Reference number(s)
2666-A

Standard Medicare Part B Management Entyvio Intravenous (IV)

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name	Dosage Form
Entyvio	vedolizumab	intravenous (IV)

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, the member has no exclusions to the prescribed therapy, and the drug or biological is usually not self-administered. The criteria outlined in this policy is only applicable to drugs not usually self-administered and are furnished incident to a physician's service. Requests for drugs on a region's self-administered drug list are not covered. Members enrolled in Medicare Part D may seek coverage under the Medicare Part D plan.

FDA-Approved Indications[1]

- Adult patients with moderately to severely active ulcerative colitis (UC)
- Adult patients with moderately to severely active Crohn's disease (CD)

Compendial Uses[5,6,10]

- Immune checkpoint inhibitor-related toxicity
- Acute graft versus host disease

All other indications will be assessed on an individual basis. Submissions for indications other than those in the coverage criteria should be accompanied by supporting evidence from Medicare approved compendia.

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Documentation

The following documentation must be available, upon request, for all submissions:

Ulcerative colitis (UC) and Crohn's disease (CD)

For continuation requests: Chart notes or medical record documentation supporting benefit of therapy.

Immune checkpoint inhibitor-related toxicity and acute graft versus host disease

Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

Coverage Criteria

Ulcerative colitis (UC)[1,2,4,8]

Authorization of 12 months may be granted for treatment of moderately to severely active ulcerative colitis.

Crohn's disease (CD)[1,3,9]

Authorization of 12 months may be granted for treatment of moderately to severely active Crohn's disease.

Immune checkpoint inhibitor-related toxicity[5-7]

Authorization of 6 months may be granted for treatment of immune checkpoint inhibitor-related toxicity when the member has had an inadequate response, intolerance, or contraindication to systemic corticosteroids or infliximab.

Acute graft versus host disease[5,10]

Authorization of 12 months may be granted for treatment of acute graft versus host disease when either of the following criteria is met:

- Member has had an inadequate response to systemic corticosteroids.
- Member has an intolerance or contraindication to corticosteroids.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Immune checkpoint inhibitor-related toxicity and acute graft versus host disease

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

All other indications

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with Entyvio.
- Entyvio is being used to treat an indication listed in the coverage criteria.
- The member is receiving benefit from therapy.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Entyvio.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- NCCN Guideline: Management of Immunotherapy-Related Toxicities
- NCCN Guideline: Hematopoietic Cell Transplantation (HCT)
- An evidence-based systematic review on medical therapies for inflammatory bowel disease.
- American College of Gastroenterology (ACG) Clinical Guideline: Management of Crohn's Disease in Adults
- American Gastroenterological Association (AGA) Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis
- AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Entyvio are covered in addition to the following:

- Immune checkpoint inhibitor-related toxicity

- Acute graft versus host disease

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the continuation of therapy criteria for Crohn's disease can be found in the American College of Gastroenterology guidelines for the management of Crohn's disease (CD) and a review article by Talley et al.

The American College of Gastroenterology lists mucosal healing as determined by endoscopy as a goal of therapy. Mucosal healing is defined as an absence of ulceration and endoscopic scoring systems have been developed to quantify degree of ulceration and inflammation in patients with CD within the reach of the colonoscope. There are a limited number of studies that have examined the long-term impact of mucosal healing on the clinical course of disease. In patients with early-stage CD, complete mucosal healing after 2 years of therapy predicts sustained steroid-free, clinical remission 3 and 4 years out from initiation of treatment. Other clinical outcomes associated with mucosal healing in CD have been decreased surgery and hospitalizations. The simple endoscopic score for Crohn's disease (SES-CD) scoring system has been used prospectively to assess mucosal healing in patients treated with anti-tumor necrosis factor (anti-TNF) therapy as well as with anti-TNF/thiopurines combination therapy, demonstrating that changes can be measured; furthermore, there is a strong correlation between improvement in the SES-CD (mucosal) healing and clinical remission. Better clinical outcomes such as decreased hospitalizations, surgery, and steroid use is associated with improved findings on CTE and MRE in patients with small bowel Crohn's disease.

Improvement in the symptoms of CD is also a goal of therapy. The most common symptom of Crohn's disease is chronic diarrhea, but some patients may not experience this symptom. Abdominal pain, often localized to the right lower quadrant of the abdomen and worsened postprandially, is common. Improvement in these symptoms as well as fatigue, weight loss, anemia, and recurrent fistulas is considered sufficient evidence to continue with therapy.

Support for the continuation of therapy for ulcerative colitis can be found in the American Gastroenterological Association guidelines for the management of moderate to severe ulcerative colitis. The Truelove and Witts criteria for classifying the severity of UC include the number of stools per day, the presence of blood in the stool, hemoglobin, colonic features on radiograph and other clinical signs such as abdominal tenderness and distention. Improvement in any of these factors while on Entyvio therapy is sufficient to continue using the requested medication.

Additionally, the American College of Gastroenterology indicates an elevation in C-reactive protein and erythrocyte sedimentation rate are indicators of active UC. The guidelines go on to indicate the goal of treatment is to achieve mucosal healing (defined as resolution of inflammatory changes [Mayo endoscopic subscore 0 or 1] to increase the likelihood of sustained steroid-free remission and prevent hospitalizations and surgery). Fecal calprotectin can be used as a surrogate for endoscopy when endoscopy is not feasible or available to assess for mucosal healing. If the patient's condition appears to

be improving based on either of these factors, it is then considered acceptable to continue using the requested medication.

Support for using Entyvio for immune checkpoint inhibitor-related toxicities can be found in the National Comprehensive Cancer Network's guideline for management of immunotherapy-related toxicities. The NCCN Guideline supports the use of Entyvio for the management of mild (G1) diarrhea or colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin. Entyvio can also be used for the management of immunotherapy-related moderate (G2) and severe (G3-4) diarrhea or colitis.

Support for acute graft versus host disease (GVHD) can be found in the National Comprehensive Cancer Network's guideline for hematopoietic cell transplantation. The NCCN Guideline for hematopoietic cell transplantation supports the use of vedolizumab in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options. Therapy for steroid-refractory acute GVHD is often used in conjunction with the original immunosuppressive agent.

References

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4. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. 2019 ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019;114:384-413.
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