# Pharmacy Management Drug Policy

**SUBJECT: Ustekinumab (Stelara [ustekinumab], Yesintek [ustekinumab-kfce], Steqeyma [ustekinumab-stba], Selarsdi [ustekinumab-aekn], Wezlana [ustekinumab-auub], ustekinumab-ttwe, Otulfi [ustekinumab-aauz], Pyzchiva [ustekinumab-ttwe], ustekinumab [Janssen Biotech])**
**POLICY NUMBER: PHARMACY-59**
**EFFECTIVE DATE: 09/25/2014**
**LAST REVIEW DATE: 05/08/2025**

*If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:*

**Policy Application**

| | | |
|---|---|---|
| **Category**: | ☒ Commercial Group (e.g., EPO, HMO, POS, PPO) | ☒ Medicare Advantage |
| | ☒ On Exchange Qualified Health Plans (QHP) | ☐ Medicare Part D |
| | ☒ Off Exchange Direct Pay | ☒ Essential Plan (EP) |
| | ☒ Medicaid & Health and Recovery Plans (MMC/HARP) | ☒ Child Health Plus (CHP) |
| | ☐ Federal Employee Program (FEP) | ☐ Ancillary Services |
| | ☒ Dual Eligible Special Needs Plan (D-SNP) | |

## DESCRIPTION:

Ustekinumab is a human monoclonal antibody that binds to and interferes with the proinflammatory cytokines, interleukin 12 (IL-12) and IL-23. Biological effects of IL-12 and IL-23 include natural killer cell activation and CD4+ T-cell differentiation and activation. Ustekinumab also interferes with the expression of monocyte chemotactic protein-1, tumor necrosis factor-alpha, interferon-inducible protein-10, and IL-8. Significant clinical improvement in psoriasis and psoriatic arthritis patients is seen in association with reduction of these proinflammatory signalers

**Ustekinumab** is indicated for:

- the treatment of patients 6 years or older with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy
- the treatment of patients 6 years or older with active psoriatic arthritis
- the treatment of adult patients with moderately to severely active Crohn's disease
- the treatment of adult patients with moderately to severely active ulcerative colitis

**Ustekinumab** can be administered by a healthcare professional or can be self-administered if individual has been trained by a health care professional.

- If administered by a healthcare professional, it goes under the medical benefit.
- If self-administered, it goes under the pharmacy (Rx) benefit.

## POLICY:

**Stelara (ustekinumab) is the preferred ustekinumab product for all lines of business under the medical benefit and for all Commercial (including Exchange and Essential Plan) and SafetyNet formularies on the pharmacy benefit.**

Based on comparable indications, efficacy, safety profile, and equivalent strengths of **Stelara**, the member will be required to use **Stelara** unless there is medical reason why **Stelara** cannot be used due to formulation differences in the inactive ingredient(s) (e.g., differences in stabilizing agent, buffering agent, and/or surfactant) which, according to the prescriber, would result in a significant allergy or serious adverse reaction (documentation required)

# Pharmacy Management Drug Policy
## Ustekinumab

### Ustekinumab Product Coverage by Benefit Type

| Ustekinumab Product | Pharmacy Benefit | Medical Benefit |
|---|---|---|
| **Stelara** | Preferred | Preferred |
| **Yesintek** | Non-Preferred | Non-Preferred |
| **Steqeyma** | Non-Preferred | Non-Preferred |
| **Selarsdi** | Non-Preferred | Non-Preferred |
| **Otulfi** | Non-Preferred | Non-Preferred |
| **Pyzchiva** | Non-Preferred | Non-Preferred |
| **ustekinumab (Janssen Biotech)** | Non-Preferred | Non-Preferred |
| **Wezlana (Optum-Nuvalia)** | Excluded | Non-Preferred |
| **ustekinumab-ttwe (Quallent)** | Excluded | Non-Preferred |

*Preferred and Non-Preferred drugs require a medical necessity review

Based upon our assessment and review of the peer-reviewed literature **ustekinumab** has been medically proven to be effective and therefore, **medically necessary** for the treatment of the following diagnoses if specific criteria are met:

### A. Plaque Psoriasis

1. Must be prescribed by or in consultation with a Dermatologist or Rheumatologist **AND**
2. Member must be at least 6 years of age **AND**
3. Member must have moderate to severe chronic plaque psoriasis that involves at least 10% of their body surface area. Consideration will be given to those who have less than 10% body surface area involvement but have severe disease of sensitive areas or areas causing significant disruption in normal activities (such as the hands, feet, face, genitalia) **AND**
4. The patient must be a candidate for systemic therapy or phototherapy and meet for **ONE** of the following (**a or b**)
   a. The patient must have had a 3-month trial of systemic therapy (i.e., acitretin, methotrexate, or cyclosporine) that resulted in an inadequate response (failure). A 3-month trial will not be required if the member experienced serious side effects during a trial of one of the aforementioned agents **OR**
   b. The patient must have had a 3-month trial of Ultraviolet B (UVB) Phototherapy or Psoralen Ultraviolet A (PUVA) Phototherapy that resulted in an inadequate response (failure)
5. Approved dosing is in chart **F** listed below on page 3.

### B. Psoriatic Arthritis

1. Must be prescribed by or in consultation with a Rheumatologist or Dermatologist **AND**
2. Member must be at least 6 years of age **AND**
3. Must have a diagnosis of active Psoriatic Arthritis
4. Approved dosing is in chart **G** listed on page 3.

### C. Crohn's Disease

1. Must be prescribed by or in consultation with a Gastroenterologist **AND**
2. The patient must have a diagnosis of moderately to severely active Crohn's Disease **AND**
3. Patient must be at least 18 years of age **AND**
4. There must be documentation that azathioprine, 6-mercaptopurine, or methotrexate is ineffective, contraindicated, or not tolerated
   a. Treatment with a biologic medication as first-line therapy will be assessed on a case-by-case basis through a letter of medical necessity and clinical progress notes based on severity of the disease

5. Approved dosing:
   a. Induction dosing - At week 0, a one-time weight-based IV loading dose (260 mg [55 kg or less], 390 mg [more than 55 kg to 85 kg], or 520 mg [more than 85 kg]) is given by a healthcare professional. This will be covered under the medical benefit.
   b. Maintenance dosing - starting at week 8, ustekinumab 90mg is given subcutaneously every 8 weeks. This can be self-injected under the Rx benefit or given subcutaneously by a healthcare professional under the medical benefit.
   c. Dose Escalation – Dose escalation coverage criteria can be found in section **H** on page 4.

**D. Ulcerative Colitis**

1. Must be prescribed by or in consultation with a Gastroenterologist **AND**
2. The patient must have a diagnosis of moderately to severely active Ulcerative Colitis **AND**
3. The patient must be at least 18 years of age **AND**
4. Must meet for ONE of the following (a or b):
   a. Must have tried and failed or has documented intolerance to at least ONE of the following conventional therapies for at least 3 months:
      i. Thiopurines: azathioprine/6-mercaptopurine (6-MP)
      ii. 5-Aminosalicylates: sulfasalazine, mesalamine, olsalazine
      iii. IV or oral steroids - note, a 3-month trial of systemic steroid therapy will not be required
   b. The patient has been diagnosed with pouchitis and has tried an antibiotic, corticosteroid enema, or mesalamine enema
5. Approved dosing:
   a. Induction dosing - At week 0, a one-time weight-based IV loading dose (260 mg [55 kg or less], 390 mg [more than 55 kg to 85 kg], or 520 mg [more than 85 kg]) is given by a healthcare professional. This will be covered under the medical benefit.
   b. Maintenance dosing - starting at week 8, ustekinumab 90mg is given subcutaneously every 8 weeks. This can be self-injected under the Rx benefit or given subcutaneously by a healthcare professional under the medical benefit.

**E. Quantity Limit:**

   a. 45mg SC syringe/vial: 0.5mL per 84 days
   b. 90mg SC syringe: 1mL per 84 days

**F. Dosing guidelines for Plaque Psoriasis (PP):**

| If patient weighs: | Initial and maintenance dose |
|---|---|
| **≤ 100kg** | 45mg at week 0 and 4, followed by 45mg every 12 weeks |
| **> 100kg** | 90mg at week 0 and 4, followed by 90mg every 12 weeks |

- **Pediatric dosing SC ( ≥ 6 years of age):**
  - **< 60kg:** 0.75mg/kg at weeks 0, 4, and every 12 weeks thereafter
  - **60kg to 100kg:** 45mg at weeks 0, 4, and every 12 weeks thereafter
  - **> 100kg:** 90mg at weeks 0, 4, and every 12 weeks thereafter

**G. Dosing guidelines for Psoriatic Arthritis (PsA):**

| If patient weighs: | Initial and maintenance dose |
|---|---|
| **Any weight** | 45mg at week 0 and 4, followed by 45mg every 12 weeks |
| **> 100kg and co-existent PP and PsA, regardless of TNF-history** | 90mg at week 0 and 4, followed by 90mg every 12 weeks |

***** If there is **no response** to initial dosing other than increasing from 45mg to 90mg at week 16 if patient weighs > 100kg, then the dose increase request will **NOT** be allowed.

- **Pediatric dosing SC ( ≥ 6 years of age):**
  - **< 60kg:** 0.75mg/kg at weeks 0, 4, and every 12 weeks thereafter
  - **60kg to 100kg:** 45mg at weeks 0, 4, and every 12 weeks thereafter
  - **> 100kg:** 90mg at weeks 0, 4, and every 12 weeks thereafter

**H. Crohn's Disease Dose Escalation Criteria**

**Coverage of ustekinumab at a dose of *up to* 90 mg every 4 weeks will require the following:**

1. Documentation must be submitted confirming that the patient has been treated with the standard maintenance dose of 90 mg every 8 weeks for at least 16 weeks (2 doses) **AND**
2. The patient must have lost response to an initial, adequate response OR the patient must have had a partial, inadequate response to standard maintenance therapy **AND**
3. Documentation must be submitted confirming that provider has ruled out other potential causes of symptoms (i.e., acute infection) **AND**
4. Documentation must be submitted showing severe disease despite use of standard maintenance therapy (imaging, colonoscopy, lab, endoscopy, etc.). Support for increasing the dosing interval may include one or more of the following:
   a. Elevated Harvey-Bradshaw Index (>7 points)
   b. Elevated C-reactive protein (> 5 mg/dL)
   c. Elevated fecal calprotectin (≥ 200 ug/dL)
   d. Endoscopy that reveals active disease (presence of ulcers)
   e. Imaging that reveals active disease (mucosal inflammation)
5. Initial approval will be for 4-months
   a. After initial approval, continued coverage of ustekinumab at a dose of up to 90 mg every 4 weeks will require documentation confirming the patient regained or obtained an adequate response to therapy (improvement in signs/symptoms of disease) **AND**
   b. The provider must attest that the patient is able to tolerate treatment with ustekinumab at the requested dose
6. Ongoing approval will be for 6-months
   a. After each 6-month approval, continued coverage of ustekinumab at a dose of **up to** 90 mg every 4 weeks will require documentation confirming the patient has maintained their response to therapy **AND**
   b. The provider must attest that the patient is able to tolerate treatment with ustekinumab at the requested dose
7. Requests for ustekinumab at a dose of 90 mg every 4 weeks for patients naïve to ustekinumab therapy will not be covered and will be considered experimental/investigational
8. Anti-drug antibody and/or therapeutic drug levels will not be accepted as rationale for dose intensification in the absence of objective evidence

9. Primary non-responders (defined those with no clinical response after the initial treatment period) will not be considered for coverage
10. Requests for treatment at a dose and/or frequency above 90 mg every 4 weeks will be considered experimental/investigational

## APPROVAL TIME PERIODS:

| Line of Business | Rx Initial approval | Rx Recertification | Medical Initial approval | Medical Recertification |
|---|---|---|---|---|
| **Commercial, Exchange, Safety Net** (Medicaid, HARP, CHP, EP) | 1 year<br><br>*Does not apply to Medicaid and HARP | 1 year<br><br>*Does not apply to Medicaid and HARP | All sites of service: 1 year | All sites of service: 1 year |
| **Medicare** | Already defined in policy | Already defined in policy | All sites of service: 2 years | All sites of service: 2 years |

## POLICY GUIDELINES:

1. Wezlana (ustekinumab-auub) products manufactured by Optum-Nuvalia and ustekinumab-ttwe manufactured by Quallent Pharma are excluded from coverage.
2. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
3. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
4. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
5. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
6. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
7. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference Non-Formulary Medication Exception Review Policy for all Lines of Business policy (Pharmacy-69)
8. If ustekinumab is being self-administered, it will be paid for under the pharmacy benefit. If ustekinumab is being given in the office or by a healthcare professional, it would then go under the medical benefit.
9. Requests for 45mg every 8 weeks will be denied as off label as there is no efficacy data for any weight.
10. While the FDA-approved dosing for persons weighing > 100kg with psoriasis is to start with 90mg dose, the 45mg dose was effective in clinical trials (PASI 75 response at week 12: 54% vs 68% in

45mg and 90mg, respectively). We will allow the dose increase to 90mg by week 16 if little to no improvement.

11. **Concurrent use of Inflammatory Agents**
    a. Ustekinumab as well as other immunomodulating therapies or Targeted Synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) (Enbrel, Cimzia, Remicade, biosimilars, etc.) should not be administered in combination with another biologic or targeted synthetic DMARD used for an inflammatory condition. Combination therapy is generally not recommended due to the added risk of immunosuppression, potential for a higher rate of adverse effects, and lack of evidence for additive therapy. NOTE: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with biologics and targeted synthetic DMARDs.
    b. Requests for the concurrent use of inflammatory agents will be evaluated for safety and efficacy and subject to off-label review.
    c. Otezla in combination with biologic DMARD therapy (such as adalimumab, Enbrel, Cosentyx, etc.) is not FDA approved or supported with a high level of clinically valid medical evidence for the treatment of plaque psoriasis or psoriatic arthritis. Therefore, these requests are considered combination therapy and are considered not medically necessary.
12. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
13. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.

**UPDATES:**

| Date: | Revision: |
|---|---|
| 05/08/2025 | Reviewed / P&T Committee Approval |
| 04/24/2025 | Revised |
| 04/07/2025 | Revised |
| 03/13/2025 | Revised |
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**REFERENCES:**

1. Stelara (Ustekinumab) [package insert]. Horsham, PA: Janssen Biotech. Revised September 2016 Accessed Online June 2017.
2. Andrulonis R, Ferris LK. Treatment of severe psoriasis with ustekinumab during pregnancy. *J Drugs Dermatol*. 2012;11(10):1240.
3. Papp KA, Langley RG, Lebwohl M, et al, "Efficacy and Safety of Ustekinumab, a Human Interleukin-12/23 Monoclonal Antibody, in Patients with Psoriasis: 52-Week Results from a Randomised, Double-Blind, Placebo-Controlled Trial (PHOENIX 2)," *Lancet*, 2008, 371(9625):1675-84.
4. Papp KA, Griffiths CE, Gordon K, et al, "Long-Term Safety of Ustekinumab in Patients with Moderate-to-Severe Psoriasis: Final Results from 5 Years of Follow-Up," *Br J Dermatol*, 2013, 168(4):844-54.
5. Leonardi CL, Kimball AB, Papp KA, et al, "Efficacy and Safety of Ustekinumab, a Human Interleukin-12/23 Monoclonal Antibody, in Patients With Psoriasis: 76-Week Results from a Randomised, Double-Blind, Placebo-Controlled Trial (PHOENIX 1)," *Lancet*, 2008, 371(9625):1665-74.
6. Galvan-Banqueri M, Marin Gil R, Santos Ramos, B, et al, "Biological Treatments for Moderate-to-Severe Psoriasis: Indirect Comparison," *J Clin Pharm Ther*, 2013, 38(2):121-30.
7. Sandborn WJ, Gasink C, Gao LL, et al. "Ustekinumab induction and maintenance therapy in refractory Crohn's disease." *N Engl J Med*. 2012 Oct;367(16):1519-28.
8. McInnes IB, Kavanaugh A, PSUMMIT 1 Study Group, et al. Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1-year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial." *Lancet*. 2013;382(9894):780.
9. Gottlieb A, Menter A, et al. "Ustekinumab, a human interleukin 12/23 monoclonal antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial." *Lancet*.2009;373(9664):633
10. Alice Gottlieb, Neil J. Korman, Kenneth B. Gordon, Steven R. Feldman, Mark Lebwohl, John Y.M. Koo, Abby S. Van Voorhees, Craig A. Elmets, Craig L. Leonardi, Karl R. Beutner, Reva Bhushan, Alan Menter Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: Overview and guidelines of care for treatment with an emphasis on the biologics *Journal of the American Academy of Dermatology*, *Volume 58, Issue 5*, *May 2008*, *Pages 851-864*
11. Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. *Archives of dermatology.* Jan 2012;148(1):95-102.
12. Ritchlin C, Rahman P, Kavanaugh A, et al: Efficacy and safety of the anti-IL-12/23 p40 monoclonal antibody, ustekinumab, in patients with active psoriatic arthritis despite conventional non-biological and biological anti-tumour necrosis factor therapy: 6-month and 1-year results of the phase 3, multicentre, double-blind, placebo-controlled, randomised PSUMMIT 2 trial. Ann Rheum Dis 2014;
13. Engel T, Kopylov U: Ustekinumab in Crohn's disease; evidence to date and place in therapy. *Ther Adv*

*Chronic Dis*. 2016 Jul; 7(4):208-214.
14. Harris K, Horst S, et al.: Patients with Refractory Crohn's Disease Successfully Treated with Ustekinumab. *Inflamm Bow Dis.* 02/2016 Volume 22, Issue 2.
15. Feagen BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2016;375:1946-1960.