Reference number
2666-A

STANDARD MEDICARE PART B MANAGEMENT

ENTYVIO (vedolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Adult patients with moderately to severely active ulcerative colitis (UC)
2. Adult patients with moderately to severely active Crohn's disease (CD)

B. Compendial Uses
Immune checkpoint inhibitor-related toxicity

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

II. DOCUMENTATION

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

A. Ulcerative colitis (UC) and Crohn's disease (CD)
For continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

B. Immune checkpoint inhibitor-related toxicity (initial requests only)
Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.

III. CRITERIA FOR INITIAL APPROVAL

A. Ulcerative colitis (UC)
Authorization of 12 months may be granted for treatment of moderately to severely active ulcerative colitis.

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

C. Immune checkpoint inhibitor-related toxicity

Authorization of 6 months may be granted for treatment of immune checkpoint inhibitor-related toxicity when the member meets either of the following criteria:
1. Member has not responded to systemic corticosteroids or infliximab.
2. Member has moderate or severe diarrhea or colitis.

IV. CONTINUATION OF THERAPY

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

A. Ulcerative colitis (UC)

Authorization for 12 months may be granted for moderately to severely active ulcerative colitis when both of the following criteria are met:
1. The member is currently receiving therapy with Entyvio.
2. The member is receiving benefit from therapy. Benefit is defined as one of the following:
    i. Member has achieved or maintained remission.
    ii. Member has achieved or maintained a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
        a. Stool frequency
        b. Rectal bleeding
        c. Urgency of defecation
        d. C-reactive protein (CRP)
        e. Fecal calprotectin (FC)
        f. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
        g. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

B. Crohn's disease (CD)

Authorization for 12 months may be granted for moderately to severely active Crohn's disease when both of the following criteria are met:
1. The member is currently receiving therapy with Entyvio.
2. The member is receiving benefit from therapy. Benefit is defined as one of the following:
    i. Member has achieved or maintained remission.
    ii. Member has achieved or maintained a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
        a. Abdominal pain or tenderness
        b. Diarrhea
        c. Body weight
        d. Abdominal mass
        e. Hematocrit
        f. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
        g. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

C. Immune checkpoint inhibitor-related toxicity

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

V. SUMMARY OF EVIDENCE

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

1. The prescribing information for Entyvio.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. NCCN Guideline: Management of Immunotherapy-Related Toxicities
4. An evidence-based systematic review on medical therapies for inflammatory bowel disease.
5. American College of Gastroenterology (ACG) Clinical Guideline: Management of Crohn's Disease in Adults
6. American Gastroenterological Association (AGA) Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis
7. 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 immune checkpoint inhibitor-related toxicity.

VI. 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.

VII. REFERENCES

1. Entyvio [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; June 2022.
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3. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113:481-517.
4. Rubin DT, Ananthakrishnan AN, et al. 2019 ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol.* 2019;114:384-413.
5. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 16, 2023.
6. NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®). Management of Immunotherapy-Related Toxicities. Version 1.2022. Available at: www.nccn.org. Accessed January 16, 2023.
7. Schneider BJ, Naidoo J, Santomasso BD, et al. Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Guideline Update. *J Clin Oncol.* 2021; 39(36):4073-4126.
8. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020; 158:1450-1461.
9. 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: 2496-2508.