09-J1000-16

Original Effective Date: 02/15/10

Reviewed: 05/13/26

Revised: 07/01/26

Subject: Ustekinumab Products (Stelara® and biosimilars)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Ustekinumab (Stelara), an interleukin (IL)-12 and IL-23 antagonist, was first approved by the US Food and Drug Administration (FDA) in September 2009 for the treatment of adults with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy, and then approved for the treatment of adults with active psoriatic arthritis (PsA) in September 2013. In September 2016, ustekinumab received an additional approval for the treatment of adult patients with moderately to severely active Crohn's disease (CD) who have: (1) failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker, or (2) failed or were intolerant to treatment with one or more TNF blockers. In October 2017, the plaque psoriasis indication was expanded to include adolescent patients (12 to 18 years of age). In October 2019, ustekinumab received approval for the treatment of adult patients with moderately to severely active ulcerative colitis (UC). In addition, the CD indication was modified to no longer include prior treatment failure (i.e., now reads "for the treatment of adult patients with moderately to severely active CD"). In July 2020, the plaque psoriasis indication was expanded to include pediatric patients (6 to 11 years of age). In July 2022, the PsA indication was expanded to include pediatric and adolescent patients (6 to 17 years of age). In April 2026, the approval for CD was expanded to include pediatric patients 2 years of age and older. New weight-based dosing recommendations are included in the package labeling for pediatric patients below certain weights. Unlike for treatment of psoriasis and PsA, treatment for CD and UC (both adults and pediatric patients) requires a single, initial weight based IV loading dose.

As of May 2026, eight unique biosimilars for Stelara have been approved by the FDA – Wezlana (ustekinumab-auub) in October 2023 (both IV and SC), Selarsdi (ustekinumab-aekn) in April 2024 (for SC) and October 2024 (for IV), Pyzchiva (ustekinumab-ttwe) in June 2024 (both IV and SC), Otulfi (ustekinumab-aauz) in September 2024 (both IV and SC), Imuldosa (ustekinumab-srlf) in October 2024 (both IV and SC), Yesintek (ustekinumab-kfce) in November 2024 (both IV and SC), Steqeyma (ustekinumab-stba) in December 2024 (both IV and SC), and Starjemza (ustekinumab-hmny) in May 2025 (both IV and SC). Also FDA-approved, are unbranded versions of Selarsdi (October 2024), Pyzchiva (March 2025), Otulfi (April 2025), Steqeyma (April 2025), and Stelara (April 2025). Despite approval, not all unbranded products may launch.

Ustekinumab (as sponsored by the innovator drug company) has been granted orphan drug designation by the FDA for “treatment of pediatric Crohn's disease (0 through 16 years of age)” in May 2016 and for “treatment of pediatric ulcerative colitis” in February 2017. In 2018 the National Comprehensive Cancer Network (NCCN) began publishing its guideline Management of Immunotherapy-Related-Toxicities. The NCCN eventually separated this guideline into two separate guidelines - Management of Immune Checkpoint Inhibitor-Related Toxicities and Management of CAR T-Cell and Lymphocyte Engager-Related Toxicities. Intravenous ustekinumab is recommended (category 2A) for immunotherapy-related and infliximab- and/or vedolizumab-refractory mild (Grade 1) diarrhea or colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin, and moderate (Grade 2) or severe (Grade 3 or 4) diarrhea or colitis.

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.

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
- Phototherapy:
    - Psoralen plus ultraviolet A (PUVA)
    - Ultraviolet B (UVB)
- 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)

- Response to treatment with ustekinumab should be assessed after 12 weeks of continuous therapy. In patients weighing 100 kg or less who have a partial response to ustekinumab 45 mg every 12 weeks, the maintenance dose may be increased to 90 mg.

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

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

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

INFLAMMATORY BOWEL DISEASE

Crohn's Disease (CD)

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

Patients are considered to have moderate to severe disease if they have failed to respond to treatment for mild to moderate disease, or if they present with more prominent symptoms of CD. Inflammation-related biomarkers are more likely to be abnormal, and greater endoscopic disease burden is typical. This includes larger or deeper ulcers, strictures, or extensive areas of disease and/or evidence of stricturing, penetrating, or perianal disease. The International Organization for the Study of Inflammatory Bowel Diseases characterizes patients with severe disease as having at least 10 loose stools per day, daily abdominal pain, presence of anorectal symptoms, systemic corticosteroid use within the prior year, lack of symptomatic improvement despite prior exposure to biologics and/or immunosuppressive agents, or significant impact of the disease on activities of daily living. They are also at a high risk for adverse disease-related complications, including surgery, hospitalization, and disability, based on a combination of structural damage, inflammatory burden, and impact of quality of life. Patients with severe disease may have large or deep mucosal lesions on endoscopy or imaging, presence of fistula and/or perianal abscess, presence of strictures, prior intestinal resections, presence of a stoma, and/or extensive disease (e.g., involvement of long bowel segments, pancolitis).

The choice of therapy in CD is dependent on the anatomic location of the disease, the severity of disease, and whether the treatment is needed to induce remission or maintain remission. The goal of treatment for induction of remission is to achieve clinical response and control of inflammation within 3

months of treatment initiation. After inducing clinical remission, patients should be transitioned to steroid-sparing maintenance therapy. In the absence of immunomodulator or biologic treatment, corticosteroid dependency and/or resistance occurs in up to half of patients. In general, the drug(s) used for induction of remission should be continued as maintenance therapy, with the exception of corticosteroids.

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

- Biologic therapy:
    - The AGA suggest early introduction with a biologic, with or without an immunomodulator, rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids (Conditional recommendation, low certainty of evidence)
        - Earlier therapy with a biologic may result in overtreating some patients and potentially exposing them to treatment-related risks and costs with limited benefit. However, step-up therapy comes with a potential risk of harm from disease progression related to inadequate disease therapy.
    - Anti-tumor necrosis factor (TNF) (i.e., infliximab or adalimumab) and ustekinumab are recommended over no treatment for the induction and maintenance of remission
    - Vedolizumab is suggested over no treatment for the induction and maintenance of remission
    - AGA suggests against the use of natalizumab over no treatment for the induction and maintenance of remission
    - Patients naïve to biologic therapy, the AGA recommends infliximab, adalimumab, or ustekinumab over certolizumab pegol and suggests the use of vedolizumab over certolizumab pegol for the induction of remission
    - Patients with primary non-response to anti-TNF, the AGA recommends ustekinumab and suggests vedolizumab for induction of remission
    - Patients with secondary non-response to infliximab, the AGA recommends use of adalimumab or ustekinumab and suggests the use of vedolizumab for the induction of remission (if adalimumab was the first line drug, there is indirect evidence to suggest using infliximab as a second-line agent)
- Corticosteroid therapy:
    - Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission
        - In patients with CD involving the distal ileum and/or ascending colon who are more concerned about systemic corticosteroids and less concerned about the lower efficacy, they may reasonably choose budesonide over systematic corticosteroids for inducing remission
- Disease modifying antirheumatic drug (DMARD) therapy:
    - Patients in corticosteroid induced remission or with quiescent moderate to severe CD, the AGA suggests thiopurines for maintenance of remission
    - Subcutaneous or intramuscular methotrexate are suggested over no treatment for the induction and maintenance of remission
    - The AGA recommends against the use of 5-aminosalicylates or sulfasalazine over no treatment for the induction or maintenance of remission
    - The AGA suggests against the use of thiopurines over no treatment for achieving remission and recommends biologic drug monotherapy over thiopurine monotherapy for induction of remission
    - The AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission

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

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

- Biologic therapy:
    - Biologic agents are effective for treating patients with active CD and previous inadequate response to corticosteroids, thiopurines, and/or methotrexate
    - Suggest against requiring failure of conventional therapy before initiation of advanced therapy for the management of CD (conditional recommendation, low level of evidence)
        - The risk of adverse effects and high cost of biologic agents may not be justifiable in a lower risk population
    - Recommend the following drugs for induction and maintenance of remission for moderately to severely active CD:
        - Anti-TNF agents (i.e., infliximab, adalimumab, certolizumab), vedolizumab, ustekinumab, risankizumab, mirikizumab, guselkumab
    - Recommend combination therapy of intravenous infliximab with immunomodulators (thiopurines) as compared with treatment with either immunomodulators alone or intravenous infliximab alone in patients with CD who are naïve to those agents
    - Recommend the use of risankizumab as compared with ustekinumab in patients with moderate to severe CD and prior exposure to anti-TNF therapy
    - Biosimilar infliximab, adalimumab, and ustekinumab are effective treatments for patients with moderate-to-severe CD and can be used for de novo induction and maintenance therapy
    - There are data to support the safety and efficacy of transitioning or switching to biosimilar infliximab or adalimumab for patients with CD in stable disease maintenance
- Janus kinase (JAK) inhibitor therapy:
    - Recommend upadacitinib use for induction and maintenance of remission for patients with moderate-to-severe CD who have previously been exposed to anti-TNF agents
- Corticosteroid therapy:
    - Recommend oral corticosteroids for short-term induction of remission in patients with moderately to severely active CD
        - Recommend controlled ileal release budesonide at a dose of 9 mg daily for induction of symptomatic remission in patients with mildly to moderately active ileocecal CD
    - Corticosteroids should not be used for maintaining remission, and their use should not exceed 3 continuous months without attempting to introduce a steroid-sparing agent (such as an immunomodulator)

- DMARD therapy:
    - Recommend against azathioprine or 6-mercaptopurine for induction of remission in moderately to severely active CD
        - Due to their slow onset of action of 8 to 12 weeks, thiopurines are not effective agents for induction of remission
    - Suggest azathioprine or 6-mercaptopurine for maintenance of remission in patients with moderately to severely active CD who had induction of remission with corticosteroids
    - Suggest methotrexate (up to 25 mg once weekly intramuscular or subcutaneous) for maintenance of remission in patients with moderately to severely active CD who had induction of remission with corticosteroids
    - Azathioprine, 6-mercaptopurine, or methotrexate may be used in the treatment of active CD and as adjunctive therapy for reducing immunogenicity associated with anti-TNF therapy

Ulcerative Colitis (UC)

Ulcerative colitis (UC) is a chronic inflammatory bowel disease affecting the large intestine. It typically starts with inflammation of the rectum, but often extends proximally to involve additional areas of the colon. The most common symptom is bloody diarrhea, but urgency, tenesmus, abdominal pain, malaise, weight loss, and fever can also be associated. UC commonly has a gradual onset and will present with periods of spontaneous remission and subsequent relapses.

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

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

<u>General treatment information</u>:

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

<u>Corticosteroid therapy</u>:

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

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 Food and Drug Administration has deemed the subcutaneous formulations of the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a

caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) of the subcutaneous formulations in certain provider-administered setting such as an outpatient hospital, ambulatory surgical suite, or emergency facility is not considered medically necessary.

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

SUBCUTANEOUS USTEKINUMAB PRODUCTS (MEDICAL AND PHARMACY BENEFIT)

Initiation of subcutaneous Stelara (ustekinumab), Steqeyma (ustekinumab-stba), Ustekinumab* (an unbranded version of Stelara), or Yesintek (ustekinumab-kfce) [i.e., a preferred subcutaneous ustekinumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "5"):

*__NOTE__: Subcutaneous unbranded Ustekinumab is a preferred agent only when provider-administered and billed under the medical benefit. It is **NOT** a preferred agent when self-administered and billed under the pharmacy benefit.

1. **ONE** of the following ("a", "b", or "c"):
    a. The member has been treated with the requested preferred subcutaneous ustekinumab product (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with the requested preferred subcutaneous ustekinumab product (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. The requested preferred subcutaneous ustekinumab product 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 the requested preferred subcutaneous ustekinumab product
            II. The prescriber has provided information in support of using the requested preferred subcutaneous ustekinumab product 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., rheumatologist for PsA; gastroenterologist for CD, UC; dermatologist for PS) 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 the requested preferred subcutaneous ustekinumab product
4. Member will **NOT** be using the requested preferred subcutaneous ustekinumab product in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
5. **ANY** of the following ("a", "b", "c", or "d"):
    a. The dosage does not exceed:
        - Loading dose:
            - CD or UC: Initial dose is a single IV weight-based dose, followed by maintenance doses starting 8 weeks after the initial IV dose

- PS and PsA (adult, 18 years or older): 90 mg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)
- PS and PsA (pediatric, 6 to 17 years old):
  - Less than 60 kg (132 lbs.): 0.75 mg/kg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)
  - 60 to 100 kg: 45 mg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)
  - More than 100 kg: 90 mg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)

- Maintenance dose – **ANY** of the following:
  - 0.75 mg/kg every 12 weeks (84 days), **AND ALL** of the following:
    - The member has a diagnosis of psoriasis **OR** psoriatic arthritis
    - Member is 6 to 17 years old
    - Member is less than 60 kg (132 lbs.)
    - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days

    OR
  - 45 mg every 12 week (84 days)
    - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days
    - QL: 45 mg/0.5 mL syringe - 1 syringe (0.5 mL)/84 days

    OR
  - 90 mg every 12 weeks (84 days), **AND EITHER** of the following:
    - Member has a diagnosis of psoriasis **AND** weighs >100 kg, **OR**
    - The member has a dual diagnosis of psoriasis **AND** psoriatic arthritis, **AND** the member is >100kg
      - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/84 days
      - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/84 days
      - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/84 days

    OR
  - 2.5 mg/kg every 8 weeks (56 days), **AND** the member has a diagnosis of pediatric Crohn's disease (for weights 35 kg or less only)
    - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days

    OR
  - 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of adult Crohn's disease, pediatric Crohn's disease (for weights greater than 35 kg only), or ulcerative colitis
    - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days
    - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/56 days
    - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/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:

- PS and PsA - 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]
- Other indications - 12 months; for CD and UC the start date will depend on if a loading dose with an IV ustekinumab product has already been received

Table 1

Diagnosis	Criteria
Active psoriatic arthritis (PsA)	**ONE** of the following:

	1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA after at least a 3-month duration of therapy **OR** 2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PsA **OR** 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PsA **OR** 4. The member has severe active PsA (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities, vision loss], highly active disease that causes major impairment in quality of life, active PsA at many sites [including dactylitis, enthesitis], function-limiting PsA at a few sites, 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 (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PsA
Moderate to severe plaque psoriasis (PS)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., acitretin, calcipotriene, calcitriol, coal tar, cyclosporine, methotrexate, pimecrolimus, phototherapy [e.g., PUVA, UVB], 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], highly active disease that causes major impairment in quality of life, active PsA at many sites [including dactylitis, enthesitis], function-limiting PsA at a few sites, rapidly progressive) **OR** 6. The member's medication history (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PS
Moderately to severely active Crohn's disease (CD)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD after at least a 3-month duration of therapy **OR** 2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of CD **OR** 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of CD **OR** 4. The member's medication history (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab 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 (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab 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 Stelara (ustekinumab), Steqeyma (ustekinumab-stba), Ustekinumab* (an unbranded version of Stelara), or Yesintek (ustekinumab-kfce) [i.e., a preferred subcutaneous ustekinumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "6"):

*__NOTE__: Subcutaneous unbranded Ustekinumab is a preferred agent only when provider-administered and billed under the medical benefit. It is **NOT** a preferred agent when self-administered and billed under the pharmacy benefit.

1. An authorization or reauthorization for the requested preferred subcutaneous ustekinumab product has been previously approved by Florida Blue (*please note ustekinumab product renewal must be for the same strength as the initial approval) [Note: members not previously approved for the requested agent will require initial evaluation review]
2. Member has had clinical benefit with the requested preferred subcutaneous ustekinumab product
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, gastroenterologist for CD, UC; dermatologist for PS) 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 the requested preferred subcutaneous ustekinumab product
5. Member will **NOT** be using the requested preferred subcutaneous ustekinumab product 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)]
6. **ANY** of the following ("a", "b", "c", or "d"):
    a. The dosage does not exceed the following:
        - 0.75 mg/kg every 12 weeks (84 days), **AND ALL** of the following:
            - The member has a diagnosis of psoriasis **OR** psoriatic arthritis

- Member is 6 to 17 years old
- Member is less than 60 kg (132 lbs.)
  - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days

OR

- 45 mg every 12 weeks (84 days)
  - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days
  - QL: 45 mg/0.5 mL syringe - 1 syringe (0.5 mL)/84 days

OR

- 90 mg every 12 weeks (84 days), **AND EITHER** of the following:
  - Member has a diagnosis of psoriasis **AND** weighs >100 kg, **OR**
  - The member has a dual diagnosis of psoriasis **AND** psoriatic arthritis, **AND** the member is >100kg
    - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/84 days
    - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/84 days
    - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/84 days

OR

- 2.5 mg/kg every 8 weeks (56 days), **AND** the member has a diagnosis of pediatric Crohn's disease (for weights 35 kg or less only)
  - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days

OR

- 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of adult Crohn's disease, pediatric Crohn's disease (for weights greater than 35 kg only), or ulcerative colitis
  - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days
  - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/56 days
  - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/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

Initiation of subcutaneous Imuldosa (ustekinumab-srlf), Otulfi (ustekinumab-aauz), Pyzchiva (ustekinumab-ttwe), Selarsdi (ustekinumab-aekn), Starjemza (ustekinumab-hmny), Ustekinumab (an unbranded version of Stelara), Ustekinumab-aekn (an unbranded version of Selarsdi), Ustekinumab-ttwe (an unbranded version of Pyzchiva), or Wezlana (ustekinumab-auub) [i.e., a non-preferred subcutaneous ustekinumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "5"):

*__NOTE__: Subcutaneous unbranded Ustekinumab is a non-preferred agent when self-administered and billed under the pharmacy benefit. It is a preferred agent when provider-administered and billed under the medical benefit.

1. **BOTH** of the following ("a" and "b")

   a. The requested non-preferred subcutaneous ustekinumab product will be used for the treatment of an indication listed in Table 2, and **ALL** of the indication-specific criteria are met

   b. **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 the requested non-preferred subcutaneous ustekinumab product

      ii. The prescriber has provided information in support of using the requested non-preferred subcutaneous ustekinumab product 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., rheumatologist for PsA; gastroenterologist for CD, UC; dermatologist for PS) 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 the requested non-preferred subcutaneous ustekinumab product

4. Member will **NOT** be using the requested non-preferred subcutaneous ustekinumab product in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Olumiant (baricitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
5. **ANY** of the following ("a", "b", "c", or "d"):
   a. The dosage does not exceed:
      - Loading dose:
        - CD or UC: Initial dose is a single IV weight-based dose, followed by maintenance doses starting 8 weeks after the initial IV dose
        - PS and PsA (adult, 18 years or older): 90 mg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)
        - PS and PsA (pediatric, 6 to 17 years old):
          - Less than 60 kg (132 lbs.): 0.75 mg/kg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)
          - 60 to 100 kg: 45 mg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)
          - More than 100 kg: 90 mg at week 0 and week 4, followed by maintenance doses starting 12 weeks later (week 16)
      - Maintenance dose – **ANY** of the following:
        - 0.75 mg/kg every 12 weeks (84 days), **AND ALL** of the following:
          - The member has a diagnosis of psoriasis OR psoriatic arthritis
          - Member is 6 to 17 years old
          - Member is less than 60 kg (132 lbs.)
            - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days

          OR
        - 45 mg every 12 week (84 days)
          - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days
          - QL: 45 mg/0.5 mL syringe - 1 syringe (0.5 mL)/84 days

          OR
        - 90 mg every 12 weeks (84 days), **AND EITHER** of the following:
          - Member has a diagnosis of psoriasis **AND** weighs >100 kg, **OR**
          - The member has a dual diagnosis of psoriasis **AND** psoriatic arthritis, **AND** the member is >100kg
            - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/84 days
            - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/84 days
            - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/84 days

          OR
        - 2.5 mg/kg every 8 weeks (56 days), **AND** the member has a diagnosis of pediatric Crohn's disease (for weights 35 kg or less only)

- QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days

OR

- 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of adult Crohn's disease, pediatric Crohn's disease (for weights greater than 35 kg only), or ulcerative colitis
  - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days
  - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/56 days
  - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/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:

- PS and PsA - 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]
- Other indications - 12 months; for CD and UC the start date will depend on if a loading dose with an IV ustekinumab product has already been received

Table 2

Diagnosis	Criteria
Active psoriatic arthritis (PsA)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA after at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PsA **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PsA **OR** d. 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], highly active disease that causes major impairment in quality of life, active PsA at many sites [including dactylitis, enthesitis], function-limiting PsA at a few sites, rapidly progressive) **OR** e. 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** f. The member's medication history (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PsA **AND** 2. **ANY** of the following (submitted medical records/chart notes are required for confirmation):

	a. The member has tried and had an inadequate response to at least **THREE** preferred ustekinumab products after at least a 6-month trial per agent **OR** b. The member has tried and had an inadequate response to **TWO** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** c. The member has tried and had an inadequate response to **ONE** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** d. The member has an intolerance or hypersensitivity to **THREE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product: **OR** e. The member has an FDA labeled contraindication to **ALL** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **The preferred ustekinumab products are:** • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce)
Moderate to severe plaque psoriasis (PS)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., acitretin, calcipotriene, calcitriol, coal tar, cyclosporine, methotrexate, pimecrolimus, phototherapy [e.g., PUVA, UVB], tacrolimus, tazarotene, topical corticosteroids) used in the treatment of PS after at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PS **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PS **OR** d. 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** e. 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], highly active disease that causes major impairment in quality of life, active PsA at many sites [including dactylitis, enthesitis], function-limiting PsA at a few sites, rapidly progressive) OR f. The member's medication history (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PS **AND** 2. **ANY** of the following (submitted medical records/chart notes are required for confirmation): a. The member has tried and had an inadequate response to at least **THREE** preferred ustekinumab products after at least a 6-month trial per agent **OR** b. The member has tried and had an inadequate response to **TWO** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** c. The member has tried and had an inadequate response to **ONE** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** d. The member has an intolerance or hypersensitivity to **THREE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** e. The member has an FDA labeled contraindication to **ALL** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **The preferred ustekinumab products are:** • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba)

	• Yesintek (ustekinumab-kfce)
Moderately to severely active Crohn's disease (CD)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD after at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of CD **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of CD **OR** d. The member's medication history (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** e. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors **AND** 2. **ANY** of the following (submitted medical records/chart notes are required for confirmation): a. The member has tried and had an inadequate response to at least **THREE** preferred ustekinumab products after at least a 6-month trial per agent **OR** b. The member has tried and had an inadequate response to **TWO** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** c. The member has tried and had an inadequate response to **ONE** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR**

	d. The member has an intolerance or hypersensitivity to **THREE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** e. The member has an FDA labeled contraindication to **ALL** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **The preferred ustekinumab products are:** • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce)
Moderately to severely active ulcerative colitis (UC)	**BOTH** of the following ("1" and "2"): 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., 6-mercaptopurine, azathioprine, balsalazide, corticosteroids, cyclosporine, mesalamine, sulfasalazine) used in the treatment of UC after at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of UC **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of UC **OR** d. The member's medication history (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** e. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors **AND** 2. **ANY** of the following (submitted medical records/chart notes are required for confirmation): a. The member has tried and had an inadequate response to at least **THREE** of the following preferred ustekinumab products after at least a 6-month trial per agent: **OR**

	b. The member has tried and had an inadequate response to **TWO** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product: **OR** c. The member has tried and had an inadequate response to **ONE** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **OR** d. The member has an intolerance or hypersensitivity to **THREE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product: **OR** e. The member has an FDA labeled contraindication to **ALL** preferred ustekinumab products that is not expected to occur with the requested non-preferred product **The preferred ustekinumab products are:** • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce)
Other indications	The member has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a

Continuation of subcutaneous Imuldosa (ustekinumab-srlf), Otulfi (ustekinumab-aauz), Pyzchiva (ustekinumab-ttwe), Selarsdi (ustekinumab-aekn), Starjemza (ustekinumab-hmny), Ustekinumab* (an unbranded version of Stelara), Ustekinumab-aekn (an unbranded version of Selarsdi), Ustekinumab-ttwe (an unbranded version of Pyzchiva), or Wezlana (ustekinumab-auub) [i.e., a non-preferred subcutaneous ustekinumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "7"):

*__NOTE__: Subcutaneous unbranded Ustekinumab is a non-preferred agent when self-administered and billed under the pharmacy benefit. It is a preferred agent when provider-administered and billed under the medical benefit.

1. An authorization or reauthorization for the requested non-preferred subcutaneous ustekinumab product has been previously approved by Florida Blue (*please note ustekinumab product renewal must be for the same strength as the initial approval) [Note: members not previously approved for the requested agent will require initial evaluation review]
2. Member has had clinical benefit with the requested non-preferred subcutaneous ustekinumab product
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for PsA, gastroenterologist for CD, UC; dermatologist for PS) 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 the requested non-preferred subcutaneous ustekinumab product
5. Member will **NOT** be using the requested non-preferred subcutaneous ustekinumab product 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)]
6. **ANY** of the following (submitted medical records/chart notes are required for confirmation):
    a. The member has tried and had an inadequate response to at least **THREE** preferred ustekinumab products after at least a 6-month trial per agent

        OR

    b. The member has tried and had an inadequate response to **TWO** preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product

        OR

    c. The member has tried and had an inadequate response to **ONE** preferred ustekinumab product after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** preferred ustekinumab products that is not expected to occur with the requested non-preferred product:

        OR

    d. The member has an intolerance or hypersensitivity to **THREE** preferred ustekinumab products that is not expected to occur with the requested non-preferred product

        OR

    e. The member has an FDA labeled contraindication to **ALL** preferred ustekinumab products that is not expected to occur with the requested non-preferred product

    The preferred ustekinumab products are:

    - Stelara (ustekinumab)
    - Steqeyma (ustekinumab-stba)
    - Yesintek (ustekinumab-kfce)
7. **ANY** of the following ("a", "b", "c", or "d"):
    a. The dosage does not exceed the following:
        - 0.75 mg/kg every 12 weeks (84 days), **AND ALL** of the following:
            - The member has a diagnosis of psoriasis **OR** psoriatic arthritis
            - Member is 6 to 17 years old
            - Member is less than 60 kg (132 lbs.)
                - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days

        OR

        - 45 mg every 12 weeks (84 days)
            - QL: 45 mg/0.5 mL vial - 1 vial (0.5 mL)/84 days
            - QL: 45 mg/0.5 mL syringe - 1 syringe (0.5 mL)/84 days

OR

- 90 mg every 12 weeks (84 days), **AND EITHER** of the following:
  - Member has a diagnosis of psoriasis **AND** weighs >100 kg, **OR**
  - The member has a dual diagnosis of psoriasis **AND** psoriatic arthritis, **AND** the member is >100kg
    - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/84 days
    - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/84 days
    - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/84 days

OR

- 2.5 mg/kg every 8 weeks (56 days), **AND** the member has a diagnosis of pediatric Crohn's disease (for weights 35 kg or less only)
    - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days

OR

- 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of adult Crohn's disease, pediatric Crohn's disease (for weights greater than 35 kg only), or ulcerative colitis
  - QL: 45 mg/0.5 mL vial - 2 vials (1 mL)/56 days
  - QL: 45 mg/0.5 mL syringe - 2 syringes (1 mL)/56 days
  - QL: 90 mg/1 mL syringe - 1 syringe (1 mL)/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 USTEKINUMAB PRODUCTS (MEDICAL BENEFIT)

Initiation of intravenous (IV) Stelara (ustekinumab), Steqeyma (ustekinumab-stba), Ustekinumab (an unbranded version of Stelara), or Yesintek (ustekinumab-kfce) [i.e., a preferred IV ustekinumab product] **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. The preferred IV ustekinumab product will be used for the treatment of an indication listed in Table 3, 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 the preferred IV ustekinumab product
   b. The prescriber has provided information in support of using the preferred IV ustekinumab product 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, 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 the preferred IV ustekinumab product
5. Member will **NOT** be using the preferred IV ustekinumab product 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); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. Member has not received a previous dose of an ustekinumab product (IV or SC) in the past 6 months [this criterion is not applicable for immune checkpoint inhibitor-related adverse effects]

Approval duration:

- CD, immune checkpoint inhibitor-related adverse effects, and UC - 1 month (to allow for one dose)
- Other indications - 12 months

Table 3

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** 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 (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors	Adults (18 years and older): • ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose Pediatric patients (less than 18 years of age): • 10 to 25 kg: 10 mg/kg X 1 dose • >25 to ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose
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**	• ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose

	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 (excluding samples) indicates use of another biologic immunomodulator agent OR a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors	
Immune checkpoint inhibitor-related adverse effects	**ALL** of the following: 1. Member has been receiving treatment with an immune checkpoint inhibitor (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, darvalumab) **AND** 2. **EITHER** of the following: a. The member has mild (Grade 1) diarrhea or colitis if persistent or progressive symptoms **AND** positive lactoferrin/calprotectin b. The member has moderate or severe diarrhea and colitis (Grades 2 to 4) **AND** 3. Member has had an inadequate response to, intolerable adverse effects with, or a contraindication to an adequate trial of **BOTH** of the following ("a" and "b"):	• ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose

	a. Systemic corticosteroid treatment b. An infliximab product **OR** vedolizumab (Entyvio) **AND** 4. The members immune checkpoint inhibitor therapy will be either permanently discontinued or held during treatment with ustekinumab	
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

Initiation of intravenous (IV) Imuldosa (ustekinumab-srlf), Otulfi (ustekinumab-aauz), Pyzchiva (ustekinumab-ttwe), Selarsdi (ustekinumab-aekn), Starjemza (ustekinumab-hmny), Ustekinumab-ttwe (an unbranded version of Pyzchiva), or Wezlana (ustekinumab-auub) [i.e., a NON-preferred IV ustekinumab product] **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. The non-preferred IV ustekinumab product will be used for the treatment of an indication listed in Table 4, 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 the non-preferred IV ustekinumab product
    b. The prescriber has provided information in support of using the non-preferred IV ustekinumab product for the member's age for the requested indication
3. The member has an FDA labeled contraindication, intolerance, and/or hypersensitivity to **ALL** of the following preferred IV ustekinumab products that is not expected to occur with the requested non-preferred IV product – documentation of the contraindications, intolerances, and/or hypersensitivities; and rationale as to why it is not expected to occur with the requested non-preferred IV product must be submitted:
    - Stelara (ustekinumab) **OR** Ustekinumab
    - Steqeyma (ustekinumab-stba)
    - Yesintek (ustekinumab-kfce)
4. The prescriber is a specialist in the area of the member's diagnosis (e.g., gastroenterologist for CD, UC) 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 the non-preferred IV ustekinumab product
6. Member will **NOT** be using the preferred IV ustekinumab product 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); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

7. Member has not received a previous dose of an ustekinumab product (IV or SC) in the past 6 months [this criterion is not applicable for immune checkpoint inhibitor-related adverse effects]

Approval duration:

- CD, immune checkpoint inhibitor-related adverse effects, and UC - 1 month (to allow for one dose)
- Other indications - 12 months

Table 4

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** 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 (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors	Adults (18 years and older): • ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose Pediatric patients (less than 18 years of age): • 10 to 25 kg: 10 mg/kg X 1 dose • >25 to ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose

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 (excluding samples) indicates use of another biologic immunomodulator agent **OR** a systemic targeted synthetic small molecule drug (e.g., oral JAK inhibitor) that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with ustekinumab is deemed clinically necessary - provider must include additional details regarding disease severity and/or risk factors	• ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose
Immune checkpoint inhibitor-related adverse effects	**ALL** of the following: 1. Member has been receiving treatment with an immune checkpoint inhibitor (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, darvalumab) **AND** 2. **EITHER** of the following: a. The member has mild (Grade 1) diarrhea or colitis if persistent or	• ≤55 kg: 260 mg (two 130 mg vials) X 1 dose • >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose • >85 kg: 520 mg (four 130 mg vials) X 1 dose

	progressive symptoms **AND** positive lactoferrin/calprotectin b. The member has moderate or severe diarrhea and colitis (Grades 2 to 4) **AND** 3. Member has had an inadequate response to, intolerable adverse effects with, or a contraindication to an adequate trial of **BOTH** of the following ("a" and "b"): a. Systemic corticosteroid treatment b. An infliximab product **OR** vedolizumab (Entyvio) **AND** 4. The members immune checkpoint inhibitor therapy will be either permanently discontinued or held during treatment with ustekinumab	
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: ustekinumab products are indicated for: (1) the treatment of patients 6 years or older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy, (2) the treatment of patients 6 years or older with active psoriatic arthritis, (3) the treatment of adults and pediatric patients 2 years of age and older with moderately to severely active Crohn's disease, and (4) the treatment of adult patients with moderately to severely active ulcerative colitis (UC).

The recommended dose is based on weight for the treatment of plaque psoriasis:

- Adult dosage (18 years and older)
  - 100 kg or less: 45 mg at week 0 and 4 week later at week 4, followed by 45 mg every 12 weeks beginning at week 16.
  - Greater than 100 kg: 90 mg at week 0 and 4 week later at week 4, followed by 90 mg every 12 weeks beginning at week 16.
- Pediatric/Adolescent dosage (6 to less than 18 years)

- Less than 60 kg: 0.75 mg/kg at week 0 and 4 week later at week 4, followed by 0.75 mg/kg every 12 weeks beginning at week 16 – refer to the prescribing information for a table of the injection volumes based on weight
- 60 to 100 kg: 45 mg at week 0 and 4 week later at week 4, followed by 45 mg every 12 weeks beginning at week 16
- Greater than 100 kg: 90 mg at week 0 and 4 weeks at weeks 4, followed by 90 mg every 12 weeks beginning at week 16

The recommended dose for the treatment of active psoriatic arthritis in adults is 45 mg every 4 weeks at weeks 0 and 4, followed by 45 mg every 12 weeks beginning at week 16. In persons with co-existent moderate to severe plaque psoriasis who weight greater than 100 kg, the recommended dose is 90 mg every 4 weeks at weeks 0 and 4, followed by 90 mg every 12 weeks beginning at week 16.

The recommended dose for pediatric patients (6 to 17 years old) is based on body weight. The dose is the following given at weeks 0 and 4, then every 12 weeks thereafter: less than 60 kg - 0.75 mg/kg, 60 kg or more - 45 mg, or greater than 100 kg with co-existent moderate-to-severe plaque psoriasis – 90 mg.

The recommended dosage for the treatment of Crohn's disease is weight-based for the initial IV loading dose but then a fixed maintenance dosage.

- For adults (18 years and older), the loading dose is: ≤55 kg: 260 mg (two 130 mg vials) X 1 dose; >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose; >85 kg: 520 mg (four 130 mg vials) X 1 dose (on week 0) given as an IV infusion in 250 mL (using 0.45% sodium chloride or normal saline) over at least one hour. The maintenance dose is 90 mg given as a subcutaneous injection 8 weeks after the initial IV dose (week 8), then every 8 weeks thereafter.
- For pediatric patients (2 to less than 18 years), the loading dose is: 10 kg to 25 kg, 10 mg/kg, 25 to ≤55 kg: 260 mg (two 130 mg vials) X 1 dose; >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose; >85 kg: 520 mg (four 130 mg vials) X 1 dose (on week 0) given as an IV infusion in 100 mL (if 10 kg to 25 kg) or 250 mL(if >25 kg), using normal saline, over at least one hour. The maintenance dose is:
  - 10 kg to 35 kg: 2.5 mg/kg given as a subcutaneous injection 8 weeks after the initial IV dose (week 8), then every 8 weeks thereafter
  - >35 kg: 90 mg given as a subcutaneous injection 8 weeks after the initial IV dose (week 8), then every 8 weeks thereafter

The recommended dosage for the treatment of UC is weight-based for the initial IV loading dose but then a fixed maintenance dosage. The loading dose is: ≤55 kg: 260 mg (two 130 mg vials) X 1 dose; >55 to 85 kg: 390 mg (three 130 mg vials) X 1 dose; >85 kg: 520 mg (four 130 mg vials) X 1 dose (on week 0) given as an IV infusion in 250 mL (using 0.45% sodium chloride or normal saline) over at least one hour. The maintenance dose is 90 mg given as a subcutaneous injection 8 weeks after the initial IV dose (week 8), then every 8 weeks thereafter.

The ustekinumab product should be administered as a subcutaneous injection with the exception of the initial IV infusion loading dose for Crohn's disease and UC.

Drug availability:

- Imuldosa
  - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
  - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Otulfi and unbranded Ustekinumab-aauz:
  - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
  - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Pyzchiva and unbranded Ustekinumab-ttwe:

    - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Selarsdi and unbranded Ustekinumab-aekn:
    - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Starjemza
    - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Stelara and unbranded Ustekinumab:
    - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Steqeyma and unbranded Ustekinumab-stba:
    - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose vial: 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Wezlana:
    - Single-dose prefilled ConfiPen autoinjector: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)
- Yesintek:
    - Single-dose prefilled syringe: 45 mg/0.5 mL, 90 mg/1 mL (both for SQ use)
    - Single-dose vial: 45 mg/0.5 mL (for SQ use), 130 mg/26 mL (5 mg/mL) (for IV infusion)

PRECAUTIONS:

Boxed Warning:

- None

Contraindication:

- Persons with clinically significant hypersensitivity to the ustekinumab product or any of the excipients.

Precautions/Warnings

- **Infections**: Serious infections have occurred. Do not start the ustekinumab product during any clinically important active infection. If a serious infection develops, discontinue therapy until the infection resolves.
- **Theoretical Risk for Vulnerability to Particular Infections**: Serious infections from mycobacteria, salmonella and Bacillus Calmette-Guerin (BCG) vaccinations have been reported in persons genetically deficient in IL-12/IL-23. Diagnostic tests for these infections should be considered as dictated by clinical circumstances.
- **Pre-treatment Evaluation for Tuberculosis (TB)**: Evaluate individuals for TB prior to initiating treatment with an ustekinumab product. Initiate treatment of latent TB before administering an ustekinumab product.
- **Malignancies**: An ustekinumab product may increase risk of malignancy. The safety of an ustekinumab product in persons with a history of or a known malignancy has not been evaluated.

- **Hypersensitivity Reactions:** Anaphylaxis or other clinically significant hypersensitivity reactions may occur.
- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS)**: One case was reported. If suspected, treat promptly and discontinue ustekinumab.
- **Immunization**: Do not administer live vaccines with an ustekinumab product.
- **Posterior Reversible Encephalopathy Syndrome (PRES)**): If PRES is suspected, treat promptly and discontinue the ustekinumab product.
- **Concomitant Therapies**: In clinical studies of psoriasis the safety of an ustekinumab product in combination with other immunosuppressive agents or phototherapy was not evaluated
- **Noninfectious Pneumonia**: Cases of interstitial pneumonia, eosinophilic pneumonia and cryptogenic organizing pneumonia have been reported during post-approval use of ustekinumab. Clinical presentations included cough, dyspnea, and interstitial infiltrates following one to three doses. Serious outcomes have included respiratory failure and prolonged hospitalization. Patients improved with discontinuation of therapy and in certain cases administration of corticosteroids. If diagnosis is confirmed, discontinue the ustekinumab product and institute appropriate treatment,

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J3357	Ustekinumab, for subcutaneous injection, 1 mg
J3358	Ustekinumab, for intravenous injection, 1 mg
Q5098*	Injection, ustekinumab-srlf (imuldosa), biosimilar, 1 mg
Q5099*	Injection, ustekinumab-stba (steqeyma), biosimilar, 1 mg
Q5100*	Injection, ustekinumab-kfce (yesintek), biosimilar, 1 mg
Q5137	Injection, ustekinumab-auub (wezlana), biosimilar, subcutaneous, 1 mg
Q5138	Injection, ustekinumab-auub (wezlana), biosimilar, intravenous, 1 mg
Q5164	Injection, ustekinumab-hmny (starjemza), biosimilar, 1 mg
Q9996	Injection, ustekinumab-ttwe (pyzchiva), subcutaneous, 1 mg
Q9997	Injection, ustekinumab-ttwe (pyzchiva), intravenous, 1 mg
Q9998*	Injection, ustekinumab-aekn (selarsdi), biosimilar, 1 mg
Q9999*	Injection, ustekinumab-aauz (otulfi), biosimilar, 1 mg

*Should be billed with either the JA modifier for the intravenous infusion of the drug or the JB modifier for subcutaneous injection of the drug.

ICD-10 Diagnosis Codes That Support Medical Necessity of Intravenous Injection (J3358, Q5098, Q5099, Q5100, Q5138, Q5164, Q9997, Q9998, Q9999):

K50.00 – K50.919	Crohn's disease [regional enteritis]
K51.00 – K51.919	Ulcerative colitis
T45.AX5A	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, initial encounter
T45.AX5D	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, subsequent encounter
T45.AX5S	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, sequela

ICD-10 Diagnosis Codes That Support Medical Necessity of Subcutaneous Injection (J3357, Q5098, Q5099, Q5100, Q5137, Q5164, Q9996, Q9998, Q9999):

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
L40.54	Psoriatic juvenile arthropathy
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 Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

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

DMARDs: An acronym for disease-modifying antirheumatic drugs. These are drugs that modify the rheumatic disease processes, and slow or inhibit structural damage to cartilage and bone. These drugs are unlike symptomatic treatments such as NSAIDs that do not alter disease progression. DMARDs can be further subcategorized. With the release of biologic agents (e.g., anti-TNF drugs), DMARDs were divided into either: (1) conventional, traditional, synthetic, or non-biological DMARDs; or as (2) biological DMARDs. However, with the release of newer targeted non-biologic drugs and biosimilars, DMARDs are now best categorized as: (1) conventional synthetic DMARDs (csDMARD) (e.g., MTX, sulfasalazine), (2) targeted synthetic DMARDs (tsDMARD) (e.g., baricitinib, tofacitinib, apremilast), and (3) biological DMARDs (bDMARD), which can be either a biosimilar DMARD (bsDMARD) or biological originator DMARD (boDMARD).

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.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): a neurological disorder, which is not caused by demyelination or a known infectious agent. RPLS can present with headache, seizures, confusion and visual disturbances. Conditions with which it has been associated include preeclampsia, eclampsia, acute hypertension, cytotoxic agents and immunosuppressive therapy. Fatal outcomes have been reported.

RELATED GUIDELINES:

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), 02-10000-16
Risankizumab (Skyrizi), 09-J3000-45
Secukinumab (Cosentyx), 09-J2000-30
Tildrakizumab-asmn (Ilumya), 09-J3000-04
Tofacitinib (Xeljanz, Xeljanz XR) Tablets, 09-J1000-86
Upadacitinib (Rinvoq), 09-J3000-51
Vedolizumab (Entyvio), 09-J2000-18

OTHER:

NOTE: The list of biologic immunomodulator agents not permitted as concomitant therapy can be found at Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.

Table 3: Conventional Synthetic DMARDs

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

REFERENCES:

1. Armstrong AW, Siegel MP, Bagel J, et al. From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. J Am Acad Dermatol. 2017 Feb;76(2):290-298.

2. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2025. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 10/29/25.
3. Coates LC, Soriano ER, Corp N, et al; GRAPPA Treatment Recommendations domain subcommittees. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. Nat Rev Rheumatol. 2022 Aug;18(8):465-479. Epub 2022 Jun 27. Erratum in: Nat Rev Rheumatol. 2022 Dec;18(12):734.
4. Dogra S, Jain A, Kanwar AJ. Efficacy and safety of acitretin in three fixed doses of 25, 35 and 50 mg in adult patients with severe plaque type psoriasis: a randomized, double blind, parallel group, dose ranging study. J Eur Acad Dermatol Venereol. 2013 Mar;27(3):e305-11.
5. Dogra S, Krishna V, Kanwar AJ. Efficacy and safety of systemic methotrexate in two fixed doses of 10 mg or 25 mg orally once weekly in adult patients with severe plaque-type psoriasis: a prospective, randomized, double-blind, dose-ranging study. Clin Exp Dermatol. 2012 Oct;37(7):729-34.
6. Elmets CA, Leonardi CL, Davis DM, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities. J Am Acad Dermatol. 2019 Apr;80(4):1073-1113. Epub 2019 Feb 13.
7. Elmets CA, Lim HW, Stoff H, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy. J Am Acad Dermatol. Epub 2019 July 25.
8. FDA Orphan Drug Designations and Approvals [Internet]. Washington, D.C. [cited 2025 Oct 29]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/.
9. Feuerstein JD, Ho EY, Shmidt E, Singh H, Falck-Ytter Y, Sultan S, Terdiman JP; American Gastroenterological Association Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021 Jun;160(7):2496-2508.
10. Feuerstein JD, Isaacs KL, Schneider Y, et al.; AGA Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020 Apr;158(5):1450-1461. 2020 Jan 13.
11. Gottlieb A, Menter A, Mendelsohn A, et al. Ustekinumab, a human interleukin 12/23 monoclonal antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial. Lancet. Feb 21, 2009; 373(9664):633-640.
12. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. Lancet. 2021;397(10281): 1301-1315.
13. Griffiths CE, Strober BE, van de Kerkhof P, et al. Comparison of Ustekinumab and Etanercept for Moderate-to-Severe Psoriasis. N Engl J Med 2010; 362:118-28.
14. Hazelwood GS, Rezaie A, Borman M, et al. Comparative effectiveness of immunosuppressants and biologics for inducing and maintaining remission in Crohn’s disease: a network meta-analysis. Gastroenterology 2014; doi: 10.1053/j.gastro.2014.10.011.
15. Imuldosa (ustekinumab-srlf) [package insert]. Accord BioPharma Inc., Raleigh, NC: November 2025.
16. Kalb RE, Strober B, Weinstein G, Lebwohl M. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. J Am Acad Dermatol 2009; 60:824-37.
17. Kavanaugh A, Ritchlin C, Rahman P et al. Ustekinumab, an anti-IL-12/23 p40 monoclonal antibody, inhibits radiographic progression in patients with active psoriatic arthritis: results of an integrated analysis of radiographic data from the phase 3, multicentre, randomised, double-blind, placebo-controlled PSUMMIT-1 and PSUMMIT-2 trials. Ann Rheum Dis 2014; 73: 1000-6.
18. Khanna R, Preiss JC, MacDonald JK, et al. Anti-IL-12/23p40 antibodies for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2015 May 5;(5):CD007572.

19. Kimball AB, Papp KA, Wasfi Y, et al. Long-term efficacy of ustekinumab in patients with moderate-to-severe psoriasis treated for up to 5 years in the PHOENIX 1 study. J Eur Acad Dermatol Venereol. 2013 Dec;27(12):1535-45. doi: 10.1111/jdv.12046. Epub 2012 Dec 20.
20. Ko CW, Singh S, Feuerstein JD, et al; American Gastroenterological Association Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology. 2019 Feb;156(3):748-764.
21. Krause ML, Amin A, and Makol A. Use of DMARDs and biologics during pregnancy and lactation in rheumatoid arthritis: what the rheumatologist needs to know. Ther Adv Musculoskelet Dis. 2014 Oct; 6(5): 169–184.
22. LeBlanc K, Mosli M, Parker CE, et al. The impact of biological interventions for ulcerative colitis on health-related quality of life. Cochrane Database Syst Rev. 2015 Sep 22;9:CD008655.
23. Lebwohl M, Yeilding N, Szapary P, et al. Impact of weight on the efficacy and safety of ustekinumab in patients with moderate to severe psoriasis: rationale for dosing recommendations. J Am Acad Dermatol 2010;63(4):571-79.
24. Leonardi CL, Kimball AB, Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomized, double-blind, placebo-controlled trial (PHOENIX 1). Lancet 2008;371(9625):1665-74.
25. Lichtenstein GR, Loftus EV, Afzali A, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2025 Jun 3;120(6):1225-1264.
26. Marwaha AK, Tan S, Dutz JP.Targeting the IL-17/IFN-γ axis as a potential new clinical therapy for type 1 diabetes. Clin Immunol. 2014 Sep;154(1):84-9. doi: 10.1016/j.clim.2014.06.006. Epub 2014 Jun 16. Review.
27. Mcinnes IB, Kavanaugh A, Gottlieb AB, et al. Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1-year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial. Lancet 2013; 382: 780-9.
28. Menter A, Cordoro KM, Davis DMR, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients. J Am Acad Dermatol. 2020 Jan;82(1):161-201. Epub 2019 Nov 5. Erratum in: J Am Acad Dermatol. 2020 Mar;82(3):574.
29. 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 Jun;82(6):1445-1486.
30. Mentor A, Korman NJ, Elmets CA, et al. Guidelines for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011; 65:137-74.
31. 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 Apr;80(4):1029-1072. Epub 2019 Feb 13.
32. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 10/29/25.
33. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 10/29/25.
34. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Management of Immune Checkpoint Inhibitor-Related Toxicities. Version 1.2026 - October 23, 2025. Available athttps://www.nccn.org/professionals/physician_gls/pdf/ici_tox.pdf. Accessed 10/29/25.
35. Otulfi (ustekinumab-aauz) [package insert]. Fresenius Kabi USA, LLC, Lake Zurich, IL: May 2025.

36. Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomized, double-blind, placebo-controlled trial (PHOENIX 2). Lancet 2008;371(9625):1675-84.
37. Pyzchiva (ustekinumab-ttwe) [package insert]. Samsung Bioepis Co., Ltd.. Republic of Korea: November 2025.
38. Rahimi R, Nikfar S, Rezaie A, et al. Pregnancy outcome in women with inflammatory bowel disease following exposure to 5-aminosalicylic acid drugs: a meta-analysis. Reprod. Toxicol; 2008:25,271–275.
39. Reich K, Leonardi C, Griffiths CEM et al. Update on the Cumulative Safety Experience of Ustekinumab: Result from the Ustekinumab Psoriasis Clinical Development Program with Up to 4 Years of Follow-up: Proceeding of the 22nd World Congress of Dermatology; 2011 May 29-29; Seoul, Korea. FC07-03.
40. Ritchlin C, Rahman P, Kavanaugh A et al. Efficacy and safety of the anti-IL-12/23 p40 monoclonal antibody, ustekinumab, in patients with active psoriatic arthritis despite conventional non-biological and biological anti-tumour necrosis factor therapy: 6-month and 1-year results of the phase 3, multicentre, double-blind, placebo-controlled, randomised PSUMMIT 2 trial. Ann Rheum Dis 2014; 73: 990-9.
41. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline Update: Ulcerative Colitis in Adults. Am J Gastroenterol. 2025 Jun 3;120(6):1187-1224.
42. Sandborn WJ, Feagan BG, Fedorak RN, et al.; Ustekinumab Crohn's Disease Study Group. A randomized trial of Ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with moderate-to-severe Crohn's disease. Gastroenterology. 2008 Oct;135(4):1130-41.
43. Sandborn WJ, Gasink C, Gao LL, et al.; CERTIFI Study Group. Ustekinumab induction and maintenance therapy in refractory Crohn's disease. N Engl J Med. 2012 Oct 18;367(16):1519-28.
44. Sands BE, Sandborn WJ, Panaccione R, et al. Ustekinumab as Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med. 2019 Sep 26;381(13):1201-1214.
45. Sbidian E, Chaimani A, Garcia-Doval, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2021 Apr 19;4(4):CD011535. Update in: Cochrane Database Syst Rev. 2022 May 23;5:CD011535.
46. Selarsdi (ustekinumab-aekn) [package insert]. Alvotech USA Inc. Leesburg, VA: December 2025.
47. Singh JA, Guyatt G, Ogdie A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019 Jan;71(1):5-32. Epub 2018 Nov 30.
48. Smith CH, Jabbar-Lopez JK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. Br J Dermatol 2017; 177: 628-136.Stelara (ustekinumab) [package insert]. Janssen Biotech, Inc. Horsham (PA): October 2019.
49. Steqeyma (ustekinumab-stba) [package insert]. Celltrion, Inc. Republic of Korea: February 2025.
50. Stelara (ustekinumab) [package insert]. Janssen Biotech, Inc. Horsham, PA: April 2026.
51. Ustekinumab [package insert]. Janssen Biotech, Inc. Horsham, PA: April 2025.
52. Ustekinumab-aekn [package insert]. Alvotech USA Inc. Leesburg, VA: December 2025.
53. Ustekinumab-stba [package insert]. Celltrion, Inc. Republic of Korea: April 2024.
54. Ustekinumab-ttwe [package insert]. Quallent Pharmaceuticals Health LLC. Grand Cayman, Cayman Islands: March 2025.
55. Wezlana (ustekinumab-auub) [package insert]. Amgen Inc. Thousand Oaks, CA: October 2025.
56. Yesintek (ustekinumab-kfce) [package insert]. Biocon Biologics Inc. Cambridge, MA: November 2024.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/13/26.

GUIDELINE UPDATE INFORMATION:

02/15/10	New Medical Coverage Guideline.
04/15/10	Revision to guideline; consisting of adding specific continuation criteria.
01/01/11	Revision to guideline; consisting of updating coding.
09/15/11	Review and revision to guideline; consisting of updating position statement, coding and references.
09/15/12	Review and revision to guideline; consisting of modifying continuation criteria, reformatting position statement and updating precautions and references.
09/15/13	Review and revision to guideline; consisting of revising description, position statement, dosage/administration, and precautions; updated program exceptions and references.
01/01/14	Revision to guideline; consisting of revising position statement, updating coding and references.
04/15/14	Revision to guideline; consisting of revising position statement.
09/15/14	Review and revision to guideline; consisting of updating position statement and references.
09/15/15	Review and revision to guideline; consisting of revising position statement, updating coding and references.
11/01/15	Revision: ICD-9 Codes deleted.
11/15/15	Revision to guideline consisting of updating maximum starting dosage in the position statement.
02/24/16	Revision to guideline consisting of updating the position statement.
09/15/16	Review and revision to guideline consisting of updating position statement, related guidelines, and references.
11/15/16	Revision to guideline, based on a new FDA-approved indication and IV formulation, consisting of updating the description section, position statement, dosage/administration section, billing/coding, related guidelines, and references.
01/01/17	Revision: updated HCPCS code J3357 description.
01/15/17	Revision to guideline to separate the authorizations for the IV and SC formulations for Crohn's disease.
04/01/17	Revision to guideline consisting of adding HCPCS code C9487.
07/01/17	Addition of HCPCS code Q9989 that replaces codes C9487 and J3590
07/15/17	Revision to guideline consisting of updating the position statement.
10/15/17	Review and revision to guideline consisting of updating description, position statement, coding/billing, definitions, related guidelines, and references.
01/01/18	Revision to guideline consisting of updating the description section, position statement, and references after expanded FDA-approved indication for plaque psoriasis to include adolescent patients. The preferred self-administered biologic products were also updated according to indication for use. Addition of HCPCS code J3358 and deletion of code Q9989.
07/01/18	Revision to guideline consisting of updating the position statement.
10/15/18	Review and revision to guideline consisting of updating the position statement, precautions, and references.
10/15/19	Review and revision to guideline consisting of updating the description, position statement, billing/coding, related guidelines, and references.
01/01/20	Revision to guideline consisting of updating the description section, position statement, dosage/administration section, and references, based on the new FDA-approved indication of ulcerative colitis.

07/01/20	Revision to guideline consisting of updating the description, position statement, billing/coding, and definitions.
01/01/21	Review and revision to guideline consisting of updating the description, position statement, and references.
03/15/21	Revision to guideline consisting of updating Table 1 in the position statement.
09/15/21	Update to Table 1 in Position Statement.
11/15/21	Revision to guideline consisting of updating the position statement.
01/01/22	Review and revision to guideline consisting of updating the description, position statement, and references.
02/15/22	Revision to guideline consisting of updating the position statement.
03/15/22	Revision to guideline consisting of updating the position statement and other sections.
05/15/22	Update to Table 1 in Position Statement.
06/15/22	Revision to guideline consisting of updating the 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, billing/coding, and references.
01/01/23	Review and revision to guideline consisting of updating the description section (NCCN information information), position statement, other section, billing/coding, and references. New drugs were added to the list of drugs that are not permitted for use in combination. For UC, added allowance for Stelara to be used first-line for members with severe disease and/or risk factors for disease complications. For IV ustekinumab added use for the treatment of moderate-to-severe, steroid-refractory, immunotherapy-related diarrhea and colitis that has failed treatment with an infliximab product or vedolizumab (Entyvio).
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.
11/15/23	Revision to guideline consisting of updating the position statement to allow use of two 45 mg syringes/vial for a 90 mg dose.
01/01/24	Review and revision to guideline consisting of updating the description section (NCCN info), position statement, other section, and references. Added allowance for the use of Stelara IV for mild (Grade 1) diarrhea or colitis if persistent or progressive symptoms AND positive lactoferrin/calprotectin. For IV dose, updated that member has not received a previous dose of ustekinumab (IV or SC) in the past 6 months (vs.12 months). 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, related guidelines, and other section. Updates to the positioning of agents in Table 1. Removal of latent TB testing requirement. New drugs added to the list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.
10/01/24	Revision to guideline consisting of updating the position statement and billing/coding. Updates to Table 1. New ICD-10 codes related to adverse effect of immune checkpoint inhibitors.
11/15/24	Revision to guideline consisting of updating the position statement to clarify that the age requirement that exists for subcutaneous Stelara also applies to intravenous Stelara.
01/01/25	Review and revision to guideline consisting of updating the description, position statement, other section, and references. Added pediatric-specific dosing for PS and PsA (when under 60 kg) to the Position Statement. Update to original Table 1 which is now a link out from the Position Statement. Table titles updated. Revised wording regarding maximum dosage exceptions. New drugs added to the list of drugs that are not permitted for use in combination. New HCPCS codes.
04/01/25	Revision: Added HCPCS code Q9999.
07/01/25	Revision to guideline consisting of updating the description section, position statement,

	dosage/administration, precautions, billing/coding, and references. Selarsdi, Stelara, Steqeyma and Yesintek are the co-preferred SC and IV ustekinumab products. Unbranded Ustekinumab SC (provider-administered) and IV is also a co-preferred product on the medical benefit only.
01/01/26	Review and revision to guideline consisting of updating the description, position statement, and references. Starjemza IV and SC added as non-preferred ustekinumab products.
05/15/26	Revision to guideline consisting of clarifying the approval duration and start date for subcutaneous injection of a ustekinumab product following IV induction with a ustekinumab product.
07/01/26	Revision to guideline consisting of updating the description section, position statement, and billing/coding. Selarsdi (both IV and SC) moved from a preferred to a non-preferred ustekinumab product. Stelara indication for CD expanded to include patients 2 years of age and older. Added HCPCS code Q5164 and removed code J3590.