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Subject: Risankizumab-rzaa (Skyrizi®) Injection and Infusion

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DESCRIPTION:

Risankizumab-rzaa (Skyrizi) is an injectable humanized IgG1 monoclonal antibody that selectively inhibits interleukin-23 (IL-23) by binding to the p19 subunit. It was initially approved by the US Food and Drug Administration (FDA) in May 2019 for “the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy”. In January 2022, the FDA approved the new indication of active psoriatic arthritis in adults. In June 2022, the FDA approved an additional new indication for the treatment of moderately to severely active Crohn's disease (CD) in adults. This approval also introduced the availability of intravenous (IV) risankizumab (previously only available as a subcutaneous injection) since the treatment of CD requires three IV induction doses. Also, a new subcutaneous dosage of 360 mg given via on-body injector was introduce for the CD indication. A second on-body injector dosage of 180 mg was introduced a few months later. In June 2024, the FDA approved a new indication for the treatment of moderately to severely active ulcerative colitis (UC) in adults. Similar to CD, the treatment of UC requires three IV induction doses; however, the dose is larger for UC (1,200 mg) than for CD (600 mg). Risankizumab was the third IL-23 to be approved by the FDA [following guselkumab (Tremfya]) in July 2017 and tildrakizumab (Ilumya) in March 2018]; however, it is the first IL-23 to be approved for the treatment of an inflammatory bowel disease. Interleukin-23 is a naturally occurring cytokine that is involved in inflammatory and immune response, and its blockade inhibits the release of proinflammatory cytokines and chemokines. Skyrizi, as sponsored by the innovator drug company, was granted an orphan drug designation for treatment of pediatric Crohn's disease in November 2016.

DERMATOLOGICAL DISORDERS

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.

RHEUMATOID DISORDERS

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.

Crohn's Disease (CD)

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

Patients are considered to have moderate to severe disease if they have failed to respond to treatment for mild to moderate disease, or if they present with more prominent symptoms of CD. Inflammation-related biomarkers are more likely to be abnormal, and greater endoscopic disease burden is typical. This includes larger or deeper ulcers, strictures, or extensive areas of disease and/or evidence of stricturing, penetrating, or perianal disease. The International Organization for the Study of Inflammatory Bowel Diseases characterizes patients with severe disease as having at least 10 loose

stools per day, daily abdominal pain, presence of anorectal symptoms, systemic corticosteroid use within the prior year, lack of symptomatic improvement despite prior exposure to biologics and/or immunosuppressive agents, or significant impact of the disease on activities of daily living. They are also at a high risk for adverse disease-related complications, including surgery, hospitalization, and disability, based on a combination of structural damage, inflammatory burden, and impact of quality of life. Patients with severe disease may have large or deep mucosal lesions on endoscopy or imaging, presence of fistula and/or perianal abscess, presence of strictures, prior intestinal resections, presence of a stoma, and/or extensive disease (e.g., involvement of long bowel segments, pancolitis).

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

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

- Biologic therapy:
    - The AGA suggest early introduction with a biologic, with or without an immunomodulator, rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids (Conditional recommendation, low certainty of evidence)
        - Earlier therapy with a biologic may result in overtreating some patients and potentially exposing them to treatment-related risks and costs with limited benefit. However, step-up therapy comes with a potential risk of harm from disease progression related to inadequate disease therapy.
    - Anti-tumor necrosis factor (TNF) (i.e., infliximab or adalimumab) and ustekinumab are recommended over no treatment for the induction and maintenance of remission
    - Vedolizumab is suggested over no treatment for the induction and maintenance of remission
    - AGA suggests against the use of natalizumab over no treatment for the induction and maintenance of remission
    - Patients naïve to biologic therapy, the AGA recommends infliximab, adalimumab, or ustekinumab over certolizumab pegol and suggests the use of vedolizumab over certolizumab pegol for the induction of remission
    - Patients with primary non-response to anti-TNF, the AGA recommends ustekinumab and suggests vedolizumab for induction of remission
    - Patients with secondary non-response to infliximab, the AGA recommends use of adalimumab or ustekinumab and suggests the use of vedolizumab for the induction of remission (if adalimumab was the first line drug, there is indirect evidence to suggest using infliximab as a second-line agent)
- Corticosteroid therapy:

- Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission
    - In patients with CD involving the distal ileum and/or ascending colon who are more concerned about systemic corticosteroids and less concerned about the lower efficacy, they may reasonably choose budesonide over systematic corticosteroids for inducing remission

- Disease modifying antirheumatic drug (DMARD) therapy:

  Patients in corticosteroid induced remission or with quiescent moderate to severe CD, the AGA suggests thiopurines for maintenance of remission

  - Subcutaneous or intramuscular methotrexate are suggested over no treatment for the induction and maintenance of remission
  - The AGA recommends against the use of 5-aminosalicylates or sulfasalazine over no treatment for the induction or maintenance of remission
  - The AGA suggests against the use of thiopurines over no treatment for achieving remission and recommends biologic drug monotherapy over thiopurine monotherapy for induction of remission
  - The AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission

- Combination therapy:
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of infliximab in combination with thiopurines over infliximab monotherapy for the induction and maintenance of remission (combination infliximab with methotrexate may be more effective over infliximab monotherapy)
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of adalimumab in combination with thiopurines over adalimumab monotherapy for the induction and maintenance of remission (combination adalimumab with methotrexate may be more effective over adalimumab monotherapy)
  - No recommendations are being made regarding the use of ustekinumab or vedolizumab in combination with thiopurines or methotrexate over biologic monotherapy for induction or maintenance or remission

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

- Biologic therapy:
  - Biologic agents are effective for treating patients with active CD and previous inadequate response to corticosteroids, thiopurines, and/or methotrexate
  - Suggest against requiring failure of conventional therapy before initiation of advanced therapy for the management of CD (conditional recommendation, low level of evidence)
    - The risk of adverse effects and high cost of biologic agents may not be justifiable in a lower risk population
  - Recommend the following drugs for induction and maintenance of remission for moderately to severely active CD:

        - Anti-TNF agents (i.e., infliximab, adalimumab, certolizumab), vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab
    - Recommend combination therapy of intravenous infliximab with immunomodulators (thiopurines) as compared with treatment with either immunomodulators alone or intravenous infliximab alone in patients with CD who are naïve to those agents
    - Recommend the use of risankizumab as compared with ustekinumab in patients with moderate to severe CD and prior exposure to anti-TNF therapy
    - Biosimilar infliximab, adalimumab, and ustekinumab are effective treatments for patients with moderate-to-severe CD and can be used for de novo induction and maintenance therapy
    - There are data to support the safety and efficacy of transitioning or switching to biosimilar infliximab or adalimumab for patients with CD in stable disease maintenance
- Janus kinase (JAK) inhibitor therapy:
    - Recommend upadacitinib use for induction and maintenance of remission for patients with moderate-to-severe CD who have previously been exposed to anti-TNF agents
- Corticosteroid therapy:
    - Recommend oral corticosteroids for short-term induction of remission in patients with moderately to severely active CD
        - Recommend controlled ileal release budesonide at a dose of 9 mg daily for induction of symptomatic remission in patients with mildly to moderately active ileocecal CD
    - Corticosteroids should not be used for maintaining remission, and their use should not exceed 3 continuous months without attempting to introduce a steroid-sparing agent (such as an immunomodulator)
- DMARD therapy:
    - Recommend against azathioprine or 6-mercaptopurine for induction of remission in moderately to severely active CD
        - Due to their slow onset of action of 8 to 12 weeks, thiopurines are not effective agents for induction of remission
    - Suggest azathioprine or 6-mercaptopurine for maintenance of remission in patients with moderately to severely active CD who had induction of remission with corticosteroids
    - Suggest methotrexate (up to 25 mg once weekly intramuscular or subcutaneous) for maintenance of remission in patients with moderately to severely active CD who had induction of remission with corticosteroids
    - Azathioprine, 6-mercaptopurine, or methotrexate may be used in the treatment of active CD and as adjunctive therapy for reducing immunogenicity associated with anti-TNF therapy

Ulcerative Colitis (UC)

Ulcerative colitis (UC) is a chronic inflammatory bowel disease affecting the large intestine. It typically starts with inflammation of the rectum, but often extends proximally to involve additional areas of the colon. The most common symptom is bloody diarrhea, but urgency, tenesmus, abdominal pain, malaise,

weight loss, and fever can also be associated. UC commonly has a gradual onset and will present with periods of spontaneous remission and subsequent relapses.

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

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

General treatment information:

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

Corticosteroid therapy:

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

Disease modifying antirheumatic drug (DMARD) therapy:

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

Biologic/advanced therapy:

- Recommend the following drugs for induction of remission and continuing the same drug for maintenance of remission:
    - Anti-tumor necrosis factor (TNF) agents (e.g., infliximab, adalimumab, golimumab), ustekinumab, guselkumab, mirikizumab, risankizumab, vedolizumab, tofacitinib, upadacitinib, sphingosine-1-phosphate (S1P) receptor modulators (e.g., ozanimod, etrasimod)
    - Most clinical trials and available data demonstrate a benefit of using the steroid-sparing therapy that induces remission to maintain that remission
- When infliximab is used as induction therapy, recommend combination therapy with a thiopurine
    - Data on combination anti-TNF and immunomodulators in moderately to severely active UC only exist for infliximab and thiopurines
- Infliximab is the preferred anti-TNF therapy for patients with moderately to severely active UC
- Recommend vedolizumab as compared to adalimumab for induction and maintenance of remission
- Patients who are primary nonresponders to an anti-TNF (defined as lack of therapeutic benefit after induction and despite sufficient serum drug concentrations) should be evaluated and considered for alternative mechanisms of disease control (e.g., in a different class of therapy) rather than cycling to another drug within the anti-TNF class
- Biosimilars to anti-TNF therapies and to ustekinumab are acceptable substitutes for originator therapies. Delays in switching should not occur and patients and clinicians should be notified about such changes

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

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

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

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 SKYRIZI (PHARMACY BENEFIT)

Initiation of subcutaneous risankizumab (Skyrizi) **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 subcutaneous risankizumab (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with subcutaneous risankizumab (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 risankizumab 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 risankizumab
            II. The prescriber has provided information in support of using subcutaneous risankizumab 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., dermatologist for PS, gastroenterologist for CD or UC, rheumatologist for PsA) or the prescriber has consulted with a specialist in the area of the member's diagnosis
3. Member does **NOT** have any FDA labeled contraindications to subcutaneous risankizumab
4. Member will **NOT** be using subcutaneous risankizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
5. **ANY** of the following ("a", "b", "c" or "d"):
    a. The dosage does not exceed:
        - Plaque psoriasis and psoriatic arthritis
            - Loading dose - 150 mg at weeks 0 and 4
            - Maintenance dose - 150 mg every 12 weeks (84 days), starting 12 weeks after week 4 (i.e., on week 16)
                - QL: 150 mg/mL auto-injector - 1 pen/84 days

- QL: 150 mg/mL prefilled syringe - 1 syringe/84 days

- Crohn's disease (CD)
  - Loading dose – Induction is given by IV infusion only. The IV dosage is 600 mg every 4 weeks for 3 total doses (i.e., weeks 0, 4, and 8)
  - Maintenance dose - 360 mg subcutaneously every 8 weeks (56 days), starting 4 weeks after the last IV dose (i.e., on week 12)
    - QL: 90 mg/mL prefilled syringe – 4 syringes/56 days
    - QL: 180 mg/1.2 mL prefilled syringes - 2 syringes/56 days
    - QL: 180 mg/1.2 mL prefilled cartridge with on-body injector – 1 cartridge/56 days
    - QL: 360 mg/2.4 mL prefilled cartridge with on-body injector – 1 cartridge/56 days
- Ulcerative colitis (UC)
  - Loading dose - Induction is given by IV infusion only. The IV dosage is 1,200 mg every 4 weeks for 3 total doses (i.e., weeks 0, 4, and 8)
  - Maintenance dose - 360 mg subcutaneously every 8 weeks (56 days), starting 4 weeks after the last IV dose (i.e., on week 12)
    - QL: 90 mg/mL prefilled syringe – 4 syringes/56 days
    - QL: 180 mg/1.2 mL prefilled syringes - 2 syringes/56 days
    - QL: 180 mg/1.2 mL prefilled cartridge with on-body injector – 1 cartridge/56 days
    - QL: 360 mg/2.4 mL prefilled cartridge with on-body injector – 1 cartridge/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: For CD and UC – Approved for 9 months [this equals a 1-year total treatment duration with IV loading doses]. Other indications - Loading dose (doses on week 0 and 4) for 4 months, then maintenance dose for 8 additional months [12 months for total duration of approval].

Table 1

Diagnosis	Criteria
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
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

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

2. An authorization or reauthorization for subcutaneous risankizumab has been previously approved by Florida Blue [Note: members not previously approved for the requested agent will require initial evaluation review]
3. Member has had clinical benefit with subcutaneous risankizumab therapy
4. The prescriber is a specialist in the area of the member's diagnosis (e.g., dermatologist for PS, gastroenterologist for CD or UC, rheumatologist for PsA) or the prescriber has consulted with a specialist in the area of the member's diagnosis
5. Member does **NOT** have any FDA labeled contraindications to subcutaneous risankizumab
6. Member will **NOT** be using subcutaneous risankizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
7. **ANY** of the following ("a", "b", "c", or "d"):
    a. The dosage does not exceed the following:
        - Plaque psoriasis and psoriatic arthritis - 150 mg every 12 weeks (84 days)
            - QL: 150 mg/mL auto-injector - 1 pen/84 days
            - QL: 150 mg/mL prefilled syringe - 1 syringe/84 days
        - CD and UC - 360 mg every 8 weeks (56 days)
            - QL: 90 mg/mL prefilled syringe – 4 syringes/56 days
            - QL: 180 mg/1.2 mL prefilled syringes - 2 syringes/56 days
            - QL: 180 mg/1.2 mL prefilled cartridge with on-body injector – 1 cartridge/56 days
            - QL: 360 mg/2.4 mL prefilled cartridge with on-body injector – 1 cartridge/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 SKYRIZI (MEDICAL BENEFIT)

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

1. Intravenous risankizumab 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 risankizumab
    b. The prescriber has provided information in support of using intravenous risankizumab 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 or UC) or the prescriber has consulted with a specialist in the area of the member's diagnosis
4. Member does **NOT** have any FDA labeled contraindications to IV risankizumab
5. Member will **NOT** be using IV risankizumab in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), 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 CD and UC indications only - member has not received a previous dose of risankizumab (IV or SC) in the past 12 months, **UNLESS** the member is completing the second and/or third dose(s) of the initial 3 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** 2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of CD **OR**	• 600 mg IV every 4 weeks for a total of 3 doses (i.e., Week 0, Week 4, and Week 8) • Maintenance therapy with subcutaneous risankizumab is started 4 weeks after the last IV dose (i.e., Week 12)

	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 risankizumab 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	• 1,200 mg IV every 4 weeks for a total of 3 doses (i.e., Week 0, Week 4, and Week 8) • Maintenance therapy with subcutaneous risankizumab is started 4 weeks after the last IV dose (i.e., Week 12)

	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 risankizumab 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

- Risankizumab is indicated for (1) the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy, (2) the treatment of active psoriatic arthritis in adults, (3) the treatment of moderately to severely active Crohn's disease in adults, and (4) the treatment of moderately to severely active ulcerative colitis in adults.
    - Plaque psoriasis and psoriatic arthritis - The recommended dose is 150 mg administered by subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter. For the indication of psoriatic arthritis, the labeling states that risankizumab may be administered alone or in combination with non-biologic DMARDs. When using 75 mg/0.83 mL prefilled syringes, for a 150 mg dose, two 75 mg prefilled syringes are required. Inject one prefilled syringe after the other in different anatomic locations (such as thighs or abdomen). Do not inject into areas where the skin is tender, bruised, erythematous, indurated or affected by psoriasis. Administration in the upper, outer arm may only be performed by a healthcare professional or caregiver.
    - Crohn's disease - The recommended induction dosage is 600 mg administered by IV infusion over a period of at least one hour at Week 0, Week 4, and Week 8. The recommended maintenance dosage is 180 mg or 360 mg administered by subcutaneous injection at Week 12,

and every 8 weeks thereafter. Use the lowest effective dosage needed to maintain therapeutic response. Use the on-body injector to administer the 180 mg/1.2 mL or 360 mg/2.4 mL prefilled cartridge subcutaneously on thigh or abdomen. Alternatively, use either two or four 90 mg/mL prefilled syringes or one or two 180 mg/1.2 mL prefilled syringes, to administer a 180 mg or 360 mg dose, respectively. Inject one prefilled syringe after the other in different anatomic locations (such as thighs or abdomen). Do not inject into areas where the skin is tender, bruised, erythematous, indurated or affected by any lesions. Obtain liver enzymes and bilirubin levels prior to initiating treatment. Refer to the product labeling for more information regarding preparation and administration.

- Ulcerative colitis - The recommended induction dosage is 1,200 mg administered by IV infusion over a period of at least two hours at Week 0, Week 4, and Week 8. The recommended maintenance dosage is 180 mg or 360 mg administered by subcutaneous injection at Week 12, and every 8 weeks thereafter. Use the lowest effective dosage needed to maintain therapeutic response. Use the on-body injector to administer the 180 mg/1.2 mL or 360 mg/2.4 mL prefilled cartridge subcutaneously on thigh or abdomen. Alternatively, use either two or four 90 mg/mL prefilled syringes or one or two 180 mg/1.2 mL prefilled syringes, to administer a 180 mg or 360 mg dose, respectively. Inject one prefilled syringe after the other in different anatomic locations (such as thighs or abdomen). Do not inject into areas where the skin is tender, bruised, erythematous, indurated or affected by any lesions. Obtain liver enzymes and bilirubin levels prior to initiating treatment. Refer to the product labeling for more information regarding preparation and administration.

Dose Adjustments

- Renal impairment - specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed
- Hepatic impairment - specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.

Drug Availability

- Intravenous Infusion
  - Carton with one 600 mg/10 mL (60 mg/mL) single-dose vial
- Subcutaneous Injection
  - Carton with one 150 mg/mL singe-dose prefilled syringe
  - Carton with one 150 mg/mL singe-dose pen
  - Carton with two 90 mg/mL single-dose prefilled syringes
  - Carton with four 90 mg/mL single-dose prefilled syringes
  - Carton with one or two 180 mg/1.2 mL (150 mg/mL) single-dose prefilled syringes
  - Kit with 180 mg/1.2 mL (150 mg/mL) single-dose prefilled cartridge with on-body injector
  - Kit with 360 mg/2.4 mL (150 mg/mL) single-dose prefilled cartridge with on-body injector
- Store in a refrigerator at 2°C to 8°C (36°F to 46° F). Do not freeze. Do not shake. Keep in the outer carton to protect from light. Not made with natural rubber latex.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

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

Precautions/Warnings

- **Hypersensitivity Reactions**: Serious hypersensitivity reactions, including anaphylaxis, have been reported with use. If a serious hypersensitivity reaction occurs, discontinue and initiate appropriate therapy immediately.
- **Infections**: may increase the risk of infection. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If such an infection develops, do not administer until the infection resolves.
- **Tuberculosis (TB)**: Evaluate for TB prior to initiating treatment.
- **Hepatotoxicity in Treatment of Crohn's Disease**: Drug-induced liver injury during induction has been reported. Monitor liver enzymes and bilirubin levels at baseline and, during induction, up to at least 12 weeks of treatment. Monitor thereafter according to routine patient management.
- **Administration of Vaccines**: Avoid use of live vaccines in patients.

BILLING/CODING INFORMATION:

HCPCS Coding

J2327	Injection, risankizumab-rzaa, intravenous, 1 mg
J3590	Unclassified biologics (for the subcutaneous formulation only)

ICD-10 Diagnosis Codes That Support Medical Necessity of Intravenous Infusion (J2327):

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 (J3590):

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

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.

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: 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

Etrasimod (Velsipity), 09-J4000-72

Golimumab (Simponi, Simponi Aria), 09-J1000-11

Guselkumab (Tremfya), 09-J2000-87

Infliximab Products, 09-J0000-39

Ixekizumab (Taltz), 09-J2000-62

Mirikizumab (Omvoh), 09-J4000-71

Natalizumab (Tysabri) Injection, 09-J0000-73

Psoralens with Ultraviolet A (PUVA), 09-10000-16

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.

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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:

09/01/19	New Medical Coverage Guideline.
01/01/20	Revision to guideline consisting of updating the position statement "Note" due to changes in preferred products.
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 position statement and references.
03/15/21	Revision to guideline consisting of updating Table 1 in the position statement.
07/15/21	Revision to guideline consisting of updating the position statement, dosage/administration, other section, and references.
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.
02/15/21	Update to Table 1 in Position Statement.
03/15/22	Revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, billing/coding, other section, definitions, related guidelines, and references based on the new FDA-approved indication for active psoriatic arthritis in adults.
05/15/22	Update to Table 1 in Position Statement.
07/15/22	Update to Table 1 in Position Statement.
09/15/22	Revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, billing/coding, related guidelines, and references based on the new FDA-approved indication for CD.
01/01/23	Review and revision to guideline consisting of updating the description section, position statement, dosage/administration, other section, and references. New drugs were added to the list of drugs that are not permitted for use in combination. A new 180 mg on-body injector dosage for CD was released. Added HCPCS code J2327.
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 section, position statement, 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	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 UC in adults.
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. Clarified that the age requirement that exists for subcutaneous Skyrizi also applies to intravenous Skyrizi. New drugs added to the list of drugs that are not permitted for use in combination.
01/01/26	Review and revision to guideline consisting of updating the description, position statement, dosage/administration, and references.