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.

P&T Date: 02/13/2025

Ustekinumab Products
Imuldosa™ (ustekinumab-srlf)
Otulfi™ (ustekinumab-aauz)
Pyzchiva® (ustekinumab-ttwe)
Selarsdi™ (ustekinumab-aekn)
Stelara® (ustekinumab)
Steqeyma® (ustekinumab-stba)
Wezlana™ (ustekinumab-auub)
Yesintek™ (ustekinumab-kfce)

HCPCS: Imuldosa: J3590; Otulfi: J3590; Pyzchiva IV: Q9997; Pyzchiva SQ: Q9969; Selarsdi IV: Q9998; Stelara SC: J3357; Stelara IV: J3358; Steqeyma: J3590; Wezlana SC: 5137; Wezlana IV: Q5138; Yesintek: J3590

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 indications
   b. FDA approved age
   c. Diagnosis of psoriasis (PsO)
      i. Trial and failure, contraindication, or intolerance to one topical corticosteroid
   d. Diagnosis of psoriatic arthritis (PsA)
   e. 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
   f. Diagnosis of ulcerative colitis
      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
   g. Not be used in combination with other biologic agents or targeted disease-modifying anti-rheumatic drugs (DMARDs) for the same indication
   h. Coverage will be provided for biosimilar products for FDA labeled indications of the innovator product when criteria are met

i. 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:

- Ustekinumab is an interleukin (IL)-12 and IL-23 inhibitor available as the innovator product Stelara and its biosimilars Imuldosa, Otulfi, Pyzchiva, Selarsdi, Steqeyma, Wezlana, and Yesintek. Wezlana was also granted interchangeability status by the FDA, while the FDA provisionally determined that Pyzchiva would be interchangeable with Stelara as it is currently subject to an unexpired period of exclusivity for the first interchangeable biosimilar biological products.

- Stelara and its biosimilars are approved for the treatment of psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis. They may be administered as a subcutaneous (SC) injection or via intravenous (IV) infusion. Administration via IV infusion is reserved for induction therapy in Crohn's disease and ulcerative colitis utilizing a single weight-based dose. After induction, the transition is made to subcutaneous dosing for maintenance therapy.

- Use of ustekinumab in combination with other biologic agents or targeted immunosuppressants has not been sufficiently evaluated for safety and efficacy and therefore is not recommended.

- 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 (AAD) - National Psoriasis Foundation (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 2020 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), IL-12/23 inhibitors, IL-23 inhibitors, and IL-17 inhibitors have a category "A" recommendation as a monotherapy treatment option for use in adult patients with moderate-to-severe plaque psoriasis. Stelara and Wezlana are approved to treat moderate to severe plaque psoriasis in patients 6 years of age and older who are candidates for phototherapy or systemic therapy. Guidelines do not recommend one product over another and note the similar efficacy seen across biologics within the same class.

- Psoriatic Arthritis

  - PsA is a chronic inflammatory disease often associated with psoriasis. 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)/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 is most commonly achieved within 3 months of therapy.

  - If PsA remains active despite OSM therapy, switching to a TNFi, an IL-17i, or an IL-12/23i biologic is recommended over switching to a different OSM; switching to a TNFi biologic over an IL-17i or IL-12/23i biologic is conditionally recommended in this scenario based on moderate quality evidence. Stelara and Wezlana are indicated to treat patients 6 years of age and older with active PsA and may be used alone or in combination with methotrexate The detailed recommendations for 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 (ACG) guidelines establish therapeutic recommendations for patients with 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 ACG 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 effective for treatment of moderately active steroid-dependent/resistant CD. Cyclosporine, tacrolimus, and mycophenolate are not recommended for treatment of CD.

  - Biologics, such as TNFi are recommended to treat CD that is resistant to treatment with corticosteroids, thiopurines, or methotrexate. The ACG 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.

  - Ustekinumab is recommended in patients with moderate to severe CD who have had prior treatment failures with corticosteroids, thiopurines, methotrexate, or TNFi.

  - 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 clinical 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

immunomodulator 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

  - The 2019 ACG guidelines and the 2020 AGA guidelines for ulcerative colitis (UC) 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-aminosalicylates (5-ASA), corticosteroids, or biologic agents. In patients with mild to moderately active disease, treatment with 5-ASA therapy has proven to be safe and efficacious for induction. Recommended dosing is 2 grams per day of oral 5-ASA or at least 1 gram per day of rectal 5-ASA with improvement usually seen within 4 weeks. A typical treatment course may be up to 8 weeks.

  - Oral steroids are recommended for induction for patients with severe disease or those who did not respond to 5-ASA therapy. The typical starting doses of oral prednisone are 40 – 60 mg per day, and clinical response is expected within 5 – 7 days of treatment. A typical treatment course with oral prednisone is 14 days. The duration of systemic corticosteroids should be as short as possible with early initiation of steroid-sparing therapy. The speed of the taper should be guided by clinical symptoms, cumulative steroid exposure, and onset of action of alternate therapies. Those unable to taper off of 10-20 mg of prednisone per day without relapsing are considered steroid dependent. Use systemic corticosteroids for maintenance of remission is not recommended.

  - Thiopurines, such as azathioprine and mercaptopurine, can be used to maintain remission. Guidelines recommend use of thiopurines over no medication or corticosteroids for maintenance therapy. Thiopurines are slow acting with maximum effectiveness of these agents being seen between 8 to 12 weeks from therapy initiation. They do not induce remission in moderately to severely active ulcerative colitis. Similarly, methotrexate is not an effective induction agent for induction or maintenance of remission.

  - In patients with moderate to severe disease, TNFi, Entyvio® (vedolizumab), and ustekinumab are recommended for the induction and maintenance of remission. For patients with moderate to severe disease in remission, guidelines do not recommend biologic monotherapy over thiopurine monotherapy. Thiopurines can be used as adjunctive therapy for reducing immunogenicity against biologic therapy and are guideline recommended.

References:

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15. Selardsi [prescribing information]. Leesburg, VA: Alvotech USA Inc; April 2024.
16. Otulfi [prescribing information]. Lake Zurich, IL: Fresenius Kabi; September 2024.
17. Imuldosa [prescribing information]. Raleigh, NC: Accord BioPharma Inc; October 2024.
18. Yesintek [prescribing information]. Cambridge, MA: Biocon Biologics, Inc; November 2024.
19. Steqeyma [prescribing information]. Jersey City, NJ: Celltrion USA, Inc.; December 2024.

Policy History		
#	Date	Change Description
4.2	Effective Date: 07/01/2025	UM medical management system update for MAPPO and BCNA for Selarsdi IV
4.1	Effective Date: 03/03/2025	UM medical management system update for MAPPO and BCNA for Steqeyma
4.0	Effective Date: 02/13/2025	Updated policy to include biosimilars Steqeyma and Yesintek
3.9	Effective Date: 02/03/2025	UM medical management system update for MAPPO and BCNA for Imuldosa, Pyzchiva IV, and Yesintek
3.8	Effective Date: 01/06/2025	UM medical management system update for MAPPO and BCNA for Otulfi
3.7	Effective Date: 12/12/2024	Updated include Otulfi and Imuldosa
3.6	Effective Date: 11/03/2024	UM medical management system update for MAPPO and BCNA for Wezlana
3.5	Effective Date: 10/03/2024	Added "for the same indication" to the not to be used in combination with other biologics or targeted DMARDs criteria
3.4	Effective Date: 08/08/2024	Updated policy to include biosimilar Pyzchiva
3.3	Effective Date: 06/06/2024	Updated policy to include biosimilar Selardsi
3.2	Effective Date: 12/14/2023	Changed policy name to Ustekinumab Products Policy. Updated to add Wezlana, FDA approved indications criteria, and coverage for biosimilar products for FDA labeled indications of the innovator product when criteria are met
3.1	Effective Date: 11/23/2023	UM medical management system update for BCBS and BCN for Wezlana

3.0	Effective Date: 12/01/2022	Annual review of criteria was performed, no changes were made
2.9	Effective Date: 12/09/2021	Removed FDA approved indications, phototherapy and oral DMARD for psoriasis, the oral DMARD for psoriatic arthritis, and added a trial of one topical corticosteroid for psoriasis.
2.8	Effective Date: 02/04/2021	Removal of the topical steroid critera for psoriasis indication
2.7	Effective Date: 12/03/2020	Criteria updated to align management between pharmacy and medical benefit for all listed indications
2.6	Effective Date: 12/05/2019	Added new indication of ulcerative colitis
2.5	Effective Date: 08/15/2019	Added t/f of preferred product statement
2.4	Effective Date: 02/14/2019	Criteria updated to prevent use with other biologic agents and added required length for DMARD trial
2.3	Effective Date: 02/01/2019	UM medical management system update for MAPPO and BCNA
2.2	Effective Date: 08/09/2018	Annual Review of Medical Policy
2.1	Effective Date: 08/02/2018	Updated the QL for psoriasis/psoriatic arthritis indication in patients weighing >100kg to reflect prescribing information recommendations
2.0	Effective Date: 03/16/2018	Removed Humira requirement from Crohn's disease
1.9	Effective Date: 08/10/2017	Criteria updated to remove step therapy for preferred biologics on medical.
1.8	Effective Date: 03/23/2017	Criteria updated to clarify preferred biologics for each indication based on current contracting.
1.7	Effective Date: 02/09/2017	FDA approval Stelara Intravenous/Crohn's
1.6	Effective Date: 11/10/2016	Preliminary Criteria Approved for Crohn's disease including trial and failure of Humira or Remicade.
1.5	Effective Date: 01/01/2016	Document updated with specified drugs required
1.4	Effective Date: 12/16/2013	Criteria update to include psoriatic arthritis
1.3	Effective Date: 08/08/2013	Criteria updates, include self-injectable
1.2	Effective Date: 05/02/2013	Criteria updates
1.1	Effective Date: 07/10/2012	Criteria updates
1.0	Effective Date: 10/2010	New policy

** 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.*