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Subject: Vedolizumab (Entyvio®) Injection and Infusion

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DESCRIPTION:

Vedolizumab (Entyvio) intravenous (IV) infusion was approved by the US Food and Drug Administration (FDA) in May 2014 for the treatment of moderately to severely active ulcerative colitis (UC) and moderately to severely active Crohn's disease (CD) in adults who have had an inadequate response with lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids. In March 2020, the indication was broadened to read as "indicated in adults for the treatment of moderately to severely active ulcerative UC and moderately to severely active CD". In September 2023, a subcutaneous (SC) formulation of vedolizumab was approved by the FDA for the treatment of adults with moderately to severely active UC. In April 2024, SC Entyvio received FDA approval for the addition indication for the treatment of adults with moderately to severely active CD.

Vedolizumab binds to and blocks the interaction between integrin alpha-4-beta-7 and mucosal addressing cell adhesion molecule-1 (MAdCAM-1) in the gut which inhibits the migration of specific memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. The action reduces the chronic inflammatory process present in both UC and Crohn's disease. FDA approval of the IV formulation was based on the results of three pivotal trials: GEMINI 1 (UC) and GEMINI 2 and GEMINI 3 (Crohn's disease). The approval of the SC formulation was based on the SC UC Trial (NCT02611830). In 2018 the National Comprehensive Cancer Network (NCCN) began publishing its guideline Management of Immunotherapy-Related-Toxicities. The NCCN eventually separated this guidelines into two separate guidelines - Management of Immune Checkpoint Inhibitor-Related Toxicities and Management of CAR T-Cell and Lymphocyte Engager-Related Toxicities. Vedolizumab IV is recommended (category 2A) as a consideration for the management of the following immunotherapy-related toxicities: (1) moderate to severe esophagitis, gastritis, or duodenitis if no improvement on corticosteroids or budesonide, (2) mild (Grade 1) diarrhea or colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin, (3) and moderate (Grade 2) diarrhea or colitis, and strongly consider for severe (Grade 3 or 4) diarrhea or colitis if colonoscopy or flexible sigmoidoscopy shows significant ulceration or extensive non-ulcerative inflammation. The NCCN guidelines also recommend (category 2A) vedolizumab IV as an adjunctive steroid sparing agent in cases of steroid-refractory diarrhea or for recurrent diarrhea with steroid taper in patients with Immune Effector Cell-Associated enterocolitis specific

to B-Cell Maturation Antigen (BCMA)-directed CAR T-cell therapy. The NCCN guidelines for Hematopoietic Cell Transplantation recommend (category 2A) vedolizumab IV for acute graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.

INFLAMMATORY BOWEL DISEASE

Crohn's Disease (CD)

Crohn's disease (CD) is a chronic inflammatory bowel disease with genetic, immunologic, and environmental influences. It can affect any portion of the gastrointestinal tract but involves the small intestine and proximal colon most often. The most common symptom is diarrhea, but abdominal pain, fatigue, fever, weight loss, and vomiting are also prevalent. Symptoms typically occur as a chronic, intermittent course, with only a minority of patients having continuously active symptomatic disease or a prolonged remission. In most cases, CD is a chronic, progressive, destructive disease. Early diagnosis and management of CD can lead to better outcomes and less negative impact on quality of life.

Patients are considered to have moderate to severe disease if they have failed to respond to treatment for mild to moderate disease, or if they present with more prominent symptoms of CD. Inflammation-related biomarkers are more likely to be abnormal, and greater endoscopic disease burden is typical. This includes larger or deeper ulcers, strictures, or extensive areas of disease and/or evidence of stricturing, penetrating, or perianal disease. The International Organization for the Study of Inflammatory Bowel Diseases characterizes patients with severe disease as having at least 10 loose stools per day, daily abdominal pain, presence of anorectal symptoms, systemic corticosteroid use within the prior year, lack of symptomatic improvement despite prior exposure to biologics and/or immunosuppressive agents, or significant impact of the disease on activities of daily living. They are also at a high risk for adverse disease-related complications, including surgery, hospitalization, and disability, based on a combination of structural damage, inflammatory burden, and impact of quality of life. Patients with severe disease may have large or deep mucosal lesions on endoscopy or imaging, presence of fistula and/or perianal abscess, presence of strictures, prior intestinal resections, presence of a stoma, and/or extensive disease (e.g., involvement of long bowel segments, pancolitis).

The choice of therapy in CD is dependent on the anatomic location of the disease, the severity of disease, and whether the treatment is needed to induce remission or maintain remission. The goal of treatment for induction of remission is to achieve clinical response and control of inflammation within 3 months of treatment initiation. After inducing clinical remission, patients should be transitioned to steroid-sparing maintenance therapy. In the absence of immunomodulator or biologic treatment, corticosteroid dependency and/or resistance occurs in up to half of patients. In general, the drug(s) used for induction of remission should be continued as maintenance therapy, with the exception of corticosteroids.

The American Gastroenterological Association (AGA) 2021 guideline provides the following recommendations and guidance:

- Biologic therapy:
    - The AGA suggest early introduction with a biologic, with or without an immunomodulator, rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids (Conditional recommendation, low certainty of evidence)
        - Earlier therapy with a biologic may result in overtreating some patients and potentially exposing them to treatment-related risks and costs with limited benefit. However, step-up therapy comes with a potential risk of harm from disease progression related to inadequate disease therapy.
    - Anti-tumor necrosis factor (TNF) (i.e., infliximab or adalimumab) and ustekinumab are recommended over no treatment for the induction and maintenance of remission
    - Vedolizumab is suggested over no treatment for the induction and maintenance of remission

- AGA suggests against the use of natalizumab over no treatment for the induction and maintenance of remission
- Patients naïve to biologic therapy, the AGA recommends infliximab, adalimumab, or ustekinumab over certolizumab pegol and suggests the use of vedolizumab over certolizumab pegol for the induction of remission
- Patients with primary non-response to anti-TNF, the AGA recommends ustekinumab and suggests vedolizumab for induction of remission
- Patients with secondary non-response to infliximab, the AGA recommends use of adalimumab or ustekinumab and suggests the use of vedolizumab for the induction of remission (if adalimumab was the first line drug, there is indirect evidence to suggest using infliximab as a second-line agent)

- Corticosteroid therapy:
  - Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission
    - In patients with CD involving the distal ileum and/or ascending colon who are more concerned about systemic corticosteroids and less concerned about the lower efficacy, they may reasonably choose budesonide over systematic corticosteroids for inducing remission
- Disease modifying antirheumatic drug (DMARD) therapy:
  - Patients in corticosteroid induced remission or with quiescent moderate to severe CD, the AGA suggests thiopurines for maintenance of remission
  - Subcutaneous or intramuscular methotrexate are suggested over no treatment for the induction and maintenance of remission
  - The AGA recommends against the use of 5-aminosalicylates or sulfasalazine over no treatment for the induction or maintenance of remission
  - The AGA suggests against the use of thiopurines over no treatment for achieving remission and recommends biologic drug monotherapy over thiopurine monotherapy for induction of remission
  - The AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission
- Combination therapy:
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of infliximab in combination with thiopurines over infliximab monotherapy for the induction and maintenance of remission (combination infliximab with methotrexate may be more effective over infliximab monotherapy)
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of adalimumab in combination with thiopurines over adalimumab monotherapy for the induction and maintenance of remission (combination adalimumab with methotrexate may be more effective over adalimumab monotherapy)
  - No recommendations are being made regarding the use of ustekinumab or vedolizumab in combination with thiopurines or methotrexate over biologic monotherapy for induction or maintenance or remission

The American College of Gastroenterology (ACG) 2025 guideline provides the following recommendations and guidance:

- Biologic therapy:
  - Biologic agents are effective for treating patients with active CD and previous inadequate response to corticosteroids, thiopurines, and/or methotrexate

- Suggest against requiring failure of conventional therapy before initiation of advanced therapy for the management of CD (conditional recommendation, low level of evidence)
    - The risk of adverse effects and high cost of biologic agents may not be justifiable in a lower risk population
- Recommend the following drugs for induction and maintenance of remission for moderately to severely active CD:
    - Anti-TNF agents (i.e., infliximab, adalimumab, certolizumab), vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab
- Recommend combination therapy of intravenous infliximab with immunomodulators (thiopurines) as compared with treatment with either immunomodulators alone or intravenous infliximab alone in patients with CD who are naïve to those agents
- Recommend the use of risankizumab as compared with ustekinumab in patients with moderate to severe CD and prior exposure to anti-TNF therapy
- Biosimilar infliximab, adalimumab, and ustekinumab are effective treatments for patients with moderate-to-severe CD and can be used for de novo induction and maintenance therapy
- There are data to support the safety and efficacy of transitioning or switching to biosimilar infliximab or adalimumab for patients with CD in stable disease maintenance

- Janus kinase (JAK) inhibitor therapy:
    - Recommend upadacitinib use for induction and maintenance of remission for patients with moderate-to-severe CD who have previously been exposed to anti-TNF agents
- Corticosteroid therapy:
    - Recommend oral corticosteroids for short-term induction of remission in patients with moderately to severely active CD
        - Recommend controlled ileal release budesonide at a dose of 9 mg daily for induction of symptomatic remission in patients with mildly to moderately active ileocecal CD
    - Corticosteroids should not be used for maintaining remission, and their use should not exceed 3 continuous months without attempting to introduce a steroid-sparing agent (such as an immunomodulator)
- DMARD therapy:
    - Recommend against azathioprine or 6-mercaptopurine for induction of remission in moderately to severely active CD
        - Due to their slow onset of action of 8 to 12 weeks, thiopurines are not effective agents for induction of remission
    - Suggest azathioprine or 6-mercaptopurine for maintenance of remission in patients with moderately to severely active CD who had induction of remission with corticosteroids
    - Suggest methotrexate (up to 25 mg once weekly intramuscular or subcutaneous) for maintenance of remission in patients with moderately to severely active CD who had induction of remission with corticosteroids
    - Azathioprine, 6-mercaptopurine, or methotrexate may be used in the treatment of active CD and as adjunctive therapy for reducing immunogenicity associated with anti-TNF therapy

Ulcerative Colitis (UC)

Ulcerative colitis (UC) is a chronic inflammatory bowel disease affecting the large intestine. It typically starts with inflammation of the rectum, but often extends proximally to involve additional areas of the colon. The most common symptom is bloody diarrhea, but urgency, tenesmus, abdominal pain, malaise, weight loss, and fever can also be associated. UC commonly has a gradual onset and will present with periods of spontaneous remission and subsequent relapses.

Disease severity is based on patient-reported outcomes (e.g., bleeding, bowel habits, bowel urgency), inflammatory burden (e.g., endoscopic assessment, inflammatory markers), disease course, and disease impact. Commonly assessed symptoms include frequency and timing of bowel movements, rectal bleeding, bowel urgency, abdominal pain, bowel cramping, and weight loss. Poor prognostic factors include less than 40 years of age at diagnosis, extensive colitis, severe endoscopic disease, hospitalization for colitis, elevated C-reactive protein (CRP), and low serum albumin. Therapeutic management in UC should be guided by the extent of bowel involvement, assessment of disease activity (i.e., quiescent, mild, moderate, or severe), and disease prognosis. Treatment response should be evaluated 12 weeks after initiation of therapy to confirm efficacy and safety.

The American College of Gastroenterology (ACG) published recommendations and guidance (2025) for the management of moderate-to-severe UC:

General treatment information:

- Patients with mildly to moderately active UC and a number of prognostic factors associated with an increased risk of hospitalization or surgery should be treated with therapies for moderate-to-severe disease
- Patients with mildly to moderately active UC who are not responsive (or are intolerant) to 5-aminosalicylate (5-ASA) therapies (e.g., balsalazide, mesalamine, sulfasalazine) should be treated as patients with moderate-to-severe disease

Corticosteroid therapy:

- In patients with moderately active UC, recommend oral budesonide multi-matrix system (MMX) for induction of remission
    - In patients with moderately active UC, consider nonsystemic corticosteroids such as budesonide MMX before the use of systemic therapy
- Recommend oral systemic corticosteroids to induce remission in UC of any extent
    - In patients with severely active UC, consider systemic corticosteroids rather than topical corticosteroids
- Recommend against systemic, budesonide MMX, or topical corticosteroids for maintenance of remission

Disease modifying antirheumatic drug (DMARD) therapy:

- Recommend against monotherapy with thiopurines or methotrexate for induction of remission
- 5-ASA therapy could be used as monotherapy for induction of moderately but not severely active UC
- 5-ASA therapy for maintenance of remission is likely not as effective in prior severely active UC as compared with prior moderately active UC
- Suggest thiopurines for maintenance of remission in patients now in remission due to corticosteroid induction
- Suggest against using methotrexate for maintenance of remission

Biologic/advanced therapy:

- Recommend the following drugs for induction of remission and continuing the same drug for maintenance of remission:

- Anti-tumor necrosis factor (TNF) agents (e.g., infliximab, adalimumab, golimumab), ustekinumab, guselkumab, mirikizumab, risankizumab, vedolizumab, tofacitinib, upadacitinib, sphingosine-1-phosphate (S1P) receptor modulators (e.g., ozanimod, etrasimod)
- Most clinical trials and available data demonstrate a benefit of using the steroid-sparing therapy that induces remission to maintain that remission

- When infliximab is used as induction therapy, recommend combination therapy with a thiopurine
  - Data on combination anti-TNF and immunomodulators in moderately to severely active UC only exist for infliximab and thiopurines
- Infliximab is the preferred anti-TNF therapy for patients with moderately to severely active UC
- Recommend vedolizumab as compared to adalimumab for induction and maintenance of remission
- Patients who are primary nonresponders to an anti-TNF (defined as lack of therapeutic benefit after induction and despite sufficient serum drug concentrations) should be evaluated and considered for alternative mechanisms of disease control (e.g., in a different class of therapy) rather than cycling to another drug within the anti-TNF class
- Biosimilars to anti-TNF therapies and to ustekinumab are acceptable substitutes for originator therapies. Delays in switching should not occur and patients and clinicians should be notified about such changes

The American Gastroenterology Association (AGA) published recommendations and guidance (2018) for the management of mild-to-moderate UC:

- In patients with moderate disease activity, suggest using high dose mesalamine (greater than 3 g/day) with rectal mesalamine for induction of remission and maintenance of remission
- Add either oral prednisone or budesonide MMX in patients that are refractory to optimized oral and rectal 5-ASA, regardless of disease extent
- If progression to moderate-to-severe disease activity occurs, or if the patient is at high risk for colectomy despite therapy, consider escalating to treatment for moderate-to-severe disease with immunomodulators and/or biologics

The American Gastroenterology Association (AGA) published recommendations and guidance (2024) for the management of moderate-to-severe UC:

<u>General treatment information</u>:

- Suggest early use of advanced therapy (e.g., biologics, ozanimod, etrasimod), with or without immunomodulator therapy (e.g., thiopurines), rather than treatment with 5-ASA and a gradual step up to biologic/immunomodulator therapy after 5-ASA treatment failure (conditional recommendation, very low certainty of evidence)
  - Patients with less severe disease or those who place a higher value on the safety of 5-ASA therapy over the efficacy of immunosuppressives may reasonably choose gradual step therapy with 5-ASA therapy

<u>DMARD therapy</u>:

- Suggest against using thiopurine monotherapy for inducing remission
- Suggest thiopurine monotherapy may be used for maintaining remission typically induced with corticosteroids
- Suggest against using methotrexate monotherapy for inducing or maintaining remission

<u>Advanced therapy</u>:

- Recommend using one of the following advanced therapies over no treatment:

- Infliximab, golimumab, vedolizumab, tofacitinib, upadacitinib, ustekinumab, ozanimod, etrasimod, risankizumab, guselkumab

- Suggest using one of the following advanced therapies over no treatment:
  - Adalimumab, filgotinib*, mirikizumab (*not currently approved by the Food and Drug Administration)
- Biosimilars of infliximab, adalimumab, and ustekinumab can be considered equivalent to their originator drug in their efficacy
- Suggest the use of infliximab in combination with an immunomodulator over infliximab or an immunomodulator alone
- Suggest the use of adalimumab or golimumab in combination with an immunomodulator over adalimumab, golimumab or immunomodulator monotherapy

Advanced therapy-naïve patients (first-line therapy):

- Suggest that a higher or intermediate efficacy medication be used rather than a lower efficacy medication
  - Higher efficacy: infliximab, vedolizumab, ozanimod, etrasimod, upadacitinib, risankizumab, guselkumab
  - Intermediate efficacy: golimumab, ustekinumab, tofacitinib, filgotinib, mirikizumab
  - Lower efficacy: adalimumab

Prior exposure to one or more advanced therapies, particularly TNF antagonists:

- Suggest that a higher or intermediate efficacy medication be used rather than a lower efficacy medication
  - Higher efficacy: tofacitinib, upadacitinib, ustekinumab
  - Intermediate efficacy: filgotinib, mirikizumab, risankizumab, guselkumab
  - Lower efficacy: adalimumab, vedolizumab, ozanimod, etrasimod

POSITION STATEMENT:

Site of Care: If intravenous vedolizumab (Entyvio) is administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to 09-J3000-46: Site of Care Policy for Select Specialty Medications.

Comparative Effectiveness

The Food and Drug Administration has deemed the subcutaneously-administered drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) of the subcutaneous formulation of vedolizumab in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary. This statement does not apply to the intravenous (IV) formulation of vedolizumab (Entyvio).

NOTE: The list of self-administered products with prerequisites for certain indications can be found at Preferred Agents and Drug List.

SUBCUTANEOUS ENTYVIO (PHARMACY BENEFIT)

Initiation of subcutaneous vedolizumab (Entyvio) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "5"):

1. **ONE** of the following ("a", "b", or "c"):
    a. The member has been treated with intravenous or subcutaneous vedolizumab (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with intravenous or subcutaneous vedolizumab (starting on samples is not approvable) within the past 90 days **AND** is at risk if therapy is changed
    c. **BOTH** of the following ('i" and "ii"):
        i. Subcutaneous vedolizumab will be used for the treatment of an indication listed in Table 1, and **ALL** of the indication-specific criteria are met
        ii. **EITHER** of the following if the member has an FDA-approved indication ("I" or "II")
            i. The member's age is within FDA labeling for the requested indication for subcutaneous vedolizumab
            ii. The prescriber has provided information in support of subcutaneous vedolizumab for the member's age for the requested indication
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., gastroenterologist for CD or UC) or the prescriber has consulted with a specialist in the area of the member's diagnosis
3. Member does **NOT** have any FDA labeled contraindications to subcutaneous vedolizumab
4. Member will **NOT** be using subcutaneous vedolizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
5. **ANY** of the following ("a". "b", "c", or "d"):
    a. The dosage does not exceed 108 mg subcutaneously once every 2 weeks [to be started 4 weeks after the second loading dose of IV vedolizumab]
        - QL: 108 mg/0.68 mL pen – 2 pens/28 days
        - QL: 108 mg/0.68 mL syringe – 2 syringes/28 days
    b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
        i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
        ii. **ALL** of the following ("1", "2", and "3"):
            1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication
            2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)
            3. **EITHER** of the following ("a" or "b"):
                a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be

achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit

b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

c. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, AND the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit

ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

d. The member does **NOT** have an FDA labeled indication **NOR** a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):

i. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

Approval duration: 12 months; the start date will depend on the number of Entyvio IV doses already received

Table 1

Indications and Specific Criteria	
Indication	**Specific Criteria**
Moderately to severely active Crohn's disease (CD)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD after at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of CD **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of CD **OR**

	d. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** e. The member has severe disease and/or risk factors for disease complications for which initial treatment with Entyvio is deemed clinically necessary – provider must include additional details regarding disease severity and/or risk factors **AND** 2. The member has received or will receive at least two doses of Entyvio IV therapy
Moderately to severely active ulcerative colitis (UC)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, balsalazide, corticosteroids, cyclosporine, mesalamine, sulfasalazine) used in the treatment of UC after at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of UC **OR** c. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of UC **OR** d. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** e. The member has severe disease and/or risk factors for disease complications for which initial treatment with Entyvio is deemed clinically necessary – provider must include additional details regarding disease severity and/or risk factors **AND** 2. The member has received or will receive at least two doses of Entyvio IV therapy

Continuation of subcutaneous vedolizumab (Entyvio) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "6"):

1. An authorization or reauthorization for subcutaneous vedolizumab has been previously approved by Florida Blue [Note: members not previously approved for the requested agent will require initial evaluation review]

2. Member has had clinical benefit with subcutaneous vedolizumab
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., gastroenterologist for CD or UC) or the prescriber has consulted with a specialist in the area of the member's diagnosis
4. Member does **NOT** have any FDA labeled contraindications to subcutaneous vedolizumab
5. Member will **NOT** be using subcutaneous vedolizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. **ANY** of the following ("a", "b", "c", or "d"):
    a. The dosage does not exceed 108 mg subcutaneously once every 2 weeks
        - QL: 108 mg/0.68 mL pen – 2 pens/28 days
        - QL: 108 mg/0.68 mL syringe – 2 syringes/28 days
    b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
        i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
        ii. **ALL** of the following ("1", "2", and "3"):
            1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication
            2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)
            3. **EITHER** of the following ("a" or "b"):
                a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit
                b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, AND there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)
    c. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
        i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit
        ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)
    d. The member does **NOT** have an FDA labeled indication **NOR** a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):

i. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

Approval duration: 12 months

INTRAVENOUS ENTYVIO (MEDICAL BENEFIT)

Initiation of intravenous (IV) vedolizumab (Entyvio) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "4"):

1. Intravenous vedolizumab will be used for the treatment of an indication listed in Table 2, and **ALL** indication-specific and maximum-allowable dosage criteria are met
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., gastroenterologist for CD, UC) or the prescriber has consulted with a specialist in the area of the member's diagnosis
3. Member does **NOT** have any FDA labeled contraindications to intravenous vedolizumab
4. For CD and UC diagnoses only - member will **NOT** be using intravenous vedolizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

Approval duration: 6 months (except for immune checkpoint inhibitor-related toxicity and IEC-associated enterocolitis specific to BCMA-directed CAR T-cell therapy, approve for 14 weeks only)

Table 2

Indications and Specific Criteria		
Indication	**Specific Criteria**	**Maximum Allowable Dose***
Moderately to severely active Crohn's disease (CD)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD after at least a 3-month duration of therapy **OR** 2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of CD **OR** 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of CD	**Initial** • 300 mg at week 0, 2, 6 and 14 **Maintenance:** • 300 mg every 8 weeks starting on week 22

	OR 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with Entyvio is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors	
Moderately to severely active ulcerative colitis (UC)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, balsalazide, corticosteroids, cyclosporine, mesalamine, sulfasalazine) used in the treatment of UC after at least a 3-month duration of therapy **OR** 2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of UC **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of UC **OR** 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with Entyvio is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors	**Initial:** • 300 mg at week 0, 2, 6 and 14 **Maintenance:** • 300 mg every 8 weeks starting on week 22

Immune checkpoint inhibitor-related adverse effects/toxicity	**ALL** of the following: 1. Member has been receiving treatment with an immune checkpoint inhibitor (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab) **AND** 2. **ANY** of the following: a. Member has moderate to severe esophagitis, gastritis, or duodenitis, **AND** has had no improvement on corticosteroids or budesonide **OR** b. Member has mild (Grade 1) diarrhea or colitis if persistent or progressive symptoms, **AND** positive lactoferrin/calprotectin **OR** c. Member has moderate (Grade 2) or severe (Grade 3 or 4) diarrhea or colitis [i.e., at least 4 or more bowel movements above baseline per day and colitis symptoms], **AND** colonoscopy or flexible sigmoidoscopy shows significant ulceration or extensive non-ulcerative inflammation	300 mg at weeks 0 and 2. May repeat up to two additional 300 mg doses at weeks 6 and 10 if the member does not have adequate improvement in symptoms.
Immune effector cell (IEC)-associated enterocolitis specific to B-cell maturation antigen (BCMA)-directed CAR T-cell therapy	**BOTH** of the following: 1. The member has previously received a BCMA-directed CAR T-cell therapy [e.g., idecabtagene vicleucel (Abecma), ciltacabtagene autoleucel (Carvykti)] **AND** 2. Member has steroid-refractory diarrhea **OR** recurrent diarrhea following a steroid taper	300 mg at weeks 0 and 2. May repeat up to two additional 300 mg doses at weeks 6 and 10 if the member does not have adequate improvement in symptoms.
Acute graft-versus-host disease (GVHD)	**ALL** of the following: 1. The member has previously received an allogeneic hematopoietic stem cell transplantation (HSCT) **AND** 2. Vedolizumab will be used as additional therapy in conjunction with systemic corticosteroids **AND** 3. The member has steroid-refractory disease	300 mg at week 0, 2, 6 and then every for 4 weeks not to exceed 6 months of treatment.

Other indications	The member has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a	Maximum dose supported by the FDA labeled indication or maximum dose supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a
*The maximum allowable dose can be exceeded if – (1) the dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication **OR** (2) the prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)		

Continuation of intravenous (IV) vedolizumab **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. An authorization or reauthorization for IV vedolizumab has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of a condition listed in Table 1 (except for acute GHVD, IEC-associated enterocolitis specific to BCMA-directed CAR T-cell therapy, and immune checkpoint inhibitor-related toxicity– see initiation criteria), **OR** the member previously met **ALL** indication-specific initiation criteria
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., gastroenterologist for CD, UC) or the prescriber has consulted with a specialist in the area of the member's diagnosis
3. Member does **NOT** have any FDA labeled contraindications to IV vedolizumab
4. Member has had clinical benefit with IV vedolizumab therapy, **UNLESS** the current maintenance dosage is 300 mg every 8 weeks and a shortened dosage interval (e.g., every 4 or 6 weeks) may be appropriate (see criteria in bullet point 6bi below)
5. Member will **NOT** be using IV vedolizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)], and Xeljanz XR (tofacitinib extended release)]; Otezla/Otezla XR (apremilast), Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. The dosage does not exceed **ANY** of the following ("a", "b", or "c"), **UNLESS** previously approved by Florida Blue **OR** another health plan (if another health plan, documentation of health plan-paid claims for Entyvio supporting the higher dosage during the 6 months immediately before the authorization request must be submitted):
    a. The dosage does not exceed 300 mg IV every 8 weeks (if for CD or UC)
    b. **BOTH** of the following if being used for CD or UC ('i" and ii"):
        i. Member has had a loss-of-response following an initial primary response (i.e., secondary non-response) after at least 6 months of continuous vedolizumab treatment
        ii. The dosage does not exceed 300 mg IV every 4 weeks
    c. The dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication **OR** the prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Vedolizumab is indicated for the treatment of adults with either of the following:

- Moderately to severely active ulcerative colitis (UC)
- Moderately to severely active Crohn's disease (CD)

Intravenous Administration for UC and CD

The recommended dose for both indications is 300 mg infused intravenously over approximately 30 minutes at weeks 0, 2, 6 and then every eight weeks. The manufacturer recommends discontinuation if there is no evidence of benefit at week 14.

Subcutaneous Injection for UC and CD

Following the first two IV doses administered at weeks 0 and 2, vedolizumab may be switched to subcutaneous injection at week 6. The recommended dose week 6 and thereafter is 108 mg injected subcutaneously once every 2 weeks. The manufacturer recommends discontinuation if there is no evidence of benefit at week 14. Vedolizumab may be switched from intravenous infusion to subcutaneous injection, for patients in clinical response or remission beyond week 6. To switch patients to subcutaneous injection, administer the first subcutaneous dose in place of the next scheduled intravenous infusion and every 2 weeks thereafter.

Product availability

- 300 mg of vedolizumab as a white to off-white lyophilized cake in a single-dose vial for reconstitution
- 108 mg/0.68 mL vedolizumab as a clear to moderately opalescent, colorless to slightly yellow solution in a single-dose prefilled syringe with needle safety device
- 108 mg/0.68 mL vedolizumab as a clear to moderately opalescent, colorless to slightly yellow solution in a single-dose prefilled pen (ENTYVIO PEN).

PRECAUTIONS:

Boxed Warning:

- None

Contraindication:

- Known serious or severe hypersensitivity reaction to vedolizumab or any of its excipients (such as dyspnea, bronchospasm, urticaria, flushing, rash and increased heart rate)

Precautions/Warnings:

- **Infusion-Related Reactions and Hypersensitivity Reactions**: Infusion-related reactions and hypersensitivity reactions have been reported, including anaphylaxis, dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate. These reactions may occur with the first or subsequent infusions and may vary in their time of onset from during infusion or up to

several hours post-infusion. Discontinue vedolizumab if anaphylaxis or other serious allergic reactions occur.

- **Infections**: Treatment with vedolizumab is not recommended in persons with active, severe infections until the infections are controlled. Consider withholding vedolizumab in those who develop a severe infection while on treatment with vedolizumab.
- **Progressive Multifocal Leukoencephalopathy**: PML, a rare and often fatal opportunistic infection of the central nervous system (CNS), has been reported with systemic immunosuppressants, including another integrin receptor antagonist. PML is caused by the John Cunningham (JC) virus and typically only occurs in patients who are immunocompromised. One case of PML in an vedolizumab -treated patient with multiple contributory factors has been reported in the post-marketing setting (e.g., human immunodeficiency virus [HIV] infection with a CD4 count of 300 cells/mm3 and prior and concomitant immunosuppression). Although unlikely, a risk of PML cannot be ruled out. Monitor individuals administered vedolizumab for any new or worsening neurological signs or symptoms.
- **Liver Injury**: There have been reports of elevations of transaminase and/or bilirubin in patients receiving vedolizumab. In general, the combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients. Vedolizumab should be discontinued in patients with jaundice or other evidence of significant liver injury.
- **Live and Oral Vaccines**: Prior to initiating treatment, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving vedolizumab may receive non-live vaccines (e.g., influenza vaccine injection) and may receive live vaccines if the benefits outweigh the risks. There are no data on the secondary transmission of infection by live vaccines in patients receiving vedolizumab.

BILLING/CODING INFORMATION:

HCPCS Coding

J3380	Injection, vedolizumab, intravenous, 1 mg
J3590	Unclassified biologics [for the subcutaneous formulation only]

ICD-10 Diagnosis Codes That Support Medical Necessity for J3380 (IV formulation)

D89.810	Acute graft-versus-host disease
D89.812	Acute on chronic graft-versus-host disease
K50.00 – K50.919	Crohn’s disease (regional enteritis)
K51.00 – K51.919	Ulcerative colitis
T45.AX5A	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, initial encounter
T45.AX5D	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, subsequent encounter
T45.AX5S	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, sequela
T80.82XA	Complication of immune effector cellular therapy, initial encounter
T80.82XD	Complication of immune effector cellular therapy, subsequent encounter
T80.82XS	Complication of immune effector cellular therapy, sequela

ICD-10 Diagnosis Codes That Support Medical Necessity for J3590 (SC formulation)

K50.00 – K50.919	Crohn’s disease (regional enteritis)
K51.00 – K51.919	Ulcerative colitis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date. The Site of Care Policy for Select Specialty Medications does not apply to Medicare Advantage members.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Crohn's Disease: is an inflammatory bowel disease characterized by severe, chronic inflammation of the intestinal wall or any portion of the gastrointestinal tract. The lower portion of the small intestine (ileum) and the rectum are most commonly affected by this disorder. Symptoms may include watery diarrhea and abdominal pain. The symptoms of Crohn's Disease can be difficult to manage, and diagnosis is often delayed.

DMARDs: An acronym for disease-modifying antirheumatic drugs. These are drugs that modify the rheumatic disease processes, and slow or inhibit structural damage to cartilage and bone. These drugs are unlike symptomatic treatments such as NSAIDs that do not alter disease progression. DMARDs can be further subcategorized. With the release of biologic agents (e.g., anti-TNF drugs), DMARDs were divided into either: (1) conventional, traditional, synthetic, or non-biological DMARDs; or as (2) biological DMARDs. However, with the release of newer targeted non-biologic drugs and biosimilars, DMARDs are now best categorized as: (1) conventional synthetic DMARDs (csDMARD) (e.g., MTX, sulfasalazine), (2) targeted synthetic DMARDs (tsDMARD) (e.g., baricitinib, tofacitinib, apremilast), and (3) biological DMARDs (bDMARD), which can be either a biosimilar DMARD (bsDMARD) or biological originator DMARD (boDMARD).

Mild-Moderate Crohn's Disease: Mild-moderate Crohn's disease applies to ambulatory members able to tolerate oral alimentation without manifestations of dehydration, toxicity (high fevers, rigors, prostration), abdominal tenderness, painful mass, obstruction, or >10% weight loss.

Moderate-Severe Crohn's Disease: Moderate-severe disease applies to members who have failed to respond to treatment for mild-moderate disease or those with more prominent symptoms of fevers, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia.

Ulcerative colitis: a chronic inflammatory disease of the colon that is of unknown cause and is characterized by diarrhea with discharge of mucus and blood, cramping abdominal pain, and inflammation and edema of the mucous membrane with patches of ulceration.

RELATED GUIDELINES:

Abatacept (Orencia), 09-J0000-67
Adalimumab Products, 09-J0000-46
Anakinra (Kineret), 09-J0000-45

Etanercept (Enbrel), 09-J0000-38
Etrasimod (Velsipity), 09-J4000-72
Golimumab (Simponi, Simponi Aria), 09-J1000-11
Infliximab Products, 09-J0000-39
Mirikizumab (Omvoh), 09-J4000-71
Natalizumab (Tysabri) Injection, 09-J0000-73
Rituximab Products, 09-J0000-59
Tocilizumab Products (Actemra, Tofidence, Tyenne), 09-J1000-21
Tofacitinib (Xeljanz, Xeljanz XR), 09-J1000-86
Ustekinumab (Stelara), 09-J1000-16

OTHER:

NOTE: The list of biologic immunomodulator agents not permitted as concomitant therapy can be found at Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.

Table 3: Conventional Synthetic DMARDs

DMARD Generic Name	DMARD Brand Name
Auranofin (oral gold)	Ridaura
Azathioprine	Imuran
Cyclosporine	Neoral, Sandimmune
Hydroxychloroquine	Plaquenil
Leflunomide	Arava
Methotrexate	Rheumatrex, Trexall
Sulfasalazine	Azulfidine, Azulfidine EN-Tabs

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maintenance of remission in inflammatory Crohn's disease. Gastroenterology. 2013 Dec;145(6):1459-63.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/12/25.

GUIDELINE UPDATE INFORMATION:

09/15/14	New Medical Coverage Guideline.
09/15/15	Review and revision to guideline; consisting of updating position statement, billing/coding, and references.
11/01/15	Revision: ICD-9 Codes deleted.
01/01/16	Annual HCPCS coding update: added code J3380 and deleted codes C9026 and J3590.
09/15/16	Review and revision to guideline consisting of updating position statement and references.
5/15/17	Revision to guideline consisting of updating the references and position statement to allow use in adolescents (age 12 to 17 years).
10/15/17	Review and revision to guideline consisting of updating description, position statement, dosage/administration, coding/billing, definitions, related guidelines, and references.
07/15/18	Revision to guideline consisting of updating the description section, position statement, coding/billing, and references based on the new NCCN guideline for management of immunotherapy-related toxicities.
10/15/18	Review and revision to guideline consisting of updating the position statement and references.
01/15/19	Revision to guideline consisting of updating the description section, position statement, and references based on the updated NCCN guideline for management of immunotherapy-related toxicities.
10/15/19	Review and revision to guideline consisting of updating the position statement and references.
11/11/19	Revision to guideline consisting of adding a reference to the Site of Care Policy for Select Specialty Medications and updating the Program Exceptions.
07/01/20	Revision to guideline consisting of updating the description and position statement.
01/01/21	Review and revision to guideline consisting of updating the description, position statement, precautions, and references.
01/01/22	Review and revision to guideline consisting of updating the description, position statement, other section, and references.
03/15/22	Revision to guideline consisting of updating the position statement and other section.
01/01/23	Review and revision to guideline consisting of updating the position statement, other section, and references. New drugs were added to the list of drugs that are not permitted for use in combination. For CD and UC, added allowance for infliximab products to be used first line for members with severe disease and/or risk factors for disease complications. Allowing higher continuation dosage when approved by another health plan when supportive claims are submitted.
04/15/23	New drugs were added to the list of drugs that are not permitted for use in combination.
07/01/23	Revision to guideline consisting of updating the other section. Humira biosimilar products added to list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.
01/01/24	Review and revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, billing/coding, other section, and references. Added Entyvio SC as a 3c agent (stepped through preferred agents). Amjevita low-concentration [10 mg/0.2 mL, 20 mg/0.4 mL, and 40 mg/0.8 mL concentrations only] clarified as the preferred prerequisite product. Added Table 1 to Position Statement. Position statement divided into one section for “SUBCUTANEOUS ENVYVIO (PHARMACY BENEFIT)” and one section for “INTRAVENOUS ENTYVIO (MEDICAL BENEFIT)” as criteria are different.

	Updated immune checkpoint inhibitor-related diarrhea or colitis criteria. Removed prevention and treatment of GVHD. New drugs were added to the list of drugs that are not permitted for use in combination.
04/01/24	Revision to guideline consisting of updating the position statement regarding continuation of therapy in members not previously approved by Florida Blue.
07/01/24	Revision to guideline consisting of updating the description section, position statement. dosage/administration, billing/coding, related guidelines, other section, and references. Entyvio SC for UC was changed from a Step 3c agent to a Step 3b agent (i.e., now stepped though two preferred agents vs. three). Amjevita low-concentration removed as a preferred agent. New indication of CD added for Entyvio SC (Step 3b). Removal of latent TB testing requirement. New drugs added to the list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.
10/01/24	Revision to guideline consisting of updating the position statement and billing/coding. Updates to Table 1. Simlandi added among the required prerequisite agents for self-administered Entyvio for CD and UC. Skyrizi added among the required prerequisite agents for self-administered Entyvio for UC. ICD-10 codes related to adverse effect of immune checkpoint inhibitors.
11/15/24	Revision to guideline consisting of updating the position statement and other section. Tremfya added as Step 1a agent for UC.
01/01/25	Review and revision to guideline consisting of updating the description, position statement, billing/coding, other section, and references. Entyvio SC moved from step 3b agent (double step) to step 1a (no biologic agent step) for CD and UC. Refractory acute GVHD added as an indication for Entyvio IV. Update to original Table 1 which is now a link out from the Position Statement. Table titles updated. Revised wording regarding maximum dosage exceptions for Entyvio SC. New drugs were added to the list of drugs that are not permitted for use in combination.
01/01/26	Review and revision to guideline consisting of updating the description, position statement, billing/coding, and references. IEC-associated enterocolitis specific to BCMA-directed CAR T-cell therapy added as an indication for Entyvio IV. New ICD-10 codes. Revised criteria for Immune checkpoint inhibitor-related toxicity.
05/15/26	Revision to guideline consisting of clarifying the approval duration and start date for Entyvio subcutaneous injection following Entyvio IV treatment.