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Subject: Ustekinumab Products (Stelara® and biosimilars)

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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). Unlike for treatment of psoriasis and PsA, treatment for CD and UC requires a single, initial weight based IV loading dose.

As of May 2025, seven 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), and Steqeyma

(ustekinumab-stba) in December 2024 (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).

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. 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, most commonly presenting with peripheral arthritis, dactylitis, enthesitis, and spondylitis. Treatment involves the use of a variety of interventions, including many agents used for the treatment of other inflammatory arthritis, particularly spondyloarthritis and RA, and other management strategies of the cutaneous manifestations of psoriasis.

The American Academy of Dermatology (AAD) recommends initiating MTX in most patients with moderate to severe PsA. After 12 to 16 weeks of MTX therapy with appropriate dose escalation, the AAD recommends adding or switching to a TNF inhibitor if there is minimal improvement on MTX monotherapy.

The American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) guidelines for PsA recommend a treat-to-target approach in therapy, regardless of disease activity, and the following:

- Active PsA is defined as symptoms at an unacceptably bothersome level as reported by the patient and health care provider to be due to PsA based on the presence of one of the following:
    - Actively inflamed joints
    - Dactylitis
    - Enthesitis
    - Axial disease
    - Active skin and/or nail involvement
    - Extraarticular manifestations such as uveitis or inflammatory bowel disease
- Disease severity includes level of disease activity at a given time point and the presence/absence of poor prognostic factors and long-term damage
- Severe PsA disease includes the presence of 1 or more of the following:
    - Erosive disease
    - Elevated markers of inflammation (ESR, CRP) attributable to PsA

- Long-term damage that interferes with function (i.e., joint deformities)
- Highly active disease that causes a major impairment in quality of life
- Active PsA at many sites including dactylitis, enthesitis
- Function limiting PsA at a few sites
- Rapidly progressive disease

- Symptomatic treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, local glucocorticoid injections
- Treatment recommendations for active disease:
  - Treatment naïve patients first line options include oral small molecules (OSM), TNF biologics, IL-17 inhibitor, and IL-12/23 inhibitor
    - OSM (i.e., methotrexate [MTX], sulfasalazine, cyclosporine, leflunomide, apremilast) should be considered if the patient does not have severe PsA, does not have severe psoriasis, prefers oral therapy, has concern over starting a biologic, or has contraindications to TNF inhibitor
    - Biologics (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) are recommended as a first line option in patients with severe PsA and/or severe psoriasis
  - Previous treatment with OSM and continued active disease:
    - Switch to a different OSM (except apremilast) in patients without severe PsA or severe PS, contraindications to TNF biologics, prefers oral therapy OR add on apremilast to current OSM therapy
    - May add another OSM (except apremilast) to current OSM therapy for patients that have exhibited partial response to current OSM in patients without severe PsA or severe PS, contraindications to TNF biologics, or prefers oral therapy
    - Biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) monotherapy
  - Previous treatment with a biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) and continued active disease:
    - Switch to another biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor, abatacept, or tofacitinib) monotherapy or add MTX to the current TNF biologic

DERMATOLOGICAL DISORDERS

Psoriasis (PS)

Psoriasis (PS) is a chronic inflammatory skin condition that is often associated with systemic manifestations, especially arthritis. Diagnosis is usually clinical, based on the presence of typical erythematous scaly patches, papules, and plaques that are often pruritic and sometimes painful.

Treatment goals for psoriasis include improvement of skin, nail, and joint lesions plus enhanced quality of life.

The American Academy of Family Physicians (AAFP) categorizes psoriasis severity into mild to moderate (less than 5% of body surface area [BSA]) and moderate to severe (5% or more of BSA). The AAFP psoriasis treatment guidelines recommend basing treatment on disease severity:

- Mild to moderate (less than 5% of BSA and sparing the genitals, hands, feet, and face):
  - Candidate for intermittent therapy: topical corticosteroids, vitamin D analogs (calcipotriene and calcitriol), or tazarotene (Tazorac)
  - Candidate for continuous therapy: calcineurin inhibitors (tacrolimus and pimecrolimus)
- Severe (5% or more of BSA or involving the genitals, hands, feet, and face):
  - Less than 20% of BSA affected: vitamin D analogs (calcipotriene and calcitriol) with or without phototherapy. These agents have a slower onset of action but a longer disease-free interval than topical corticosteroids
  - 20% or more of BSA affected: systemic therapy with MTX, cyclosporine, acitretin, or biologics. Biologics are recommended for those with concomitant PsA
- Less commonly used topical therapies include non-medicated moisturizers, salicylic acid, coal tar, and anthralin

The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) categorize psoriasis severity as limited or 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 occurs in select locations (e.g., hands, feet, scalp, face, or genital area) or when it causes intractable pruritus. The AAD psoriasis treatment guidelines recommend the following:

- Mild to moderate disease (less than 5% of BSA):
  - Topical corticosteroids (strength of recommendation A)
  - Off-label use of 0.1% tacrolimus for psoriasis involving the face as well as inverse psoriasis (strength of recommendation B)
  - Long-term use (up to 52 weeks) of topical vitamin D analogs including calcipotriene, calcitriol, tacalcitol, and maxacalcitol (strength of recommendation A)
  - Use of calcipotriene foam and calcipotriene plus betamethasone dipropionate gel for the treatment of mild to moderate scalp psoriasis (strength of recommendation A)
  - Use of tacalcitol ointment or calcipotriene combined with hydrocortisone for facial psoriasis (strength of recommendation B)
  - Vitamin D analogs in combination with topical corticosteroids (strength of recommendation A)
  - Topical tazarotene alone or in combination with narrowband ultraviolet B (NB-UVB) (strength of recommendation B), or topical corticosteroids (strength of recommendation A)
  - Topical salicylic acid alone or in combination with topical corticosteroids (strength of recommendation B)
  - Coal tar preparations (strength of evidence A)
- Moderate to severe disease without PsA (5% or more of BSA or psoriasis in vulnerable areas [e.g., face, genitals, hands, and feet] that adversely affects quality of life):

- Methotrexate (adults) (strength of evidence A)
- Methotrexate is less effective than TNF-inhibitors (strength of evidence B)
- Combination therapy with methotrexate and NB-UVB (adult patients) (strength of evidence B)
- Cyclosporine for patients with severe, recalcitrant (strength of recommendation A), erythrodermic, generalized pustular, and/or palmoplantar psoriasis (strength of recommendation B)
- Acitretin as monotherapy or in combination with psoralen plus ultraviolet light (PUVA) or broad band ultraviolet light (BB-UVA [strength of evidence B])
- If UV-therapy is unavailable, first line therapies include MTX, cyclosporine, acitretin, and biologics
- Apremilast (strength of recommendation A)
- TNF-α inhibiters monotherapy (strength of evidence A) or in combination with topical corticosteroids with or without a vitamin D analogue (strength of evidence B) or in combination with acitretin (strength of evidence C)
- TNF-α inhibitors should be considered as a preferred treatment option for patients with concomitant PsA
- Infliximab (strength of evidence A)
- IL-12/IL-23 Inhibitors monotherapy (strength of evidence A) or in combination with topical corticosteroids with or without a vitamin D analogue (strength of evidence C) or in combination with acitretin or methotrexate (strength of evidence B)
- IL-12/IL-23 inhibitors in combination with apremilast or cyclosporine (strength of evidence C)
- IL-17 inhibitors monotherapy (strength of evidence A)
- IL-23 inhibitors monotherapy for moderate to severe plaque psoriasis or as monotherapy for generalized pustular psoriasis (strength of evidence B)

*Strength of recommendation and descriptions

Strength of recommendation	Description
A	Recommendation based on consistent and good-quality patient-oriented evidence
B	Recommendation based on inconsistent or limited-quantity patient-oriented evidence
C	Recommendation based on consensus, opinion, case studies, or disease-oriented evidence

Biologics are routinely used when one or more traditional systemic agents fail to produce adequate response, but are considered first line in patients with moderate to severe psoriasis with concomitant severe PsA. Primary failure is defined as initial nonresponse to treatment. Primary failure to a TNF-α inhibitor does not preclude successful response to a different TNF-α inhibitor. Failure of another biologic therapy does not preclude successful response to ustekinumab.

The National Psoriasis Foundation (NPF) medical board recommend a treat-to-target approach to therapy for psoriasis that include the following:

- The preferred assessment instrument for determining disease severity is BSA
- Target response after treatment initiation should be BSA ≤1% after 3 months
- Acceptable response is either a BSA ≤3% or a BSA improvement ≥75% from baseline at 3 months after treatment initiation

INFLAMMATORY BOWEL DISEASE

Crohn's Disease (CD)

Crohn's Disease (CD) is an inflammatory condition that can affect any portion of the gastrointestinal tract from the mouth to the perianal area. Choice of therapy is dependent on the anatomic location of disease, the severity of disease, and whether the treatment goal is to induce remission or maintain remission. The American Gastroenterological Association (AGA) 2021 guideline recommends the following:

- 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
    - Anti-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)
- DMARD therapy:
    - Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission
    - 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 2018 American College of Gastroenterology (ACG) guidelines recommend the following:

- Mild to moderately severe disease/low risk disease:
  - Sulfasalazine (in doses of 3-6 grams daily) is effective in colonic and/or ileocolonic CD, but not those with isolated small bowel disease
  - 5-aminosalicylic (ASA) suppositories and enema preparations are effective for induction and maintenance of remission in rectal and sigmoid disease
  - Conventional corticosteroids are primarily used for the treatment of flares, and are often used as a bridge until immunomodulators and/or biologic agents become effective
  - Controlled ileal release budesonide is effective for induction of remission in ileocecal disease
- Moderate to severe disease/moderate to high risk disease
  - Corticosteroids are effective for short-term use in alleviating signs and symptoms of moderate to severely active CD, but do not induce mucosal healing and should be used sparingly
  - Azathioprine, 6-mercaptopurine, or MTX (15 mg once weekly) may be used in treatment of active disease and as adjunctive therapy for reducing immunogenicity against biologic therapy
  - TNF inhibitors should be used to treat CD that is resistant to treatment with corticosteroids and that is refractory to thiopurines or MTX
  - Vedolizumab with or without an immunomodulator should be considered for induction of symptomatic remission for patients with moderate to severely active CD and objective evidence of active disease
  - Ustekinumab should be used in patients that have failed previous treatment with corticosteroids, thiopurines, MTX, or TNF inhibitors, or in patients with no prior TNF inhibitor exposure

- Severe/fulminant disease:
    - IV corticosteroids should be used
    - TNF inhibitors can be considered
- Maintenance therapy:
    - Thiopurines or methotrexate should be considered once remission is induced with corticosteroids
    - TNF inhibitors, specifically infliximab, adalimumab, and certolizumab pegol, should be used in combination with azathioprine, MTX, or 6-mercaptopurine to maintain remission of TNF induced remission
    - Vedolizumab should be used for maintenance of remission of vedolizumab induced remission
    - Ustekinumab should be used for maintenance of remission of ustekinumab induced remission

Ulcerative Colitis (UC)

Ulcerative colitis (UC) is a chronic immune-mediated inflammatory condition affecting the large intestine associated with inflammation of the rectum, but that can extend to involve additional areas of the colon. The American College of Gastroenterology (ACG) recommends a treat-to-target approach and recommend therapeutic management should be guided by diagnosis (i.e., Montreal classification), assessment of disease activity (i.e., mild, moderate, and severe), and disease prognosis. The ACG treatment recommendations are further broken down into induction therapies and maintenance of remission. The 2019 ACG treatment guidelines recommend the following for therapeutic management of UC:

<u>Induction of remission</u>:

- Mildly active disease:
    - Rectal 5-ASA at a dose of 1 g/day with or without oral 5-ASA at a dose of at least 2 g/day for left-sided UC
    - Rectal 5-ASA at a dose of 1 g/day for ulcerative proctitis
    - Oral 5-ASA at a dose of at least 2 g/day for extensive UC
    - Add oral budesonide multi-matrix (MMX) 9 mg/day for patients that are intolerant or non-responsive to oral and/or rectal and oral 5-ASA at appropriate doses
- Moderately active disease:
    - Oral budesonide multi-matrix (MMX) 9 mg/day for induction of remission
- Moderately to severely active disease:
    - Oral systemic corticosteroids, TNF inhibitors (i.e., adalimumab, golimumab, or infliximab), tofacitinib, or vedolizumab to induce remission
    - Combination of infliximab with thiopurine therapy when using infliximab for induction
    - Switch to tofacitinib or vedolizumab for induction in patients that have failed TNF inhibitors

- Patients with initial response to TNF inhibitors that lose response should have antibody levels and serum drug levels tested to assess reason for loss of response. If serum levels are adequate, use of another TNF inhibitor is not likely to be of benefit.

Maintenance of remission:

- Previously mildly active disease:
  - Rectal 5-ASA at a dose of 1 g/day in patients with ulcerative proctitis
  - Oral 5-ASA at a dose of at least 2 g/day in patients with left-sided or extensive UC
- Previously moderately to severely active disease:
  - Thiopurines in patients that achieved remission due to corticosteroid induction
  - Continue TNF inhibitors (i.e., adalimumab, golimumab, or infliximab) for remission due to TNF induction
  - Continue vedolizumab for remission due to vedolizumab induction
  - Continue tofacitinib for remission due to tofacitinib induction

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

- Use either standard-dose mesalamine (2-3 g/day) or diazo-bonded 5-ASA for patients with extensive UC for induction of remission and maintenance of remission
- May add rectal mesalamine to oral 5-ASA in patients with extensive or left-sided UC for induction of remission and maintenance of remission
- Use high dose mesalamine (>3 g/day) with rectal mesalamine in patients with suboptimal response to standard-dose mesalamine, diazo-bonded 5-ASA, or with moderate disease activity 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

The American Gastroenterology Association (AGA) published recommendations for the management of moderate to severe UC.

- Standard of care is to continue agents initiated for induction therapy as maintenance therapy, if they are effective (excluding corticosteroids and cyclosporine)
- Adult outpatients with moderate to severe UC:
  - Infliximab, adalimumab, golimumab, vedolizumab, tofacitinib or ustekinumab are strongly recommended over no treatment
  - Biologic naïve patients:
    - infliximab or vedolizumab are conditionally recommended over adalimumab for induction of remission
    - Recommend tofacitinib only be used in the setting of a clinical or registry study

- Previous exposure to infliximab, particularly those with primary non-response, ustekinumab or tofacitinib are conditionally recommended over vedolizumab or adalimumab for induction of remission
- Conditionally recommend against use of thiopurine monotherapy for induction, but may be used for maintenance of remission over no treatment

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 Selarsdi (ustekinumab-aekn), 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 (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (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

- 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of Crohn's disease 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

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

	OR 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with 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 Selarsdi (ustekinumab-aekn), 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 (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (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

- 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of Crohn's disease 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), Ustekinumab* (an unbranded version of Stelara), 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 (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (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

- 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of Crohn's disease 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

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** of the conventional agents used in the treatment of PsA **OR** c. The member has an FDA labeled contraindication to **ALL** of the 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], 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 indicates use of another biologic immunomodulator agent OR Otezla 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** of the following preferred ustekinumab products after at least a 6-month trial per agent:

	• Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** b. The member has tried and had an inadequate response to **TWO** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** c. The member has tried and had an inadequate response to **ONE** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** d. The member has an intolerance or hypersensitivity to **THREE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** e. The member has an FDA labeled contraindication to **ALL** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • 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, anthralin, calcipotriene, calcitriol, coal tar products, cyclosporine, methotrexate, pimecrolimus, PUVA [phototherapy], tacrolimus, tazarotene, topical corticosteroids) used in the treatment of PS after at least a 3-month duration of therapy **OR** 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], rapidly progressive) OR f. The member's medication history indicates use of another biologic immunomodulator agent **OR** Otezla 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** of the following preferred ustekinumab products after at least a 6-month trial per agent: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce)

	OR b. The member has tried and had an inadequate response to **TWO** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** c. The member has tried and had an inadequate response to **ONE** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** d. The member has an intolerance or hypersensitivity to **THREE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** e. The member has an FDA labeled contraindication to **ALL** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • 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** of the conventional agents used in the treatment of CD **OR** c. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of CD **OR** d. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** 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: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** b. The member has tried and had an inadequate response to **TWO** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab)

	• Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** c. The member has tried and had an inadequate response to **ONE** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** d. The member has an intolerance or hypersensitivity to **THREE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** e. The member has an FDA labeled contraindication to **ALL** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • 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** of the conventional agents used in the treatment of UC

	OR c. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of UC **OR** d. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** 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: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** b. The member has tried and had an inadequate response to **TWO** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **ONE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** c. The member has tried and had an inadequate response to **ONE** of the following preferred ustekinumab products after at least a 6-month duration of therapy per agent **AND** an intolerance or hypersensitivity to **TWO** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn)

	• Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** d. The member has an intolerance or hypersensitivity to **THREE** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • Stelara (ustekinumab) • Steqeyma (ustekinumab-stba) • Yesintek (ustekinumab-kfce) **OR** e. The member has an FDA labeled contraindication to **ALL** of the following preferred ustekinumab products that is not expected to occur with the requested non-preferred product: • Selarsdi (ustekinumab-aekn) • 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), Ustekinumab* (an unbranded version of Stelara), 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 (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

3. **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:

      - Selarsdi (ustekinumab-aekn)
      - Stelara (ustekinumab)
      - Steqeyma (ustekinumab-stba)
      - Yesintek (ustekinumab-kfce)

      OR

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

      - Selarsdi (ustekinumab-aekn)
      - Stelara (ustekinumab)
      - Steqeyma (ustekinumab-stba)
      - Yesintek (ustekinumab-kfce)

      OR

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

      - Selarsdi (ustekinumab-aekn)
      - Stelara (ustekinumab)
      - Steqeyma (ustekinumab-stba)
      - Yesintek (ustekinumab-kfce)

      OR

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

      - Selarsdi (ustekinumab-aekn)
      - Stelara (ustekinumab)
      - Steqeyma (ustekinumab-stba)
      - Yesintek (ustekinumab-kfce)

      OR

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

- Selarsdi (ustekinumab-aekn)
- Stelara (ustekinumab)
- Steqeyma (ustekinumab-stba)
- Yesintek (ustekinumab-kfce)

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

- 90 mg every 8 weeks (56 days), **AND** the member has a diagnosis of Crohn's disease 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) Selarsdi (ustekinumab-aekn), 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 (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (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** of the conventional agents used in the treatment of CD **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of CD **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

	4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with 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** of the conventional agents used in the treatment of UC **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of UC **OR** 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with	• ≤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

	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"): a. Systemic corticosteroid treatment b. An infliximab product **OR** vedolizumab (Entyvio) **AND**	• ≤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

	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), 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:
    - Selarsdi (ustekinumab-aekn)
    - 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 (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (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** of the conventional agents used in the treatment of CD **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of CD **OR** 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of CD **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with 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

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** of the conventional agents used in the treatment of UC **OR** 3. The member has an FDA labeled contraindication to **ALL** of the conventional agents used in the treatment of UC **OR** 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of UC **OR** 5. The member has severe disease and/or risk factors for disease complications for which initial treatment with 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 adult patients 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 and 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 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: 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)

- 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
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, 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, 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

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

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.
07/01/24	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.