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Subject: Etrasimod (Velsipity) Tablet

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DESCRIPTION:

Etrasimod (Velsipity) in an oral sphingosine 1-phosphate (S1P) receptor modulator that was approved by the US Food and Drug Administration (FDA) in October 2023 for “the treatment of moderately to severely active ulcerative colitis (UC) in adults”. Etrasimod is the second S1P receptor modulator to be approved for the treatment of UC; the first being ozanimod (Zeposia). Of note, ozanimod was initially FDA-approved for the treatment of relapsing forms of multiple sclerosis (MS) in March 2020, followed by the approval for UC in May 2021. Overall, etrasimod is the fifth S1P receptor modulator available in the US market, with fingolimod (Gilenya), ponesimod (Ponvory), and siponimod (Mayzent) only being FDA-approved for the treatment of relapsing forms of MS. Etrasimod has high affinity for S1P receptors 1, 4, and 5; whereas ozanimod has high affinity for S1P receptors 1 and 5 only. Etrasimod does not require initial dosage titration, whereas ozanimod requires titration during the first week. The therapeutic effect of etrasimod in UC is unclear; but it is speculated that etrasimod reduces lymphocyte migration into the intestines.

The efficacy of etrasimod for the treatment of moderately to severely active UC in adults was studied in two randomized, double-blind, placebo-controlled trials. In ELEVATE UC 52, 27% of patients receiving etrasimod achieved clinical remission vs. 7% of patients receiving placebo at week 12 (p=0.001) and was achieved by 32% compared to 7% at week 52 (p=0.001). In ELEVATE UC 12, clinical remission was achieved among 26% of patients receiving etrasimod compared to 15% of patients receiving placebo (p<0.05). Clinical remission was defined as stool frequency subscore of 0 or 1, rectal bleeding subscore of 0, and endoscopy score of 1 or less (excluding friability) on the modified Mayo score (mMS). All key secondary efficacy endpoints were met at week 12, including endoscopic improvement and mucosal healing. Patients with certain cardiac conditions or with severe hepatic impairment should not receive etrasimod; clinicians should also review the potential for drug interactions before prescribing this drug.

INFLAMMATORY BOWEL DISEASE

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:

Comparative Effectiveness

The Food and Drug Administration has deemed the 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 formulations in certain provider-administered setting such as an outpatient hospital, ambulatory surgical suite, or emergency facility is not considered medically necessary.

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

Initiation of etrasimod (Velsipity) **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 etrasimod (starting on samples is not approvable) within the past 90 days
   b. The prescriber states the member has been treated with etrasimod (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. Etrasimod 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 etrasimod

II. The prescriber has provided information in support of using etrasimod 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 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 etrasimod
4. Member will **NOT** be using etrasimod in combination with a 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 [Zeposia (ozanimod)]
5. **ANY** of the following ("a", "b", "c". or "d"):
   a. The dosage does not exceed 2 mg orally once daily.
      - QL: 2 mg tablet – 30 tablets/30 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

Table 1

Diagnosis	Criteria
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** conventional agents used in the treatment of UC **OR** d. The member's medication history (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **AND** 2. **ANY** of the following (submitted medical records/chart notes are required for confirmation): a. The member has tried and had an inadequate response to at least **THREE** preferred products after at least a 3-month trial per product **OR** b. The member has tried and had an inadequate response to **TWO** preferred products after at least a 3-month duration of therapy per products, **AND** an intolerance or hypersensitivity to **ONE** preferred product **OR** c. The member has tried and had an inadequate response to **ONE** preferred product after at least a 3-month duration of therapy, **AND** an intolerance or hypersensitivity to **TWO** preferred products

	OR d. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to at least **THREE** preferred products **OR** e. The member has an FDA labeled contraindication to **ALL** preferred products **OR** f. **ALL** preferred products are **NOT** clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication **The preferred UC products are:** • Adalimumab-aaty • Adalimumab-adaz • Entyvio (vedolizumab) subcutaneous injection • Hadlima (adalimumab-bwwd) • Humira (adalimumab) • Simlandi (adalimumab-ryvk) • Skyrizi (risankizumab-rzaa) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Tremfya (guselkumab) • Xeljanz/Xeljanz XR (tofacitinib) • Yesintek (ustekinumab-kfce)
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

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

1. An authorization or reauthorization for etrasimod 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 etrasimod therapy
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., gastroenterologist for 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 etrasimod
5. Member will **NOT** be using etrasimod in combination with a 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 [Zeposia (ozanimod)]

6. **ANY** of the following ("a", "b", "c", or "d"):
   a. The dosage does not exceed 2 mg orally once daily.
      - QL: 2 mg tablet – 30 tablets/30 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

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:

- Etrasimod is indicated for the treatment of moderately to severely active ulcerative colitis in adults.
- The recommended dosage is 2 mg orally once daily. Swallow the tablet whole, with or without food.
- Assessments are required prior to initiating etrasimod:
    - Obtain a recent (within the last 6 months or after discontinuation of prior UC therapy) complete blood count, including lymphocyte count.
    - Obtain an electrocardiogram (ECG) to determine whether preexisting conduction abnormalities are present. In patients with certain preexisting conditions, advice from a cardiologist should be sought.
    - Obtain recent (i.e., within the last 6 months) transaminase and bilirubin levels.
    - Obtain a baseline evaluation of the fundus, including the macula, near the start of treatment.
    - Determine if patients are taking drugs that could slow heart rate or atrioventricular (AV) conduction.
    - If patients are taking anti-neoplastic, immune-modulating, or non-corticosteroid immunosuppressive therapies, or if there is a history of prior use of these drugs, consider possible unintended additive immunosuppressive effects before initiating treatment.
    - Patients without a healthcare professional-confirmed history of varicella (chickenpox) or without documentation of a full course of vaccination against varicella zoster virus (VZV) should be tested for antibodies to VZV before initiating treatment; VZV vaccination of antibody-negative patients is recommended prior to commencing treatment.
    - If live attenuated vaccine immunizations are required, administer at least 4 weeks prior to initiation.
    - Update immunizations in agreement with current immunization guidelines prior to initiating.
    - Obtain a skin examination prior to or shortly after initiation. If a suspicious skin lesion is observed, it should be promptly evaluated.

Dose Adjustment:

- Hepatic Impairment - For mild hepatic impairment (Child-Pugh class A) or moderate hepatic impairment (Child-Pugh class B), no dosage adjustments are needed. Use not recommended for severe hepatic impairment (Child-Pugh class C).
- Renal Impairment - No dosage adjustments are needed.

Drug Availability:

- 2 mg round, green film-coated tablet in a 30 count bottle
- Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F)

PRECAUTIONS:

Boxed Warning:

- None

Contraindications:

- Patients, who in the last 6 months, have experienced a myocardial infarction, unstable angina pectoris, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III or IV heart failure
- Patients who have a history or presence of Mobitz type II second-degree or third-degree AV block, sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker

Precautions/Warnings

- **Infections**: May increase the risk of infections. Obtain a complete blood count (CBC) before initiation of treatment. Monitor for infection during treatment and for 5 weeks after discontinuation. Consider interruption of treatment if a serious infection develops. Avoid use of live attenuated vaccines during and for up to 5 weeks after treatment.
- **Bradyarrhythmia and Atrioventricular Conduction Delays:** May result in a transient decrease in heart rate and AV conduction delays. Obtain an electrocardiogram (ECG) to assess for preexisting cardiac conduction abnormalities before starting treatment. Consider cardiology consultation for conduction abnormalities or concomitant use with other drugs that decrease heart rate.
- **Liver Injury**: Elevations of aminotransferases may occur. Obtain transaminase and bilirubin levels before initiating. Discontinue if significant liver injury is confirmed.
- **Macular Edema:** May increase the risk of macular edema. Obtain a baseline evaluation of the fundus, including the macula, near the start of treatment. Periodically conduct an evaluation of the fundus, including the macula, while on therapy and any time there is a change in vision. Consider discontinuing if macular edema develops.
- **Increased Blood Pressure:** Monitor blood pressure during treatment.
- **Fetal Risk**: May cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for one week after stopping.
- **Cutaneous Malignancies**: Obtain a skin examination prior to or shortly after the start of treatment and periodically during treatment, especially if risk factors. Promptly evaluate suspicious skin lesions.
- **Posterior Reversible Encephalopathy Syndrome (PRES):** If symptoms develop, obtain a physical and neurological exam, and consider MRI.
- **Respiratory Effects**: May cause a decline in pulmonary function. Assess pulmonary function (e.g., spirometry) if clinically indicated.
- **Unintended Additive Immune System Effects from Prior Treatment with Immunosuppressive or Immune-Modulating Drugs**: Consider the half-life and mode of action of prior therapies.
- **Immune System Effects After Stopping Velsipity:** If using concomitant immunosuppressants, monitor patients for infectious complications for up to 5 weeks after the last dose.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J8499	Prescription drug, oral, non chemotherapeutic, nos

ICD-10 Diagnosis Codes That Support Medical Necessity:

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.

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:

Bacillus Calmette-Guérin (BCG): a vaccine against tuberculosis that is prepared from a strain of the attenuated (weakened) live bovine tuberculosis bacillus, Mycobacterium bovis.

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).

RELATED GUIDELINES:

Adalimumab Products, 09-J0000-46
Apremilast (Otezla) Tablet, 09-J2000-19
Brodalumab (Siliq) Injection, 09-J2000-74
Certolizumab Pegol (Cimzia), 09-J0000-77
Etanercept (Enbrel), 09-J0000-38
Golimumab (Simponi, Simponi Aria), 09-J1000-11
Guselkumab (Tremfya), 09-J2000-87
Infliximab Products, 09-J0000-39
Ixekizumab (Taltz), 09-J2000-62
Natalizumab (Tysabri) Injection, 09-J0000-73
Psoralens with Ultraviolet A (PUVA), 02-10000-16
Risankizumab (Skyrizi), 09-J3000-45
Secukinumab (Cosentyx), 09-J2000-30
Tildrakizumab-asmn (Ilumya), 09-J3000-04
Vedolizumab (Entyvio), 09-J2000-18

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 2: Conventional Synthetic DMARDs

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

REFERENCES:

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COMMITTEE APPROVAL:

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

GUIDELINE UPDATE INFORMATION:

04/01/24	New Medical Coverage Guideline.
07/01/24	Revision to guideline consisting of updating the position statement, related guidelines, and other section. Amjevita low-concentration removed as a required prerequisite agent. Updates to the positioning of agents in Table 1. 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. Updates to Table 1. Simlandi and Skyrizi added among the required prerequisite agents.
01/01/25	Review and revision to guideline consisting of updating the position statement, other section, and references. Adalimumab-aaty, Adalimumab-adaz, Entyvio SC, and Tremfya added among the prerequisite therapies for UC. Update to original Table 1 which is now a link out from the Position Statement. Table titles updated. Revised wording regarding maximum dosage exceptions. New drugs were added to the list of drugs that are not permitted for use in combination.
07/01/25	Revision: Added Selarsdi, Steqeyma and Yesintek among the preferred agents for UC.
01/01/26	Review and revision to guideline consisting of updating the description, position statement and references.
07/01/26	Revision: Modified the prerequisite requirement that bypasses the conventional agent step to exclude sample use and include systemic targeted synthetic small molecule drugs as an option. Removed Selarsdi as a preferred agent for UC.