Clinical Policy: Ustekinumab (Stelara), Ustekinumab-aauz (Otulfi), Ustekinumab-ttwe (Pyzchiva), Ustekinumab-aekn (Selarsdi), Ustekinumab-auub (Wezlana)

Reference Number: CP.PHAR.264
Effective Date: 08.16
Last Review Date: 11.24
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ustekinumab (Stelara®), ustekinumab-aauz (Otulfi®), ustekinumab-ttwe (Pyzchiva®), ustekinumab-aekn (Selarsdi™), and ustekinumab-auub (Wezlana™) are human interleukin-12 (IL-12) and -23 (IL-23) antagonists.

FDA Approved Indication(s)

Stelara, Otulfi, Pyzchiva, Selarsdi, and Wezlana are indicated for the treatment of:

- Patients 6 years and older with moderate-to-severe plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy
- Patients 6 years and older with active psoriatic arthritis (PsA)

Stelara, Otulfi, Pyzchiva, and Wezlana are also indicated for the treatment of:

- Adult patients with moderately to severely active Crohn's disease (CD)
- Adult patients with moderately to severely active ulcerative colitis (UC)

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Stelara, Otulfi, Pyzchiva, Selarsdi, and Wezlana are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Crohn's Disease (must meet all)**:**

1. Diagnosis of CD;
2. Request is for Stelara, Otulfi, Pyzchiva, or Wezlana;
3. Prescribed by or in consultation with a gastroenterologist;
4. Age ≥ 18 years;
5. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], MTX) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
   b. Medical justification supports inability to use immunomodulators (*see Appendix E*);

6. Member meets ONE of the following, unless contraindicated or clinically significant adverse effects are experienced (a or b, *see Appendix D*):
   a. Failure of a ≥ 3 consecutive month trial of one* adalimumab product (e.g., *Hadlima™, Simlandi®, Yusimry™, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
   b. History of failure of two TNF blockers;

   **Prior authorization may be required for adalimumab products*
7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V (i and ii):
      i. Initial dose (IV):
         1) Weight ≤ 55 kg: 260 mg once;
         2) Weight > 55 kg to 85 kg: 390 mg once;
         3) Weight > 85 kg: 520 mg once;
      ii. Maintenance dose (SC): 90 mg 8 weeks after the initial IV dose, followed by maintenance dose of 90 mg every 8 weeks;
   b. If request is for a dose that exceeds 90 mg every 8 weeks, all of the following (i, ii, and iii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. Member meets ONE of the following, unless contraindicated or clinically significant adverse effects are experienced (1 or 2, *see Appendix D*):
         1) Failure of infliximab (*Avsola™, Inflectra®, and Renflexis® are preferred*), used for ≥ 3 consecutive months;
         2) History of failure of two TNF blockers;
      iii. Dose does not exceed 90 mg every 4 or 6 weeks.

Approval duration: 6 months

B. Plaque Psoriasis (must meet all)**:**
1. Diagnosis of moderate-to-severe PsO as evidenced by involvement of one of the following (a or b):
   a. ≥ 3% of total body surface area;
   b. Hands, feet, scalp, face, or genital area;
2. For Stelara, Otulfi, Pyzchiva, and Wezlana: Request is for SC formulation;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Age ≥ 6 years;
5. Member meets one of the following (a, b, or c):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;

c. Member has intolerance or contraindication to MTX, cyclosporine, and acitretin, and failure of phototherapy, unless contraindicated or clinically significant adverse effects are experienced;

6. If member is ≥ 18 years, ONE of the following, unless contraindicated or clinically significant adverse effects are experienced (a or b, *see Appendix D*):
   a. Failure of a ≥ 3 consecutive month trial of one* adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
   b. History of failure of two TNF blockers;
   **Prior authorization may be required for adalimumab products*
7. Failure of a ≥ 3 consecutive month trial of Taltz®*, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Taltz*
8. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
9. Request meets one of the following (a or b):
   a. Dose does not exceed one of the following (*see Appendix G for dose rounding guidelines*) (i or ii):
      i. Adult: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (1 or 2):
         1) Weight ≤ 100 kg: 45 mg per dose;
         2) Weight > 100 kg: 90 mg per dose;
      ii. Pediatric: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (1, 2, or 3):
         1) Stelara and Wezlana only: Weight < 60 kg: 0.75 mg/kg per dose;
         2) Weight 60 kg to 100 kg: 45 mg per dose;
         3) Weight > 100 kg: 90 mg per dose;
   b. If request is for a dose that exceeds 90 mg every 12 weeks, all of the following (i, ii, and iii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. Member is ≥ 18 years and meets ONE of the following, unless contraindicated or clinically significant adverse effects are experienced (1 or 2):
         1) One of the following (a, b, or c, *see Appendix D*):
            a) Failure of BOTH of the following, each used for ≥ 3 consecutive months (i and ii):
               i) One adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
               ii) Infliximab (*Avsola™, Inflectra®, and Renflexis® are preferred*);
            b) If member has had a history of failure of one TNF blocker, then failure of one of the following TNF blockers used for for ≥ 3 consecutive months: one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*) or infliximab (*Avsola, Inflectra, and Renflexis are preferred*);

c) History of failure of two TNF blockers;
2) Failure of Otezla®, used for ≥ 3 consecutive months;
iii. Dose does not exceed 90 mg every 8 weeks.

Approval duration: 6 months

C. Psoriatic Arthritis (must meet all)**:**
1. Diagnosis of PsA;
2. For Stelara, Otulfi, Pyzchiva, and Wezlana: Request is for SC formulation;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Age ≥ 6 years;
5. If member is ≥ 18 years, failure of ALL* of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, c, and d, *see Appendix D*):
   a. Failure of one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
   b. Otezla;
   c. Taltz;
   d. If member has not responded or is intolerant to one or more TNF blockers, Xeljanz®/Xeljanz XR®, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

   **Prior authorization may be required for adalimumab products, Otezla, Taltz, and Xeljanz/Xeljanz XR*
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Request meets one of the following (a or b):
   a. Dose does not exceed one of the following (i or ii):
      i. Adult: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (1 or 2):
         1) 45 mg per dose;
         2) Co-existent PsO and weight > 100 kg: 90 mg per dose;
      ii. Pediatric: weight-based dosing initially and 4 weeks later, followed by maintenance dose every 12 weeks (1, 2, or 3):
         1) Stelara and Wezlana only: Weight < 60 kg: 0.75 mg/kg per dose;
         2) Weight ≥ 60 kg: 45 mg per dose;
         3) Co-existent PsO and weight > 100 kg: 90 mg per dose;
   b. If request is for a dose that exceeds 45 mg every 12 weeks, all of the following (i, ii, and iii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. Member is ≥ 18 years and meets one of the following, unless contraindicated or clinically significant adverse effects are experienced (1 or 2, *see Appendix D*):
         1) Failure of infliximab (*Avsola, Inflectra, and Renflexis are preferred*), used for ≥ 3 consecutive months;
         2) History of failure of two TNF blockers;

iii. Dose does not exceed 90 mg every 12 weeks.

Approval duration: 6 months

D. Ulcerative Colitis (must meet all)**:**

1. Diagnosis of UC;
2. Request is for Stelara, Otulfi, Pyzchiva, or Wezlana;
3. Prescribed by or in consultation with a gastroenterologist;
4. Age ≥ 18 years;
5. Documentation of a Mayo Score ≥ 6 (*see Appendix F*);
6. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
7. Member meets both* of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a and b, *see Appendix D*):
   a. Failure of one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), unless the member has had history of failure of two TNF blockers;
   b. If member has had a history of failure of two TNF blockers, then failure of Zeposia®;

   **Prior authorization may be required for adalimumab products and Zeposia*
8. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
9. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V:
      i. Initial dose (IV):
         1) Weight ≤ 55 kg: 260 mg once;
         2) Weight > 55 kg to 85 kg: 390 mg once;
         3) Weight > 85 kg: 520 mg once;
      ii. Maintenance dose (SC): 90 mg 8 weeks after the initial IV dose, followed by maintenance dose of 90 mg every 8 weeks;
   b. If request is for a dose that exceeds 90 mg every 8 weeks, all of the following (i, ii, and iii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. Failure of a trial of ≥ 3 consecutive months of BOTH of the following, unless contraindicated or clinically significant adverse effects are experienced (1 and 2, *see Appendix D*):
         1) Infliximab (*Avsola, Inflectra, and Renflexis are preferred*), unless the member has had a history of failure of two TNF blockers;
         2) If member has not responded or is intolerant to one or more TNF blockers, Xeljanz/Xeljanz XR, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;
      iii. Dose does not exceed 90 mg every 4 or 6 weeks.

Approval duration: 6 months

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. For Stelara, Otulfi, Pyzchiva, and Wezlana: Request is for SC formulation;
4. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
5. Member meets one of the following (a or b):
   a. If request is for a dose increase, new dose does not exceed one of the following (i, ii, or iii):
      i. PsO alone (*see Appendix G for dose rounding guidelines*) (1 or 2):
         1) Adults (a or b):
            a) Weight ≤ 100 kg: 45 mg every 12 weeks;
            b) Weight > 100 kg: 90 mg every 12 weeks;
         2) Pediatrics (a, b, or c):
            a) Stelara and Wezlana only: Weight < 60 kg: 0.75 mg/kg every 12 weeks;
            b) Weight 60 kg to 100 kg: 45 mg every 12 weeks;
            c) Weight > 100 kg: 90 mg every 12 weeks;
      ii. PsA (1 or 2):
         1) Adults (a or b):
            a) 45 mg every 12 weeks;
            b) Co-existent PsO and weight > 100 kg: 90 mg every 12 weeks;

2) Pediatrics (a, b, or c):
   a) Stelara and Wezlana only: Weight < 60 kg: 0.75 mg/kg every 12 weeks;
   b) Weight ≥ 60 kg: 45 mg every 12 weeks;
   c) Co-existent PsO and weight > 100 kg: 90 mg every 12 weeks;

iii. CD, UC: 90 mg every 8 weeks;

b. If request is for a dose increase and new maintenance dose exceeds the maximum dose and frequency indicated in Section V, all of the following (i, ii, and iii):
   i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
   ii. One of the following (1, 2, 3 or 4):
      1) CD: Member meets one of the following, unless contraindicated or clinically significant adverse effects are experienced (a, b, or c, *see Appendix D*):
         a) Failure of both of the following, each used for ≥ 3 consecutive months (i and ii):
            i) One adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
            ii) Infliximab (*Avsola, Inflectra and Renflexis are preferred*);
         b) If member has had a history of failure of one TNF blocker, then failure of one of the following TNF blockers used for ≥ 3 consecutive months: one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*) or infliximab (*Avsola, Inflectra and Renflexis are preferred*);
         c) History of failure of two TNF blockers;
      2) UC: Member meets BOTH of the following, unless clinically significant adverse effects are experienced or both are contraindicated (a and b):
         a) One of the following (i, ii, or iii, *see Appendix D*):
            i) Failure of both of the following, each used for ≥ 3 consecutive months (1 and 2):
               1. One adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
               2. Infliximab (*Avsola, Inflectra and Renflexis are preferred*);
            ii) If member has had a history of failure of one TNF blocker, then failure of one of the following TNF blockers used for ≥ 3 consecutive months: one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*) or infliximab (*Avsola, Inflectra and Renflexis are preferred*);
            iii) History of failure of two TNF blockers;
         b) Failure of both of the following, each used for ≥ 3 consecutive months (i and ii):
            i) Zeposia;

ii) If member has not responded or is intolerant to one or more TNF blockers, Xeljanz/Xeljanz, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

3) For PsO: Member is ≥ 18 years and meets ONE of the following, unless clinically significant adverse effects are experienced or both are contraindicated (a or b):
   a) One of the following (i, ii, or iii, *see Appendix D*):
      i) Failure of both of the following, each used for ≥ 3 consecutive months (1 and 2):
         1. ONE adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
         2. Infliximab (*Avsola, Inflectra and Renflexis are preferred)*;
      ii) If member has had a history of failure of one TNF blocker, then failure of one of the following TNF blockers used for ≥ 3 consecutive months: one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*) or infliximab (*Avsola, Inflectra and Renflexis are preferred);*
      iii) History of failure of two TNF blockers;
   b) Failure of both of the following, each used for ≥ 3 consecutive months: Taltz and Otezla;
4) For PsA: Member is ≥ 18 years and meets BOTH of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a and b):
   a) One of the following (i, ii, or iii, *see Appendix D*):
      i) Failure of both of the following, each used for ≥ 3 consecutive months (1 and 2):
         1. One adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*);
         2. Infliximab (*Avsola, Inflectra and Renflexis are preferred*);
      ii) If member has had a history of failure of one TNF blocker, then failure of one of the following TNF blockers used for ≥ 3 consecutive months: one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*) or infliximab (*Avsola, Inflectra and Renflexis are preferred*);
      iii) History of failure of two TNF blockers;
   b) Failure of ALL of the following, each used for ≥ 3 consecutive months (i, ii, and iii):
      i) Otezla;
      ii) Taltz;
      iii) If member has not responded or is intolerant to one or more TNF blockers, Xeljanz/Xeljanz XR unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

iii. New dose does not exceed one of the following (1, 2, or 3):
1) CD, UC: 90 mg every 4 or 6 weeks;
2) PsO: 90 mg every 8 weeks;
3) PsA: 90 mg every 12 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Combination use with biological disease-modifying antirheumatic drugs (bDMARDs) or potent immunosuppressants, including but not limited to any tumor necrosis factor (TNF) antagonists [e.g., Cimzia®, Enbrel®, Humira® and its biosimilars, Remicade® and its biosimilars (Avsola™, Inflectra™, Renflexis™, Zymfentra®), Simponi®], interleukin agents [e.g., Actemra® (IL-6RA), Arcalyst® (IL-1 blocker), Bimzelx® (IL-17A and F antagonist), Cosentyx® (IL-17A inhibitor), Ilaris® (IL-1 blocker), Ilumya™ (IL-23 inhibitor), Kevzara® (IL-6RA), Kineret® (IL-1RA), Omvoh™ (IL-23 antagonist), Siliq™ (IL-17RA), Skyrizi™ (IL-23 inhibitor), Stelara® (IL-12/23 inhibitor), Taltz® (IL-17A inhibitor), Tofidence™ (IL-6), Tremfya® (IL-23 inhibitor), Wezlana™ (IL-12/23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Cibinqo™, Olumiant™, Rinvoq™, Xeljanz®/Xeljanz® XR,], anti-CD20 monoclonal antibodies [Rituxan® and its biosimilars (Riabni™, Ruxience™, Truxima®), Rituxan Hycela®], selective co-stimulation modulators [Orencia®], integrin receptor antagonists [Entyvio®], tyrosine kinase 2 inhibitors [Sotyktu™], and sphingosine 1-phosphate receptor modulator [Velsipity™] because of the additive immunosuppression, increased risk of neutropenia, as well as increased risk of serious infections.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6-MP: 6-mercaptopurine
CD: Crohn's disease
FDA: Food and Drug Administration
GI: gastrointestinal

IL-12: interleukin-12
IL-23: interleukin-23
JAKi: Janus kinase inhibitors
MTX: methotrexate
PsO: plaque psoriasis
PsA: psoriatic arthritis
TNF: tumor necrosis factor
UC: ulcerative colitis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO daily	50 mg/day
azathioprine (Azasan®, Imuran)	**CD** 1.5 – 2.5 mg/kg/day PO	2.5 mg/kg/day
corticosteroids	**CD*** prednisone 40 mg – 60 mg PO QD for 1 to 2 weeks, then taper daily dose by 5 mg weekly until 20 mg PO QD, and then continue with 2.5 – 5 mg decrements weekly or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC®) 6 – 9 mg PO QD **UC** *Adult:* Prednisone 40 mg – 60 mg PO QD, then taper dose by 5 to 10 mg/week Budesonide (Uceris®) 9 mg PO QAM for up to 8 weeks	Various
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
6-mercaptopurine (Purixan®)	**CD** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate (Trexall®, Otrexup™, Rasuvo®, RediTrex®, Rheumatrex®, Jylamvo®)	**CD*** 15 – 25 mg/week IM or SC **PsO** 10 to 25 mg/week IM, SC or PO or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day
Hadlima (adalimumab-bwwd), Simlandi (adalimumab-ryvk), Yusimry (adalimumab-aqvh), adalimumab-aaty (Yuflyma®), adalimumab-adaz (Hyrimoz®), adalimumab-fkjp (Hulio®), adalimumab-adbm (Cyltezo®)	**CD, UC** Initial dose: 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: 40 mg SC every other week starting on Day 29 **PsA** 40 mg SC every other week **PsO** Initial dose: 80 mg SC Maintenance dose: 40 mg SC every other week starting one week after initial dose	40 mg every other week
Otezla® (apremilast)	**PsA** Initial dose: Day 1: 10 mg PO QAM Day 2: 10 mg PO QAM and 10 mg PO QPM Day 3: 10 mg PO QAM and 20 mg PO QPM Day 4: 20 mg PO QAM and 20 mg PO QPM Day 5: 20 mg PO QAM and 30 mg PO QPM Maintenance dose: Day 6 and thereafter: 30 mg PO BID	60 mg/day
Taltz® (ixekizumab)	**PsA** Initial dose: 160 mg (two 80 mg injections) SC at week 0 Maintenance dose: 80 mg SC every 4 weeks	80 mg every 4 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	PsO Initial dose: 160 mg (two 80 mg injections) SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, and 12 Maintenance dose: 80 mg SC every 4 weeks	
Xeljanz® (tofacitinib)	**PsA** 5 mg PO BID **UC** Induction: 10 mg PO BID for 8 weeks, up to 16 weeks Maintenance: 5 mg PO BID	Maintenance: 10 mg/day
Xeljanz XR® (tofacitinib extended-release)	**PsA** 11 mg PO QD **UC** Induction: 22 mg PO QD for 8 weeks, up to 16 weeks Maintenance: 11 mg PO QD	Maintenance: 11 mg/day
Zeposia® (ozanimod)	**UC** Days 1-4: 0.23 mg PO QD Days 5-7: 0.46 mg PO QD Day 8 and thereafter: 0.92 mg PO QD	**UC** 0.92 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): clinically significant hypersensitivity to ustekinumab products or any of the excipients
- Boxed warning(s): none reported

Appendix D: General Information

- Definition of failure of MTX or DMARDs
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week.

However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.

- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in erythrocyte sedimentation rate/C-reactive protein (ESR/CRP) levels
  - Improvements in activities of daily living
- TNF blockers:
  - Etanercept (Enbrel®), adalimumab (Humira®) and its biosimilars, infliximab (Remicade®) and its biosimilars (Avsola™, Renflexis™, Inflectra®), certolizumab pegol (Cimzia®), and golimumab (Simponi®, Simponi Aria®).

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:
  - Inability to induce short-term symptomatic remission with a 3-month trial of systemic glucocorticoids
  - High-risk factors for intestinal complications may include:
    - Initial extensive ileal, ileocolonic, or proximal GI involvement
    - Initial extensive perianal/severe rectal disease
    - Fistulizing disease (e.g., perianal, enterocutaneous, and rectovaginal fistulas)
    - Deep ulcerations
    - Penetrating, stricturing or stenosis disease and/or phenotype
    - Intestinal obstruction or abscess
  - High risk factors for postoperative recurrence may include:
    - Less than 10 years duration between time of diagnosis and surgery
    - Disease location in the ileum and colon
    - Perianal fistula
    - Prior history of surgical resection
    - Use of corticosteroids prior to surgery

Appendix F: Mayo Score

- Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician's global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0 – 2	Remission
3 – 5	Mild activity
6 – 10	Moderate activity
>10	Severe activity

Appendix G: Dose Rounding Guidelines for PsO

Weight-based Dose Range	Quantity Recommendation
Subcutaneous, Syringe	
≤ 46.99 mg	1 syringe of 45 mg/0.5 mL
47 to 94.49 mg	1 syringe of 90 mg/1 mL
94.5 to 141.49 mg	1 syringe of 45 mg/0.5 mL and 1 syringe of 90 mg/1 mL
Subcutaneous, Vial	
≤ 46.99 mg	1 vial of 45 mg/0.5 mL
47 to 94.49 mg	2 vials of 45 mg/0.5 mL

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ustekinumab (Stelara), Ustekinumab-aauz (Otulfi), ustekinumab-ttwe (Pyzchiva), ustekinumab-auub (Wezlana)	CD, UC	Weight based dosing IV at initial dose: Weight ≤ 55 kg: 260 mg Weight > 55 kg to 85 kg: 390 mg Weight > 85 kg: 520 mg Maintenance dose: 90 mg SC every 8 weeks	90 mg every 8 weeks
Ustekinumab (Stelara), Ustekinumab-aauz (Otulfi), ustekinumab-ttwe (Pyzchiva), Ustekinumab-aekn (Selarsdi), ustekinumab-auub (Wezlana) **Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses*	PsO	Weight based dosing SC at weeks 0 and 4, followed by maintenance dose every 12 weeks *Adult:* Weight ≤ 100 kg: 45 mg Weight > 100 kg: 90 mg *Pediatrics (age 6 years to 17 years):* **Stelara, Wezlana:** Weight < 60 kg: 0.75 mg/kg **Stelara, Otulfi, Pyzchiva, Selarsdi, Wezlana:** Weight 60 to 100 kg: 45 mg Weight > 100 kg: 90 mg	90 mg every 12 weeks
	PsA	Weight based dosing SC at weeks 0 and 4, followed by maintenance dose every 12 weeks *Adult:* 45 mg SC at weeks 0 and 4, followed by 45 mg every 12 weeks	45 mg every 12 weeks

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Pediatrics (age 6 years to 17 years): Weight based dosing SC at weeks 0 and 4, then every 12 weeks thereafter **Stelara, Wezlana:** Weight < 60 kg: 0.75 mg/kg **Stelara, Otulfi, Pyzchiva, Selarsdi, Wezlana:** Weight ≥ 60 kg: 45 mg	
	PsA with co-existent PsO	Weight > 100 kg: 90 mg SC at weeks 0 and 4, followed by 90 mg every 12 weeks	90 mg every 12 weeks

VI. Product Availability

Drug Name	Availability
Ustekinumab (Stelara)	• Single-dose prefilled syringe for SC injection: 45 mg/0.5 mL, 90 mg/mL • Single-dose vial for SC injection: 45 mg/0.5 mL • Single-dose vial for IV infusion: 130 mg/26 mL
Ustekinumab-aauz (Otulfi)	• Single-dose prefilled syringe for SC injection: 45 mg/0.5 mL, 90 mg/mL • Single-dose vial for IV infusion: 130 mg/26 mL
Ustekinumab-ttwe (Pyzchiva)	• Single-dose prefilled syringe for SC injection: 45 mg/0.5 mL, 90 mg/mL • Single-dose vial for IV infusion: 130 mg/26 mL
Ustekinumab-aekn (Selarsdi)	• Single-dose prefilled syringe for SC injection: 45 mg/0.5 mL, 90 mg/mL
Ustekinumab-auub (Wezlana)	• Single-dose prefilled syringe for SC injection: 45 mg/0.5 mL, 90 mg/mL • Single-dose vial for SC injection: 45 mg/0.5 mL • Single-dose vial for IV infusion: 130 mg/26 mL

VII. References

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Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3357	Ustekinumab, for subcutaneous injection,1 mg
J3358	Ustekinumab, for intravenous injection, 1 mg
Q5137	Injection, ustekinumab-auub (wezlana), biosimilar, subcutaneous, 1 mg
Q5138	Injection, ustekinumab-auub (wezlana), biosimilar, intravenous, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Criteria added for new FDA indication: ulcerative colitis; RT4: removed language stating for use after failure of other agents for the CD indication per updated FDA labeling; references reviewed and updated.	12.03.19	02.20
2Q 2020 annual review: no significant changes; added dose rounding guidelines for weight based dosing for PsO; references reviewed and updated.	02.28.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: updated PsO indication/criteria to reflect pediatric age extension to use in patients 6 years and older; alphabetized indications.	08.17.20	
2Q 2021 annual review: added additional criteria related to diagnosis of moderate-to-severe PsO per 2019 AAD/NPF guidelines specifying at least 3% BSA involvement or involvement of areas that severely impact daily function; added combination of bDMARDs under Section III; references reviewed and updated.	02.23.21	05.21
Per August SDC and prior clinical guidance, for PsA removed Simponi as a redirect option and modified to require a trial of all; for UC added requirement for trial of Humira, Simponi, and Zeposia in a step-wise manner. Add coverage for dose escalation with Stelara for CD (per A&G report) and UC (per SDC direction) requiring redirection to preferred agents [Humira, Simponi, Zeposia, infliximab (Avsola, Inflectra and Renflexis are preferred)] per SDC; for Xeljanz redirection requirements added bypass for members with cardiovascular risk and qualified redirection to apply only for member that has not responded or is intolerant to one or more TNF blockers; added Legacy WellCare line of business to policy (WCG.CP.PHAR.264 to be retired) and revised its initial approval duration from 12 months to 6 months.	08.16.21	11.21
2Q 2022 annual review: added Xeljanz as required agent for off-label dosing request for UC; for PsO, allowed phototherapy as alternative to systemic conventional DMARD if contraindicated or clinically significant adverse effects are experienced; reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated.	02.21.22	05.22
Fixed the following typos: removed "for CD and UC" in continued therapy section for off-label dose requests, as preferred agents should be tried for all indications prior to off-label dose escalation; in continued therapy, off-label dose escalation requests, added "for age ≥ 18 years" as qualifers of redirections to Taltz, Otezla, and infliximab due to their lack of pediatric safety and efficacy data in PsO.	05.18.22	
RT4: for PsA, updated criteria and dosing per FDA approved pediatric extension. Template changes applied to other diagnoses/indications and continued therapy section.	09.09.22	
Per February SDC, added Amjevita as an alternative option to Humira for CD and UC.	02.13.23	
2Q 2023 annual review: updated off-label dosing in Appendix B; for CD, PsO, PsA, and UC, added TNFi criteria to allow bypass if member has had history of failure of two TNF blockers; references reviewed and updated.	02.10.23	05.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Per July SDC: added criteria requiring use one adalimumab product and stating Yusimry, Hadlima, unbranded adalimumab-fkjp, and unbranded adalimumab-adaz as preferred; for PsA and PsO, removed criteria requiring use of Enbrel; for UC, removed criteria requiring use of Simponi, Humira, and Amjevita; updated Appendix B with relevant therapeutic alternatives.	07.25.23	
Per December SDC, added adalimumab-adbm to listed examples of preferred adalimumab products. RT4: added newly approved biosimilar Wezlana to criteria; for initial criteria, corrected spelling error in "dose does not exceed" criteria.	12.06.23	02.24
2Q 2024 annual review: updated Appendix D with removal of PsA guideline and pediatric pharmacokinetic studies supplemental information; added Bimzelx, Zymfentra, Omvoh, Tofidence, Sotyktu, and Velsipity to section III.B; references reviewed and updated.	01.22.24	05.24
RT4: added newly approved biosimilar Selarsdi to criteria. Added HCPCS codes [Q5137, Q5138].	05.03.24	
Per June SDC, added Simlandi to listed examples of preferred adalimumab products. RT4: added newly approved biosimilar Pyzchiva to criteria. Per SDC, added unbranded adalimumab-aaty to listed examples of preferred adalimumab products.	07.23.24	08.24
RT4: added newly approved biosimilar Otulfi to criteria.	10.03.24	11.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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