Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope	
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA	☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B DRUG

Service Description

This document addresses the use of Stelara (ustekinumab) and its biosimilars Wezlana (Ustekinumab-auub), Imuldosa (Ustekinumab-srlf), Selarsdi (ustekinumab-aekn), and Pyzchiva (Ustekinumab-ttwe), a monoclonal antibody which binds to the p40 protein subunit used by both the interleukin-12 and interleukin-23 (IL-12/23) cytokines disrupting their interaction with receptors and thereby inhibiting the release of proinflammatory cytokines and chemokines. Stelara (ustekinumab) and its biosimilars Wezlana (Ustekinumab-auub), Imuldosa (Ustekinumab-srlf), Selarsdi (ustekinumab-aekn), and Pyzchiva (Ustekinumab-ttwe) are approved for the treatment of plaque psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis.

Background Information

Plaque Psoriasis (otherwise known as psoriasis vulgaris): The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) published joint guidelines on the management and treatment of psoriasis with biologics. The guidelines do not include a treatment algorithm or compare biologics to each other or conventional therapy. The guideline notes that patients with mild- moderate disease may be adequately controlled with topical therapy and/or phototherapy while moderate to severe disease may necessitate treatment with a biologic. Biologics approved for psoriasis were studied in a population with 10% or greater BSA involvement. Moderate to severe disease is defined as involvement in > 3% of body surface area (BSA) or involvement in sensitive areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia). Tumor necrosis factor inhibitor (TNFi) biologics, ustekinumab, IL17 inhibitors, and IL23 inhibitors are all recommended as monotherapy treatment options for adult patients with moderate to severe plaque psoriasis. Combination use of TNFi biologics (etanercept, infliximab, adalimumab) and ustekinumab with apremilast is poorly studied and the AAD has given this practice a grade C recommendation based on limited-quality evidence.

Psoriatic Arthritis: The American College of Rheumatology (ACR) guidelines recommend that initial treatment of patients with active severe PsA or concomitant psoriasis should include a TNFi biologic over an oral small molecule (OSM; including methotrexate, sulfasalazine, cyclosporine, leflunomide, and apremilast). For initial therapy, OSMs are preferred over IL-17 and ustekinumab; and may be considered over TNFi biologics in mild to moderate disease without comorbid conditions or in those who prefer oral

Policy Name	Policy Number	Scope	
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA	☒ MMM Multihealth

therapy.

Recommendations involving biologics over OSMs as first line therapy are conditional and based on low quality evidence. Evidence cited includes indirect comparisons of placebo-controlled trials, studies with open-label design, and extrapolation from studies in plaque psoriasis. Furthermore, most pivotal trials for TNFi biologics included a study population that were DMARD experienced. Overall, there is a lack of definitive evidence for the safety and efficacy of biologic drugs over conventional therapy for the initial treatment of most patients with psoriatic arthritis. The ACR guidelines also include recommendations for patients whose disease remains active despite treatment with an OSM. Here, TNFi biologics are recommended over other therapies including IL-17 inhibitors, ustekinumab, tofacitinib, and abatacept. When TNFi biologics are not used, IL-17 inhibitors are preferred over ustekinumab; both of which are preferred over tofacitinib and abatacept. For disease that remains active despite TNFi monotherapy, switching to a different TNFi is recommended over other therapies.

Crohn's Disease: According to the American Gastrointestinal Association clinical practice guidelines, evidence supports the use of methotrexate, corticosteroids, TNFi +/- immunomodulator, ustekinumab, or vedolizumab for induction of remission. Among the biologics, infliximab, adalimumab, ustekinumab, or vedolizumab are recommended or suggested over certolizumab for induction of remission. Evidence supports biologic agents, thiopurines, and methotrexate for maintenance of remission. Ustekinumab and vedolizumab are options for individuals with primary nonresponse to initial treatment with TNFi. Adalimumab, ustekinumab, or vedolizumab may be used in cases where an individual previously responded to infliximab and then lost response (secondary nonresponse).

Ulcerative Colitis: The American Gastroenterological Association (AGA) guidelines define moderate to severe UC as those who are dependent on or refractory to corticosteroids, have severe endoscopic disease activity, or are at high risk of colectomy. AGA strongly recommends biologics (TNFi, vedolizumab, or ustekinumab) or tofacitinib over no treatment in induction and maintenance of remission (moderate quality of evidence). For biologic-naïve individuals, Infliximab or vedolizumab are conditionally recommended over adalimumab for induction of remission (moderate quality evidence).

Immune-checkpoint Inhibitor Therapy-Related Toxicity: The National Comprehensive Cancer Network (NCCN) guidelines on Management of Immunotherapy-Related Toxicities provide a 2A recommendation for the use of ustekinumab in mild persistent diarrhea or colitis for positive lactoferrin/calprotectin and for moderate or severe diarrhea or colitis that is refractory to infliximab and/or vedolizumab. There is no high-quality data provided to support this use.

Approved Indications

A. Plaque psoriasis
B. Psoriatic arthritis,
C. Crohn's disease
D. Ulcerative colitis

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope	
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA	☒ MMM Multihealth

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	
J3358	Ustekinumab, for intravenous injection, 1 mg [Stelara IV]
Q5137	Injection, ustekinumab-auub (wezlana), biosimilar, subcutaneous, 1 mg
Q5138	Injection, ustekinumab-auub (wezlana), biosimilar, intravenous, 1 mg
J3590	Unclassified biologics, when specified as ustekinumab-ttwe (Pyzchiva), ustekinumab-srlf (Imuldosa), ustekinumab-aekn (Selarsdi)
ICD-10 Diagnosis	
K50.00-K50.919	Crohn's disease [regional enteritis]
K51.00-K51.919	Ulcerative colitis
L40.0	Psoriasis vulgaris
L40.1	Generalized pustular psoriasis
L40.2	Acrodermatitis continua
L40.3	Pustulosis palmaris et plantaris
L40.4	Guttate psoriasis
L40.50-L40.59	Arthropathic psoriasis
L40.8	Other psoriasis
L40.9	Psoriasis, unspecified

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Stelara (ustekinumab), Wezlana (Ustekinumab-auub), Imuldosa (Ustekinumab-srlf), Selarsdi (ustekinumab-aekn), and Pyzchiva (Ustekinumab-ttwe), may be approved for the following:

A. **Prescriber Specialties**
   i. Rheumatology
   ii. Gastroenterology
   iii. Dermatology

B. **Criteria For Initial Approval**

Initial requests for Stelara (ustekinumab), Wezlana (Ustekinumab-auub), Imuldosa (Ustekinumab-srlf), Selarsdi (ustekinumab-aekn), and Pyzchiva (Ustekinumab-ttwe), may be approved for the following:

I. Crohn's disease (CD) when the following criteria are met:
   A. For individuals requesting intravenous induction dose:
      1. Individual is 18 years of age or older with moderate to severe CD; **AND**
      2. Individual has had an inadequate response to or is intolerant of conventional therapy (such as systemic corticosteroids or immunosuppressants [such as thiopurines or methotrexate]); **OR**
      3. Individual has a contraindication to systemic corticosteroids or thiopurines or methotrexate;

   OR

   B. For individuals requesting subcutaneous maintenance therapy;
      1. Individual is 18 years of age or older with moderate to severe CD; **AND**
      2. Individual has completed the IV induction dose with ustekinumab and will be using SubQ ustekinumab for maintenance therapy;

OR

II. Psoriatic arthritis (PsA) when the following criteria are met:
   A. Individual is 6 years of age or older with moderate to severe PsA; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [nonbiologic DMARDs (such as methotrexate, sulfasalazine, cyclosporine or leflunomide)];

OR

III. Plaque psoriasis (Ps) when the following criteria are met:
   A. Individual is 6 years of age or older with chronic moderate to severe (that is, extensive or disabling) plaque Ps with either of the following (AAD 2019):
      1. Plaque Ps involving greater than three percent (3%) body surface area (BSA); **OR**
      2. Plaque Ps involving less than or equal to three percent (3%) BSA involving

Policy Name	Policy Number	Scope	
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA	☒ MMM Multihealth

sensitive areas or areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia); **AND**

B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to phototherapy or other systemic therapy (such as acitretin, or [nonbiologic DMARDs (such as methotrexate, sulfasalazine, cyclosporine or leflunomide)];

OR

IV. Ulcerative colitis (UC) when the following criteria are met:

A. For individuals requesting intravenous induction dose:

1. Individual is 18 years of age or older with moderate to severe UC; **AND**

2. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as 5-Aminosalicylic acid products, systemic corticosteroids, or immunosuppressants [such as thiopurines]).

OR

B. For individuals requesting subcutaneous maintenance therapy:

1.Individual is 18 years of age or older with moderate to severe UC; **AND**

2. Individual has completed the intravenous induction dose with ustekinumab and will be using subcutaneous ustekinumab for maintenance therapy;

OR

V. Immunotherapy-related toxicities when each of the following criteria are met (NCCN 2A):

A. Individual is undergoing immune checkpoint inhibitor therapy for a cancer diagnosis; **AND**

B. Individual is experiencing moderate to severe diarrhea or colitis as a result of immune checkpoint inhibitor treatment; **AND**

C. Symptoms persist despite treatment with steroids and biologics (infliximab and/or vedolizumab).

C. **Authorization Duration**

i. Initial Approval Duration: 1 year

ii. Reauthorization Approval Duration: 1 year

D. **Criteria For Continuation of Therapy**

i. Continuation requests for Stelara (ustekinumab) may be approved if the following criterion is met:

a. Individual has been receiving and is maintained on a stable dose of Stelara/Selarsdi/Wezlana; **AND**

b. There is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Policy Name	Policy Number	Scope	
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA	☒ MMM Multihealth

E. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Stelara (ustekinumab) may not be approved for the following:

- In combination with phototherapy; **OR**
- In combination with oral or topical JAK inhibitors, apremilast, ozanimod , etrasimod, deucravacitinib, or any of the following biologic immunomodulators: Other TNF antagonists, IL-23 inhibitors, IL-17 inhibitors, IL-6 inhibitors, IL-1 inhibitors, vedolizumab, abatacept, rituximab, or natalizumab; **OR**
- History of posterior reversible encephalopathy syndrome; **OR**
- Tuberculosis, other active serious infections, or a history of recurrent infections [repeat TB testing not required for ongoing therapy];, other active serious infections, or a history of recurrent infections; **OR**
- If initiating therapy, individual has not had a tuberculin skin test (TST) or a Centers for Disease Control (CDC-) and Prevention-recommended equivalent to evaluate for latent tuberculosis (unless switching therapy from another targeted immune modulator and no new risk factors); **OR**
- When the above criteria are not met and for all other indications.

Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Limit
Stelara 130 mg/26 mL (5 mg/mL) vial	Body weight 55 kg or less: 2 vials (8 week supply, one time fill) Body weight more than 55kg to 85 kg: 3 vials (8 week supply, one time fill) Body weight more than 85 kg [max limit]: 4 vials (8 week supply, one time fill) Body weight 55 kg or less: 2 vials (8 week supply, one time fill) Body weight more than 55kg to 85 kg: 3 vials (8 week supply, one time fill) Body weight more than 85 kg [max limit]: 4 vials (8 week supply, one time fill)
Stelara 45 mg/0.5 mL vial	1 vial per 84 days (12 weeks)
Stelara 45 mg/0.5 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Stelara 90 mg/1 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Selarsdi 45 mg/0.5 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Selarsdi 90 mg/1 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Wezlana 130 mg/26 mL (5 mg/mL) vial	Body weight 55 kg or less: 2 vials (8 week supply, one time fill) Wezlana 130 mg/26 mL (5 mg/mL) vial Body weight more than 55kg to 85 kg: 3 vials (8 week supply, one time fill) Body weight more than 85 kg [max limit]: 4 vials (8 week supply, one time fill)
Wezlana 45 mg/0.5 mL vial	1 vial per 84 days (12 weeks)
Wezlana 45 mg/0.5 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Wezlana 90 mg/1 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Pyzchiva 45 mg/0.5 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Pyzchiva 90 mg/1 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)

Policy Name	Policy Number	Scope
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA ☒ MMM Multihealth

Pyzchiva 130 mg/26 mL (5 mg/mL) vial	Body weight 55 kg or less: 2 vials (8 week supply, one time fill) Pyzchiva 130 mg/26 mL (5 mg/mL) vial Body weight more than 55kg to 85 kg: 3 vials (8 week supply, one time fill) Body weight more than 85 kg [max limit]: 4 vials (8 week supply, one time fill)
Imuldosa 45 mg/0.5 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Imuldosa 90 mg/1 mL single-use prefilled syringe	1 syringe per 84 days (12 weeks)
Imuldosa 130 mg/26 mL (5 mg/mL) vial	Body weight 55 kg or less: 2 vials (8 week supply, one time fill) Imuldosa 130 mg/26 mL (5 mg/mL) vial Body weight more than 55kg to 85 kg: 3 vials (8 week supply, one time fill) Body weight more than 85 kg [max limit]: 4 vials (8 week supply, one time fill)

Policy Name	Policy Number	Scope	
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA	☒ MMM Multihealth

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 27, 2022.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
5. Menter A, Korman NJ, Elmets CA et al for the American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. *J Am Acad Dermatol*. 2011; 65: 137-174.
6. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019; 80: 1029-72.
7. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheum. 2019; 71(1): 5-32.
8. Feuerstein JD, Issacs KL, Schneider Y, et al. American Gastroenterological Association Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology 2020; 158:1450-1461.
9. Feuerstein JD, Ho EY, Shmidt E et al. American Gastroenterological Association Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology 2021; 160:2496-2508.
10. Rubin DT, Ananthakrishnan AN, Siegel CA et al. American College of Gastroenterology Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol 2019; 114:384-413.
11. Centers for Disease Control and Prevention (CDC). Tuberculosis (TB). Available at: https://www.cdc.gov/tb/topic/basics/risk.htm. Last updated: March 18, 2016. Accessed September 29, 2022.

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Ustekinumab agents (Stelara, Selarsdi, Wezlana, Pyzchiva, Imuldosa)	MP-RX-FP-85-23	☒ MMM MA ☒ MMM Multihealth

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review	Add new interchangeable biosimilars Wezlana, Selarsdi, Pyzchiva, Imuldosa to clinical criteria and quantity limits; add immunotherapy-related toxicities indication per NCCN; add etrasimod to combination use exclusion for consistency; update contraindication to prior therapy language for clarity; update Crohn's disease and Ulcerative colitis criteria to separate criteria for IV induction dose or subcutaneous therapy; clarify repeat TB testing requirements; add continuation of use language; wording and formatting updates. Add new biosimilar Selarsdi to clinical criteria, and quantity limits. Coding Reviewed: Added HCPCS Q5137, Q5138, J3357.	11/18/2024	12/17/2024
Select Review	Remove Stelara subcutaneous HCPCS Code J3357.	N/A	N/A
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Revised: 11/7/2024