective for reducing the signs and symptoms of active CD and induction of remission in patients with moderately to severely active CD. Oral corticosteroids are effective and can be used for short-term use in alleviating signs and symptoms of moderate to severely active disease. The ACG guidelines recommend prednisone equivalent doses ranging from 40 to 60 mg per day. These doses are typically maintained for 1 –2 weeks and tapered at 5 mg weekly until 20 mg and then 2.5 –5 mg weekly. Once begun, care should be taken to ensure that corticosteroids are successfully discontinued, and steroid-sparing agents should be used.
  - In patients with moderate-to-severe CD who remain symptomatic despite current or prior corticosteroid therapy, mercaptopurine, azathioprine, and intramuscular or subcutaneous methotrexate are effective as steroid-sparing agents and are recommended by the guidelines. Maximum effectiveness of these agents can be seen between 8 to 12 weeks from therapy initiation. Methotrexate is also recommended in combination with steroids as effective for treatment of moderately active steroid-dependent/resistant CD. Cyclosporine, tacrolimus, and mycophenolate are not recommended for treatment of CD.
  - Biologics, such as anti-tumor necrosis factor (anti-TNF) agents are recommended to treat CD that is resistant to treatment with corticosteroids, thiopurines, or methotrexate. The ACG guidelines also recommend the use of biologics in combination with immunosuppressants to help decrease the formation of antibodies against the biologic therapy. There are no robust, published studies to support use of biologic agents in combination.
  - Entyvio is indicated for moderate to severely active disease; however, it only has proven efficacy in adults with moderate to severely active CD who had an inadequate response, lost response, or where intolerant to anti-TNF agents, immunomodulators, or corticosteroids.
  - The 2021 American Gastroenterological Association (AGA) guidelines include similar recommendations for the management of moderate-to-severe CD compared to the recommendations cited in the 2018 ACG guidelines. Both guidelines recommend corticosteroids over no treatment for induction of remission. Additionally, both guidelines recommend thiopurines, such as azathioprine or 6-mercaptopurine, as steroid-

sparing agents for maintenance of remission. The AGA guidelines also recommend the same biologic agents cited in the ACG guidelines for treatment of CD, with the exception of Tysabri® (natalizumab), which the AGA suggests against due to its associated risk of progressive multifocal leukoencephalopathy (PML).

- Of note, the AGA guidelines conditionally recommend earlier introduction of biologic therapy prior to failure of corticosteroids; however, this recommendation is supported by a low level of clinical evidence. To date, no blinded randomized controlled trials (RCTs) have demonstrated the superiority of early introduction of biologic therapy compared to conventional induction therapy with corticosteroids followed by steroid-sparing therapy. The 2021 AGA guideline authors also acknowledge that earlier therapy with either combination immunomodulator plus biologic therapy or biologic monotherapy may result in over-treating some patients and potentially exposing them to treatment-related risks and costs with limited benefit.

- Ulcerative Colitis (UC)

  - The 2019 American College of Gastroenterology guidelines and the 2020 American Gastroenterology Association guidelines state therapeutic management in UC should be guided by the specific diagnosis, an assessment of disease activity, and disease prognosis. Treatment selection should be based not only on inflammatory activity but also on disease prognosis.

  - Remission can be induced using a variety of medications, including, oral 5-aminosalicylates (5-ASA), corticosteroids, or biologic agents. In patients with mild to moderately active disease, treatment with 5-ASA therapy has proven to be safe and efficacious for induction. Recommended dosing is 2 grams per day of oral 5-ASA or at least 1 gram per day of rectal 5-ASA with improvement usually seen within 4 weeks. A typical treatment course may be up to 8 weeks.

  - Oral steroids are recommended for induction for patients with severe disease or those who did not respond to 5-ASA therapy. The typical starting doses of oral prednisone are 40 – 60 mg per day, and clinical response is expected within 5 – 7 days of treatment. A typical treatment course with oral prednisone is 14 days. The duration of systemic corticosteroids should be as short as possible with early initiation of steroid-sparing therapy. The speed of the taper should be guided by clinical symptoms, cumulative steroid exposure, and onset of action of alternate therapies. Those unable to taper off 10-20 mg of prednisone per day without relapsing are considered steroid dependent. Use systemic corticosteroids for maintenance of remission is not recommended.

  - Thiopurines, such as azathioprine and mercaptopurine, can be used to maintain remission. Guidelines recommend use of thiopurines over no medication or corticosteroids for maintenance therapy. Thiopurines are slow acting with maximum effectiveness of these agents being seen between 8 to 12 weeks from therapy initiation. They do not induce remission in moderately to severely active UC. Similarly, methotrexate is not an effective induction agent for induction or maintenance of remission.

  - Entyvio is also recommended for patients with moderate to severe disease with prior failure of anti-TNF therapy. Xeljanz® is recommended for patients with moderate to severe UC only after failure of, or intolerance to, anti-TNF agents.

References:

1. Entyvio [prescribing information]. Deerfield, IL: Takeda Pharmaceuticals; September 2023.
2. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of Crohn's disease in adults. AJG. 2018 April; 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. doi:10.1053/j.gastro.2021.04.022
4. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020; 158: 1450 - 61.
5. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. Am J Gastroenterol. 2019; 114: 384–413.

Policy History		
#	Date	Change Description
2.6	Effective Date: 10/03/2024	Added "for the same indication" to the not to be used in combination with other biologics or targeted DMARDs criteria
2.5	Effective Date: 03/01/2024	UM medical management system removal for MAPPO and BCNA for Entyvio SQ
2.4	Effective Date: 02/12/2024	UM medical management system update for MAPPO and BCNA for Entyvio SQ
2.3	Effective Date: 12/14/2023	Updated to include Entyvio SQ, FDA approved indication, and update the trial and failure preferred verbiage to reference pharmacy and medical benefit
2.2	Effective Date: 12/01/2022	Annual review of criteria was performed, no changes were made
2.1	Effective Date: 12/09/2021	Removed FDA approved indications criteria
2.0	Effective Date: 12/03/2020	Criteria updated to align management between pharmacy and medical benefit for all listed indications.
1.9	Effective Date: 4/16/2020	Addition of preferred therapy verbiage
1.8	Effective Date: 11/07/2019	Annual Review of Medical Policy
1.7	Effective Date: 11/01/2018	Took out step of TNF agents and added the following criteria: Not on concurrent treatment with a biologic response modifier (example: TNFs, natalizumab)
1.6	Effective Date: 08/09/2018	Updated policy to include preferred infliximab product verbiage
1.5	Effective Date: 02/08/2018	Annual Review of Medical Policy
1.4	Effective Date: 07/05/2017	UM medical management system update for MAPPO and BCNA for Entyvio IV
1.3	Effective Date: 02/09/2017	Annual Review of Policy
1.2	Effective Date: 01/01/2016	Document updated with specified drugs required
1.0	Effective Date: 10/30/2014	New Policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Entyvio IV® (vedolizumab) HCPCS CODE: J3380

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This form is to be used by participating physicians to obtain coverage for ENTYVIO®. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. What is the patient's dose and frequency of requested therapy?
   Initiation - *Dose*: _____mg *Frequency*: _____
   Maintenance - *Dose*: _____mg *Frequency* every: ☐ 2 weeks ☐ 4 weeks ☐ 6 weeks ☐ 8 weeks ☐ Other: _____
   If the frequency is **less than every 8 weeks** for maintenance dose please explain why?
   _____
3. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
4. **Please specify location of administration if hospital outpatient infusion:** _____
5. **Please provide the NPI number for the place of administration:** _____
6. **Initiation and Continuation:**
   a. What is the patient's diagnosis?
      ☐ Crohn's Disease ☐ Ulcerative Colitis ☐ Other, list diagnosis:_____
   b. Has the patient tried and failed therapy with at least one conventional therapy?
      ☐ Systemic corticosteroid daily for 7 days: please list name of drug(s): _____, Date started: _____ Date ended: ____
      ☐ Mercaptopurine, Date started: _____ Date ended: _____
      ☐ Azathioprine, Date started: _____ Date ended: _____
      ☐ Methotrexate, Date started: _____ Date ended: _____
      ☐ Other: _____, Date started: _____ Date ended: _____
   c. Will the patient be receiving Entyvio with other biologic agents (Infliximab, Humira, Kineret, Tremfya, etc) or targeted DMARD medications (for example: Otezla)? ☐ Yes ☐ No, Comment: _____
7. **Continuation request**: **Entyvio start date:** _____
   a. Have the patient's signs and symptoms improved with Entyvio?
      ☐ Yes ☐ No, Comment: _____

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached Chart Notes	☐ Prior Treatments with other medications
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

12/31/14; 11/20/2015; 4/22/2016; 7/8/2016; 10/3/2016; 2/2/2018; 7/24/2018, 9/18/2018; 10/11/2018; 3/15/2019; 12/3/2020