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Subject: Guselkumab (Tremfya®) Injection and Infusion

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DESCRIPTION:

Guselkumab (Tremfya) is an injectable human monoclonal antibody that selectively binds to the p19 subunit of interleukin 23 (IL-23) and inhibits its interaction with the IL-23 receptor. Guselkumab inhibits the release of proinflammatory cytokines and chemokines mediated by IL-23. Guselkumab was first approved by the US Food and Drug Administration (FDA) in July 2017 for "the treatment of adult patients with moderate-to-severe plaque psoriasis (PS) who are candidates for systemic therapy or phototherapy." Guselkumab was the first biologic agent that specifically targets the IL-23 pathway to be approved by the FDA for the treatment of plaque psoriasis. Ustekinumab (Stelara) was FDA-approved for plaque psoriasis in 2009, but inhibits both IL-12 and IL-23 via the p40 subunit found on both interleukins. In July 2020, the FDA approved the additional indication of treatment of adult patients with active psoriatic arthritis (PsA). In September 2024, the FDA approved a new indication for the treatment of moderately to severely active ulcerative colitis (UC) in adults. A new intravenous (IV) formulation of guselkumab was also approved at this same time for induction dosing. In March 2025, the FDA approved a new indication for the treatment of moderately to severely active Crohn's disease (CD) in adults. At the time of approval, induction with either three IV doses or three subcutaneous (SC) doses was included in the labeling. In September 2025, the FDA approved the use of SC induction for UC as well. Also, in September 2025, the indications for PS and PsA were expanded to include pediatric patients 6 years of age and older who also weigh at least 40 kg.

Psoriatic Arthritis (PsA)

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease associated with psoriasis (PS), most commonly presenting with peripheral arthritis, dactylitis, enthesitis, and spondylitis. Active PsA is defined as symptoms at an unacceptably bothersome level as reported by the patient due to one of the

following: actively inflamed joints, dactylitis, enthesitis, axial disease, active skin and/or nail involvement, and/or extraarticular manifestations such as uveitis or inflammatory bowel disease (IBD). Disease severity is based on the assessment of the level of disease activity at a given point in time, and the presence/absence of poor prognostic factors and long-term damage. Severe PsA is defined in the American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) guidelines for PsA and includes the presence of one or more of the following:

- Erosive disease
- Elevated markers of inflammation (e.g., erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) attributable to PsA
- Long-term damage that interferes with function (e.g., joint deformities, vision loss)
- Highly active disease that causes a major impairment in quality of life, such as:
    - Active PsA at many sites including dactylitis and enthesitis
    - Function-limiting PsA at a few sites
- Rapidly progressive disease

Treatment involves the use of a variety of interventions, including many agents used for the treatment of other inflammatory arthritis disorders, particularly spondyloarthritis and rheumatoid arthritis, and other management strategies of the cutaneous manifestations of psoriasis. Symptomatic treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, and local glucocorticoid injections. Only patients with very mild peripheral disease may sufficiently benefit from NSAIDs as monotherapy, and instead patients are typically treated with disease-modifying antirheumatic drugs (DMARDs) and/or biologics. Efficacy of DMARD and biologic therapies should be assessed 3 months after initiation, and if adequate improvement is not seen then the treatment regimen should be updated or changed. The ACR-NPF guidelines for PsA recommend a treat-to-target approach in therapy, regardless of disease activity, and treatment recommendations for active disease are as follows:

- Treatment naïve patients:
    - First line options include oral small molecules (OSM), tumor necrosis factor (TNF) inhibitors, interleukin (IL)-17 inhibitors, and IL-12/23 inhibitors
        - OSM (i.e., methotrexate [MTX], sulfasalazine, cyclosporine, leflunomide, apremilast) should be considered if the patient does not have severe PsA, does not have severe PS, prefers oral therapy, has concern over starting a biologic, or has contraindications to TNF inhibitors
        - Biologics (e.g., TNF inhibitor, IL-17 inhibitor, IL-12/23 inhibitor) are recommended as a first line option in patients with severe PsA and/or severe PS
- Previous treatment with OSM and continued active disease:
    - Switch to a biologic (i.e., TNF inhibitor, IL-17 inhibitor, IL-12/23 inhibitor); recommended over switching to a different OSM
        - Biologic monotherapy is conditionally recommended over biologic plus MTX combination therapy
    - Switch to a different OSM (except apremilast) OR add on apremilast to current OSM therapy; recommended over adding another OSM

- Add another OSM (except apremilast) to current OSM therapy; may consider for patients that have exhibited partial response to current OSM
- Switch to apremilast monotherapy; may be considered instead of adding apremilast to current OSM therapy if the patient has intolerable side effects with the current OSM

- Previous treatment with a biologic and continued active disease:
  - Switch to another biologic (e.g., TNF inhibitor, IL-17 inhibitor, IL-12/23 inhibitor, abatacept, or tofacitinib) as monotherapy
  - Add MTX to the current biologic; may consider adding MTX in patients with a partial response to current biologic therapy

The European Alliance of Associations for Rheumatology (EULAR) guidelines for PsA (2023 update) also recommend a treat-to-target approach in therapy. MTX (preferred) or another conventional synthetic disease-modifying antirheumatic drug (csDMARD) (e.g., sulfasalazine, leflunomide) should be used for initial therapy. If the treatment target is not achieved with a csDMARD, a biologic should be initiated with preference of product being based on patient specific disease characteristics. Biologics include TNF inhibitors, IL-12/23 inhibitors, IL-17A inhibitors, IL-17A/F inhibitors, IL-23 inhibitors, and cytotoxic T-lymphocyte–associated antigen 4 (CTLA4) analogs. No order of preference of biologics is provided since none have demonstrated superiority for joint involvement, however, CTLA4 analogs are least preferred due to limited efficacy in clinical trials. The use of a Janus kinase (JAK) inhibitor (e.g., tofacitinib, upadacitinib) may be used after failure of a biologic or if biologics are not clinically appropriate for the patient. However, careful consideration should be applied prior to using a JAK inhibitor due to the increased risk of cardiovascular and malignancy events in older patients with RA and cardiovascular risk factors. A phosphodiesterase-4 (PDE4) inhibitor (i.e., apremilast) may be considered in patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a biologic nor a JAK inhibitor is appropriate. Patients with an inadequate response to a biologic or JAK inhibitor may switch to a different drug within the same class or switch to a different mode of action. Adding MTX to a biologic may increase drug survival by limiting the development of antidrug antibodies, especially for TNF inhibitors.

Psoriasis (PS)

Psoriasis (PS) is a chronic inflammatory skin and systemic disorder. It is a complex disease that affects the skin and joints and is associated with numerous comorbidities, including obesity and inflammatory bowel disease. Psoriasis vulgaris, or plaque psoriasis, is a cutaneous form that often presents with pink plaques with silvery scale on the scalp, elbows, knees, or presacral region, but any area of the skin may be involved. Plaque psoriasis is the most common form (affecting 90% of adults with psoriasis), but others include guttate, erythrodermic, pustular, inverse, nail, and psoriatic arthritis (PsA). PS is clinically diagnosed based on the presence of cutaneous and systemic symptoms, and treatment is similar for most forms but is guided by the body surface area (BSA) involved. The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) categorize psoriasis severity as mild (less than 3% of BSA), moderate (3% to 10% of BSA), or severe (greater than 10% of BSA). The AAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when it causes serious emotional consequences, occurs in select locations (e.g., hands, feet, scalp, face, or genital area), or when it causes intractable pruritus.

Topical therapies are most commonly used to treat mild to moderate PS, but they may be used in combination with phototherapy, systemic, or biologic therapies for the treatment of moderate to severe PS. Topical therapies alone can be sufficient for managing limited disease and also have fewer significant adverse effects compared to systemic treatment options. However, topical therapies may be inadequate to obtain and maintain skin clearance, and systemic therapies may be warranted. Conventional systemic agents are widely used as monotherapy or in combination with biologics for moderate to severe disease, and they are beneficial for widespread disease and ease of administration. Biologics are routinely used when one or more conventional agents fail to produce an adequate response but are considered first line in patients with severe PS or patients with concomitant severe PsA. The NPF medical board recommends a treat-to-target approach to therapy for psoriasis that includes the following:

- The preferred assessment instrument for determining treatment response is BSA
- The preferred time to perform initial evaluation of treatment response is after 3 months
- Target response after treatment initiation should be BSA less than or equal to 1% after 3 months
- Acceptable response is either a BSA less than or equal to 3% or a BSA improvement greater than or equal to 75% from baseline at 3 months after treatment initiation

Selection of treatment is based on several factors including benefit-risk assessment, clinical presentation, disease severity, and comorbidities. The AAD/NPF psoriasis treatment guidelines support the following treatment options:

- Topical therapies:
    - Topical corticosteroids (TCS)
    - Topical calcineurin inhibitors (TCIs), such as tacrolimus and pimecrolimus
    - Vitamin D analogues (e.g., calcipotriene and calcitriol)
    - Tazarotene (topical retinoid)
    - Coal tar preparations
    - Topical anthralin
- Psoralen plus ultraviolet light (PUVA) phototherapy
- Systemic non-biologic therapies:
    - Methotrexate (MTX)
    - Cyclosporine
    - Acitretin
    - Apremilast
- Biologic therapies:
    - Tumor necrosis factor (TNF)-α inhibitors (e.g., adalimumab, certolizumab, etanercept, infliximab)
    - Interleukin (IL)-17 inhibitors (e.g., brodalumab, ixekizumab, secukinumab)
    - IL-23 inhibitors (e.g., guselkumab, risankizumab, tildrakizumab)

- IL-12/IL-23 Inhibitors (e.g., ustekinumab)

  *Note: Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics was published in 2019. No specific biologic drug/class is recommended as first-line for all patients with psoriasis, and instead choice of therapy should be individualized based on patient specific factors. Additional biologic drugs have since received FDA approval for psoriasis that are not discussed.

Primary failure for biologics is defined as initial nonresponse to treatment. Primary failure to a tumor necrosis factor (TNF)-α inhibitor does not preclude successful response to a different TNF-α inhibitor, and failure of another biologic therapy does not preclude successful response to ustekinumab. All biologics may lose efficacy in a patient who initially responds favorably to the medication (secondary failure), and loss of efficacy may be attributed to the presence of antidrug antibodies. The concomitant use of MTX with a biologic may increase drug survival by limiting antibody formation.

For the treatment of PS in the pediatric patient population, topical corticosteroids are the mainstay option based on extensive clinical experience that supports efficacy. Topical calcineurin inhibitors are also a treatment option and may be preferred for psoriasis of the face, genitalia, and body folds. Vitamin D analogues are recommended as a treatment option for childhood plaque psoriasis and are considered safe, effective, and generally well tolerated. Other topical therapies that may be used for the treatment of pediatric psoriasis include tazarotene, anthralin, and coal tar. Phototherapy may be efficacious and well tolerated for pediatric patients with generalized psoriasis or localized psoriasis refractory to topical agents. Systemic non-biologic therapies, such as methotrexate, cyclosporine, and acitretin, are options for moderate to severe psoriasis. Biologic therapies (e.g., adalimumab, etanercept, infliximab, ustekinumab) have also shown efficacy in moderate to severe plaque psoriasis in this patient population.

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:

<u>General treatment information</u>:

- 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

<u>Corticosteroid therapy</u>:

- 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

<u>Disease modifying antirheumatic drug (DMARD) therapy</u>:

- 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:

General treatment information:

- 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

DMARD therapy:

- 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

Advanced therapy:

- 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 FDA 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) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, 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.

SUBCUTANEOUS TREMFYA (PHARMACY BENEFIT)

Initiation of subcutaneous guselkumab (Tremfya) meets the definition of medical necessity when **ALL** of the following are met ("1" to "6"):

1. **ONE** of the following ("a", "b", or "c"):
    a. The member has been treated with subcutaneous guselkumab (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with subcutaneous guselkumab (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 guselkumab 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 guselkumab
            II. The prescriber has provided information in support of using subcutaneous guselkumab for the member's age for the requested indication
2. For the indications of plaque psoriasis (PS) and psoriatic arthritis (PsA) **ONLY** – if requested for a pediatric member (i.e., less than 18 years of age) then the member weighs 40 kg (88 lbs) or greater
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, dermatologist for PS, gastroenterologist for CD and 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 guselkumab
5. Member will **NOT** be using subcutaneous guselkumab 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 the following based on the indication for use:
        - Crohn's disease and ulcerative colitis:

- Induction dose - 400 mg at weeks 0, 4, and 8
  - QL: Three Induction Packs for Ulcerative Colitis or Crohn's Disease (two 200 mg/2mL single-dose prefilled syringe in a carton) per 180 days
- Maintenance dose - 100 mg every 8 weeks (starting 8 weeks after the last IV or SC induction dose), **OR** 200 mg every 4 weeks (starting 4 weeks after that last IV or SC induction dose)
  - QL: 100 mg/mL pen - 1 pen/ 56 days
  - QL: 100 mg/mL syringe - 1 syringe/56 days
  - QL: 200 mg/2 mL pen - 1 pen/28 days
  - QL: 200 mg/2 mL syringe - 1 syringe/28 days

- PS and PsA:
  - Loading dose – 100 mg at weeks 0 and 4
  - Maintenance dose - 100 mg every 8 weeks (56 days), starting 8 weeks after week 4 (i.e., on week 12)
    - QL: 100 mg/mL pen - 1 pen/56 days
    - QL: 100 mg/mL syringe - 1 syringe/56 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: CD and UC - Loading dose (doses on week 0, 4 and 8) for 3 months, then maintenance dose for 9 additional months [12 months for total duration of approval]. PS and PsA - Loading dose (doses on week 0 and 4) for 3 months, then maintenance dose for 9 additional months [12 months for total duration of approval]

Table 1

Diagnosis	**Criteria**
Active psoriatic arthritis (PsA)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA 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 PsA **OR** 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PsA **OR** 4. The member has severe active PsA (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities, vision loss], rapidly progressive)

	OR 5. The member has concomitant severe psoriasis (PS) (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences) **OR** 6. The member's medication history indicates use of another biologic immunomodulator agent **OR** Otezla/Otezla XR that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PsA
Moderate to severe plaque psoriasis (PS)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., acitretin, calcipotriene, calcitriol, coal tar, cyclosporine, methotrexate, pimecrolimus, PUVA [phototherapy], tacrolimus, tazarotene, topical corticosteroids) used in the treatment of PS 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 PS **OR** 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PS **OR** 4. The member has severe active PS (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences) **OR** 5. The member has concomitant severe psoriatic arthritis (PsA) (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities, vision loss], rapidly progressive) **OR** 6. The member's medication history indicates use of another biologic immunomodulator agent **OR** Otezla/Otezla XR that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PS

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** agents used in the treatment of CD **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 guselkumab 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** 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 guselkumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors
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 guselkumab (Tremfya) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "6"):

1. An authorization or reauthorization for subcutaneous guselkumab 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 guselkumab therapy
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, dermatologist for PS, gastroenterologist for CD and 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 guselkumab
5. Member will **NOT** be using subcutaneous guselkumab 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 the following based on the indication for use:
        - Crohn's disease and ulcerative colitis - 100 mg every 8 weeks (starting 8 weeks after the last IV or SC induction dose), **OR** 200 mg every 4 weeks (starting 4 weeks after that last IV or SC induction dose)
            - QL: 100 mg/mL pen - 1 pen/ 56 days
            - QL: 100 mg/mL syringe - 1 syringe/56 days
            - QL: 200 mg/2 mL pen - 1 pen/28 days
            - QL: 200 mg/2 mL syringe - 1 syringe/28 days
        - Other indications - 100 mg every 8 weeks (56 days)
            - QL: 100 mg/mL pen - 1 pen/56 days
            - QL: 100 mg/mL syringe - 1 syringe/56 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 TREMFYA (MEDICAL BENEFIT)

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

1. Intravenous guselkumab will be used for the treatment of an indication listed in Table 2, and **ALL** of the indication-specific and maximum-allowable dose criteria are met
2. **EITHER** of the following if the member has an FDA-approved indication ("a" or "b")
    a. The member's age is within FDA labeling for the requested indication for intravenous guselkumab
    b. The prescriber has provided information in support of using intravenous guselkumab for the member's age for the requested indication
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., gastroenterologist for CD and 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 IV guselkumab
5. Member will **NOT** be using IV guselkumab 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. For the CD and UC indication only - member has not received a previous dose of guselkumab (IV or SC) in the past 6 months, **UNLESS** the member is completing the second and/or third dose(s) of the initial three IV doses for induction

Approval duration: CD and UC - 3 months (to allow 3 total IV doses). Other indications - Up to 12 months.

Table 2

Indication	Criteria	Max Allowable Dosage
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**	• 200 mg IV every 4 weeks for a total of 3 doses (i.e., Week 0, Week 4, and Week 8) • Maintenance therapy with subcutaneous guselkumab is started either 4 weeks or 8 weeks after the last IV dose (i.e., Week 12 or 16)

	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 **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 guselkumab 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**	• 200 mg IV every 4 weeks for a total of 3 doses (i.e., Week 0, Week 4, and Week 8) • Maintenance therapy with subcutaneous guselkumab is started either 4 weeks or 8 weeks after the last IV dose (i.e., Week 12 or 16)

	3. The member has an FDA labeled contraindication to **ALL** 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 guselkumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors	
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

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

- Indicated for (1) the treatment of adults and pediatric patients 6 years of age and older who also weigh at least 40 kg with moderate-to-severe plaque psoriasis (PS) and who are candidates for systemic therapy or phototherapy, (2) the treatment of adults and pediatric patients 6 years of age and older who also weigh at least 40 kg with active psoriatic arthritis (PsA), (3) the treatment of adults with moderately to severely active ulcerative colitis (UC), and (4) the treatment of adults with moderately to severely active Crohn's disease (CD).
- For both PS and PsA, the recommended dose is 100 mg as a subcutaneous (SC) injection at Week 0, Week 4, and every 8 weeks thereafter. For psoriatic arthritis, the product labeling states that

guselkumab may be administered alone or in combination with a conventional DMARD (e.g., methotrexate). A patient may self-inject after proper training in SC injection technique. The prefilled syringe should be removed from the refrigerator to allow the solution to reach room temperature (about 30 minutes) before injection

- For CD and UC, the recommended induction dosage is either 200 mg administered by IV infusion over at least one hour at Week 0, Week 4, and Week 8; OR 400 mg administered by subcutaneous injection (given as two consecutive injections of 200 mg each) at Week 0, Week 4, and Week 8. The recommended maintenance dosage of is either:
  - 100 mg administered by SC injection at Week 16, and every 8 weeks thereafter, or
  - 200 mg administered by subcutaneous injection at Week 12, and every 4 weeks thereafter

  Use the lowest effective recommended dosage to maintain therapeutic response. The solution for IV infusion must be diluted, prepared, and infused by a healthcare professional.

Dose Adjustments

- No specific guidelines for dosage adjustments for renal or hepatic impairment are available. It appears that no dosage adjustments are needed.

Drug Availability

Subcutaneous Injection:

- 100 mg/1 mL in a single-dose prefilled syringe
- 100 mg/1 mL in a single-dose One-Press patient-controlled injector
- 100 mg/1 mL in a single-dose prefilled pen (Tremfya Pen)
- 200 mg/2 mL in a single-dose prefilled pen (Tremfya Pen)
- 200 mg/2 mL in a single-dose prefilled syringe
- Induction Pack for Ulcerative Colitis or Crohn's Disease – two 200 mg/2mL single-dose prefilled syringe in a carton

Intravenous Infusion:

- 200 mg/20 mL (10 mg/mL) solution in a single-dose vial

Store in a refrigerator at 2ºC to 8ºC (36ºF to 46ºF). Store in original carton until time of use. Protect from light until use. Do not freeze. Do not shake. Not made with natural rubber latex.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Patients with a history of serious hypersensitivity reaction to guselkumab or to any of the excipients

Precautions/Warnings

- **Adverse Reactions**: The most common (≥1%) adverse reactions associated with guselkumab treatment include upper respiratory infections, headache, injection site reactions, arthralgia, diarrhea, gastroenteritis, tinea infections, and herpes simplex infections.
- **Infections**: Guselkumab may increase the risk of infection. In clinical trials for plaque psoriasis, infections occurred in 23% of subjects in the guselkumab group versus 21% of subjects in the placebo group through 16 weeks of treatment. A similar risk of infection was seen in trials for psoriatic arthritis, Crohn's disease, and ulcerative colitis. Consider the risks and benefits prior to initiating guselkumab in patients with a chronic infection or a history of recurrent infection. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a serious infection develops or if an infection is not responding to standard therapy, monitor the patient closely and discontinue guselkumab until the infection resolves.
- **Tuberculosis (TB)**: Evaluate patients for TB infection prior to initiating treatment with guselkumab. Do not administered guselkumab to patients with active tuberculosis infection.
- **Hepatotoxicity**: Drug-induced liver injury has been reported. For the treatment of Crohn's disease or ulcerative colitis, monitor liver enzymes and bilirubin levels at baseline, for at least 16 weeks of treatment, and periodically thereafter according to routine patient management. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded.
- **Hypersensitivity Reactions**: Serious hypersensitivity reactions have been reported with postmarket use of guselkumab. Some cases required hospitalization. If a serious hypersensitivity reaction occurs, discontinue guselkumab and initiate appropriate therapy.
- **Immunizations**: Avoid using live vaccines concurrently with guselkumab.
- **CYP450 Substrates**: The formation of CYP450 enzymes can be altered by increased levels of certain cytokines during chronic inflammation, and treatment with guselkumab may modulate serum levels of some cytokines. Therefore, upon initiation or discontinuation of guselkumab in patients who are receiving concomitant drugs which are CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) and consider dosage modification of the CYP450 substrate.
- **Pregnancy**: There are no available data on use in pregnant women to inform a drug associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, guselkumab may be transmitted from the mother to the developing fetus. A study in pregnant cynomolgus monkeys given weekly guselkumab doses up to 30-times the maximum recommended human dose found no evidence of malformations or embryofetal toxicity. View the prescribing information for additional details.

BILLING/CODING INFORMATION:

HCPCS Coding

J1628	Injection, guselkumab, 1 mg [for both IV and SC formulations]

ICD-10 Diagnosis Codes That Support Medical Necessity of Intravenous Infusion (J1628; NDC 57894-0650-02):

K50.00 – K50.919	Crohn's disease [regional enteritis]
K51.00 - K51.919	Ulcerative colitis

ICD-10 Diagnosis Codes That Support Medical Necessity of Subcutaneous Injection (J1628; NDCs 57894-0640-01, 57894-0640-11, 57894-0651-02, and 57894-0651-22):

L40.0	Psoriasis vulgaris
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis
L40.59	Other psoriatic arthropathy
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 Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of guideline creation.

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:

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).

Plaque psoriasis: It is the most common form of psoriasis. It affects 80 to 90% of people with psoriasis. Plaque psoriasis typically appears as raised areas of inflamed skin covered with silvery white scaly skin. These areas are called plaques.

Psoriatic arthritis (PsA): joint inflammation that occurs in about 5% to 10% of people with psoriasis (a common skin disorder). It is a severe form of arthritis accompanied by inflammation, psoriasis of the skin or nails, and a negative test for rheumatoid factor. Enthesitis refers to inflammation of entheses, the site where ligaments or tendons insert into the bones. It is a distinctive feature of PsA and does not occur with other forms of arthritis. Common locations for enthesitis include the bottoms of the feet, the Achilles' tendons, and the places where ligaments attach to the ribs, spine, and pelvis.

RELATED GUIDELINES:

Abatacept (Orencia), 09-J0000-67
Adalimumab Products, 09-J0000-46
Apremilast (Otezla) Tablet, 09-J2000-19
Bimekizumab (Bimzelx), 09-J4000-70
Brodalumab (Siliq) Injection, 09-J2000-74
Certolizumab Pegol (Cimzia), 09-J0000-77
Deucravacitinib (Sotyktu), 09-J4000-37
Etanercept (Enbrel), 09-J0000-38
Golimumab (Simponi, Simponi Aria), 09-J1000-11
Infliximab Products, 09-J0000-39
Ixekizumab (Taltz), 09-J2000-62
Natalizumab (Tysabri) Injection, 09-J0000-73
Psoralens with Ultraviolet A (PUVA), 09-10000-16
Risankizumab (Skyrizi), 09-J3000-45
Secukinumab (Cosentyx), 09-J2000-30
Tildrakizumab-asmn (Ilumya), 09-J3000-04
Tofacitinib (Xeljanz, Xeljanz XR) Tablets, 09-J1000-86
Ustekinumab (Stelara), 09-J1000-16
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 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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7. Dogra S, Jain A, Kanwar AJ. Efficacy and safety of acitretin in three fixed doses of 25, 35 and 50 mg in adult patients with severe plaque type psoriasis: a randomized, double blind, parallel group, dose ranging study. J Eur Acad Dermatol Venereol. 2012; 27:305-311.
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COMMITTEE APPROVAL:

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

GUIDELINE UPDATE INFORMATION:

09/15/17	New Medical Coverage Guideline.
01/01/18	Revision to guideline consisting of updating the preferred self-administered biologic products according to indication for use. Secukinumab (Cosentyx) is now a preferred product for plaque psoriasis. Addition of HCPCS code C9029.
07/01/18	Revision to guideline consisting of updating the position statement.
10/15/18	Review and revision to to guideline consisting of updating the references.
01/01/19	Revision: HCPCS code updates. Added J1628 and removed C9029 and J3590.
09/01/19	Revision to guideline consisting of updating the position statement and references.

10/15/19	Review and revision to guideline consisting of updating the description, position statement, precautions, and references.
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, dosage/administration, precautions, billing/coding, definitions, related guidelines, other, and references.
03/15/21	Revision to guideline consisting of updating Table 1 in the position statement.
09/15/21	Update to Table 1 in Position Statement.
11/15/21	Revision to guideline consisting of updating the position statement.
01/01/22	Review and revision to guideline consisting of updating the position statement, other section, and references.
02/15/22	Update to Table 1 in Position Statement.
03/15/22	Revision to guideline consisting of updating the position statement and other sections.
05/15/22	Update to Table 1 in Position Statement.
07/15/22	Update to Table 1 in Position Statement.
09/15/22	Update to Table 1 in Position Statement.
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.
04/15/23	Update to Table 1 in Position Statement. 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 position statement and other section. Amjevita and Hadlima added as Step 1a agents. 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 position statement, other section, and references. Update to Table 1 in Position Statement. New drugs were added to the list of drugs that are not permitted for use in combination.
07/01/24	Revision to guideline consisting of updating the description, position statement, related guidelines, and other section. 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	Update to Table 1 in Position Statement.
11/15/24	Revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, billing/coding, related guidelines, other section, and references based on the new FDA-approved indication for UC in adults. Position statement divided into one section for “SUBCUTANEOUS TREMFYA (PHARMACY BENEFIT)” and one section for “INTRAVENOUS TREMFYA (MEDICAL BENEFIT)”.
01/01/25	Review and revision to guideline consisting of updating the position statement, other section, and references. 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 Tremfya SC. New drugs added to the list of drugs that are not permitted for use in combination.

05/15/25	Revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, billing/coding, and references based on the new FDA-approved indication for CD in adults.
11/15/25	Revision to guideline consisting of updating the description, position statement, dosage/administration, and references based on the newly FDA-approved subcutaneous induction dosing for UC and the expanded indications for PS and PsA to include pediatric patients 6 years of age and older who also weigh at least 40 kg.
01/01/26	Review and revision to guideline consisting of updating the description, position statement and references.