Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 10/03/2024

Skyrizi™ (risankizumab-rzaa)

HCPCS: Skyrizi SC: J3590; Skyrizi IV: J2327

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age.
   b. Diagnosis of psoriasis
      i. Trial and failure, contraindication, or intolerance to one topical corticosteroid
   c. Diagnosis of psoriatic arthritis
   d. Diagnosis of Crohn's disease (CD)
      i. Treatment with an adequate course of conventional therapy (such as steroids for 7 days, immunomodulators such as azathioprine for at least 2 months) has been ineffective or is contraindicated or not tolerated.
   e. Diagnosis of ulcerative colitis (UC)
      i. Treatment with an adequate course of conventional therapy (such as steroids for 7 days, immunomodulators such as azathioprine for at least 2 months) has been ineffective or is contraindicated or not tolerated.
   f. Not to be used in combination with other biologics or targeted disease-modifying anti-rheumatic drugs (DMARDs) for the same indication
   g. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing.
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Skyrizi is an interleukin (IL)-23 antagonist indicated for the treatment of moderate-to-severe psoriasis in adults who are candidates for systemic therapy or phototherapy, for the treatment of active psoriatic arthritis in adults, for the treatment of moderately to severely active Crohn's disease in adults, and for the treatment of moderately to severely active ulcerative colitis in adults.

- Psoriasis

    - Psoriasis is a chronic, painful, and life-altering immune-mediated disease which predominantly manifests with skin and joint involvement. Patients may also experience significant cardiovascular and psychological comorbidities. Approximately 2% of U.S. adults are affected by psoriasis (men and women equally), and it can occur at any age. Approximately 90% of psoriasis-affected patients have plaque psoriasis, which is characterized by well-defined round or oval plaques that vary in size and often coalesce. The severity of psoriasis is defined as: mild = less than 3% of body affected; moderate = 3-10% of body affected; and severe being more than 10% of the body affected.

    - Per the 2020 Joint American Academy of Dermatology - National Psoriasis Foundation (AAD/NPF) guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures: topical corticosteroids provide a high efficacy and good safety option for patients with localized disease. They are generally recommended as first-line therapy. Choice of steroid potency may depend on severity, location, patient preference, and patient age, while the duration of treatment may vary with steroid potency, location and severity of disease often ranging from 2-12 weeks. Therapeutic regimens may include 2-4 weeks with a topical steroid applied twice daily, followed by a maintenance regimen where topical steroids are alternated with a steroid-sparing topical agent. Treatment with topical steroids for over 12 weeks is recommended under careful supervision by a physician.

    - Per the 2019 Joint AAD/NPF guidelines of care for the management and treatment of psoriasis with phototherapy: phototherapy serves as a reasonable and effective treatment option for patients requiring more than topical medications and/or those wishing to avoid systemic medications or simply seeking an adjunct to a failing regimen. Guidelines also state that the majority of patients with mild-to-moderate disease have adequate disease control with topical therapies and phototherapy alone.

    - Per the Joint AAD/NPF guidelines of care for the management and treatment of psoriasis with systemic nonbiologic therapies: many oral medications, including methotrexate, cyclosporine, and acitretin, have been used for decades to treat psoriasis, each with its own benefits and risks. Most work by targeting the immune system, whereas others, such as acitretin, work predominantly by decreasing keratinocyte hyperproliferation, thus restoring the normal epidermal differentiation. Both methotrexate and cyclosporine are category A guideline recommendations for the treatment of moderate to severe psoriasis in adults and for severe, recalcitrant psoriasis, respectively. Studies examining the use of methotrexate and cyclosporine in psoriasis showed the primary efficacy endpoints met within 12-16 weeks. Acitretin is a category B guideline recommendation as monotherapy for plaque psoriasis, with full treatment response expected within 3-6 months.

    - Per the 2019 Joint AAD/NPF guidelines of care for the management and treatment of psoriasis with biologics: biologic agents, as monotherapy or combined with other topical or systemic medications, have a high benefit-to-risk ration. Tumor necrosis factor inhibitors (TNFi) and IL-12/IL-23, IL-23, and IL-17 products have a category "A" recommendation as a monotherapy treatment option for adult patients with moderate-to-severe plaque psoriasis. Guidelines do not recommend one product over another and note the similar

efficacy seen across biologics within the same class. There are no published, robust studies to support the use of more than one biologic or targeted DMARD in combination.

- Psoriatic Arthritis

  - Psoriatic arthritis (PsA) is a chronic inflammatory disease often associated with psoriasis. Psoriasis is an autoimmune disease affecting the skin, resulting in scaly red and white patches. These patches, called plaques, may appear anywhere on the body. The inflammation may also develop in the joints, which is classified as PsA. PsA occurs in up to 30% of patients with psoriasis, most commonly appearing between the ages of 30 and 50. PsA causes pain, stiffness, and swelling in and around the joints. If not properly treated, progressive joint damage may occur.

  - Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guideline for the treatment of psoriatic arthritis, all recommendations for treatment-naive patients with active PsA are conditional based on low- to very-low quality evidence.

  - In treatment-naïve patients, oral systemic medications (OSMs), such as methotrexate, sulfasalazine, cyclosporine, and leflunomide, may be used in patients without severe psoriatic arthritis and without severe psoriasis. OSMs have robust longitudinal safety and efficacy data in patients with PsA. Maximal response to OSMs are most commonly achieved within 3 months of therapy.

  - If PsA remains active despite OSM therapy, switching to a TNFi, an interleukin-17 inhibitor (IL-17i), or an IL-12/23i biologic is recommended over switching to a different OSM. In this scenario, a TNFi biologic is conditionally recommended over an IL-17i or IL-12/23i biologic based on moderate quality evidence. Additional treatment options include Xeljanz/Xeljanz XR (tofacitinib) and Orencia® (abatacept). Detailed recommendations regarding subsequent therapies can be found in the 2018 ACR/NPF guideline for the treatment of psoriatic arthritis.

- Crohn's disease

  - The 2018 American College of Gastroenterology guidelines establish therapeutic recommendations for patients with Crohn's disease (CD) based upon disease location, disease severity, disease-associated complications, and future disease prognosis. Therapeutic approaches are individualized according to the symptomatic response and tolerance to medical intervention. Current therapeutic approaches should be considered a sequential continuum to treat acute disease or induce clinical remission and then to maintain response/remission. In general, clinical evidence of improvement should be evident within 2 – 4 weeks and the maximal improvement should occur within 12 – 16 weeks. Those with continued symptoms should be treated with an alternative therapy for mild to moderate disease, have their medication dose adjusted in order to attempt to optimize therapy, or advance to treatment for moderate to severe disease according to their clinical status.

  - Corticosteroids are used primarily for the treatment of flares of CD. Conventional corticosteroids are effective for reducing the signs and symptoms of active CD and induction of remission in patients with moderately to severely active CD. Oral corticosteroids are effective and can be used for short-term use in alleviating signs and symptoms of moderate to severely active disease. The guidelines recommend prednisone equivalent doses ranging from 40 to 60 mg per day. These doses are typically maintained for 1 –2 weeks and tapered at 5 mg weekly until 20 mg and then 2.5 –5 mg weekly. Once begun, care should be taken to ensure that corticosteroids are successfully discontinued, and steroid-sparing agents should be used.

- In patients with moderate-to-severe CD who remain symptomatic despite current or prior corticosteroid therapy, mercaptopurine, azathioprine, and intramuscular or subcutaneous methotrexate are effective steroid-sparing agents and guideline recommended. Maximum effectiveness of these agents can be seen between 8 to 12 weeks from therapy initiation. Methotrexate is also recommended in combination with steroids as an effective treatment for moderately active steroid-dependent/resistant CD. Cyclosporine, tacrolimus, and mycophenolate are not recommended for treatment of CD.

- Biologics, such as TNFi's are recommended to treat CD that is resistant to treatment with corticosteroids, thiopurines, or methotrexate. Guidelines also recommend the use of biologics in combination with immunosuppressants to help decrease the formation of antibodies against the biologic therapy. There are no robust, published studies to support use of biologic agents in combination

- The 2021 American Gastroenterological Association (AGA) guidelines include similar recommendations for the management of moderate-to-severe CD compared to the recommendations cited in the 2018 ACG guidelines. Both guidelines recommend corticosteroids over no treatment for induction of remission. Additionally, both guidelines recommend thiopurines, such as azathioprine or 6-mercaptopurine, as steroid-sparing agents for maintenance of remission. The AGA guidelines also recommend the same biologic agents cited in the ACG guidelines for treatment of CD, with the exception of Tysabri® (natalizumab), which the ACG suggests against use of due to its associated risk of progressive multifocal leukoencephalopathy (PML).

- Of note, the AGA guidelines conditionally recommend earlier introduction of biologic therapy prior to failure of corticosteroids; however, this recommendation is supported by a low level of clincial evidence. To date, no blinded randomized controlled trials (RCTs) have demonstrated the superiority of early introduction of biologic therapy compared to conventional induction therapy with corticosteroids followed by steroid-sparing therapy. The 2021 AGA guideline authors also acknowledge that earlier therapy with either combination immunomodulotor plus biologic therapy or biologic monotherapy may result in over-treating some patients and potentially exposing them to treatment-related risks and costs with limited benefit.

- Ulcerative Colitis

  - UC and CD are two of the most common forms of inflammatory bowel disease (IBD). Both UC and CD are chronic, relapsing, remitting, inflammatory conditions of the gastrointestinal (GI) tract. UC only involves the large intestine as opposed to CD, which can affect any part of the GI tract from mouth to anus. CD can also affect the entire thickness of the bowel wall, while UC only involves the innermost lining of the large intestine. UC can present with symptoms of abdominal discomfort or loose bowel movements, including blood. The cause of UC or CD is not fully understood; however, research suggests that an interplay between environmental factors, genetics, and intestinal microbiota may contribute to the development of UC or CD. UC has an incidence of 9 to 20 cases per 100,000 persons per year. Its prevalence is 156 to 291 cases per 100,000 persons per year.

  - The 2019 ACG guidelines and the 2020 AGA guidelines state therapeutic management in UC should be guided by the specific diagnosis, an assessment of disease activity, and disease prognosis. Treatment selection should be based not only on inflammatory activity but also on disease prognosis. Remission can be induced using a variety of medications, including oral 5-aminosalicyclic-acid (ASA), corticosteroids, or biologic agents. Thiopurines, such as azathioprine and mercaptopurine, can be used to maintain remission. The TNFi agents infliximab, adalimumab, and golimumab are effective for treatment of patients with UC. Treatment guidelines do not recommend the use of one agent over another as there have been no head-to-head trials comparing the agents to one another. Vedolizumab is another guideline recommended option in patients with moderately to severely active UC for induction of remission, and in patients with moderately to severely active UC who have previously failed anti-TNF therapy, for induction of remission.

References:

1. Skyrizi [prescribing information]. North Chicago, IL. AbbVie Inc., June 2024.
2. Elmets CA, Lim HW, Stoff B, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy [published correction appears in J Am Acad Dermatol. 2020 Mar;82(3):780]. J Am Acad Dermatol. 2019;81(3):775-804. doi:10.1016/j.jaad.2019.04.042
3. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures [published online ahead of print, 2020 Jul 30]. J Am Acad Dermatol. 2020;S0190-9622(20)32288-X. doi:10.1016/j.jaad.2020.07.087
4. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol. 2020;82(6):1445-1486. doi:10.1016/j.jaad.2020.02.044
5. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029-1072. doi:10.1016/j.jaad.2018.11.057
6. Singh JA, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019 Jan; 71 (1): 5-32.
7. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of crohn's disease in adults. AJG. 2018 April; 113 (4): 481-517
8. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.2</td><td>Effective Date: 10/03/2024</td><td>Added “for the same indication” to the not to be used in combination with other biologics or targeted DMARDs criteria</td></tr>
<tr><td>2.1</td><td>Effective Date: 08/08/2024</td><td>Added ulcerative colitis indication</td></tr>
<tr><td>2.0</td><td>Effective Date: 08/10/2023</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.9</td><td>Effective Date: 08/04/2022</td><td>Added Crohn’s disease indication and new IV formulation</td></tr>
<tr><td>1.8</td><td>Effective Date: 12/09/2021</td><td>Removed FDA approved indications and phototherapy and oral DMARD requirements for psoriasis and added a trial of one topical corticosteroid for psoriasis.</td></tr>
<tr><td>1.7</td><td>Effective Date: 02/04/2021</td><td>Removal of the topical steroid critera for psoriasis indication</td></tr>
<tr><td>1.6</td><td>Effective Date: 12/03/2020</td><td>New policy replacing previously approved criteria that was embedded in the Skyrizi drug review. Previous criteria updated to align management between pharmacy and medical benefit for all listed indications. Skyrizi drug review document to be retired once new policy is approved</td></tr>
<tr><td>1.5</td><td>Effective Date: 10/08/2020</td><td>UM medical management system update for BCBS and BCN
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<tr><td>MAPPO</td><td>Yes</td></tr>
<tr><td>BCNA</td><td>Yes</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*