Medication Policy Manual

Policy No: dru444

Topic: Drugs for chronic inflammatory diseases

Date of Origin: January 8, 2016

- adalimumab (Humira; biosimilars: Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz, Idacio, Simlandi, Yuflyma, Yusimry; unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)
- Bimzelx, bimekizumab-bkzx
- Cibinqo, abrocitinib
- Cimzia, certolizumab pegol
- Cosentyx, secukinumab
- Entyvio, vedolizumab
- etanercept (Enbrel; biosimilars Erelzi, Eticovo)
- golimumab (Simponi, Simponi Aria)
- Ilumya, tildrakizumab-asmn
- Kevzara, sarilumab
- Leqselvi, deuruxolitinib
- Litfulo, ritlecitinib
- Olumiant, baricitinib
- Omvoh, mirikizumab-mrkz
- Orencia, abatacept
- Otezla, apremilast
- Siliq, brodalumab
- Skyrizi, risankizumab-rzaa
- Sotyktu, deucravacitinib
- Spevigo, spesolimab-sbzo
- Taltz, ixekizumab
- tocilizumab (Actemra; biosimilars Tofidence, Tyenne)
- tofacitinib (Xeljanz, Xeljanz XR)
- upadacitinib (Rinvoq, Rinvoq LQ)
- Tremfya, guselkumab
- ustekinumab (Stelara; biosimilars Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)
- Velsipity, etrasimod

Committee Approval Date: December 12, 2024

Next Review Date: 2025

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IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Administration of Contract

Coverage for cosmetic purposes, including removal, inhibition, or stimulation of hair growth, is defined by benefit contract language.

Description

Medications included in this policy are used to treat a group of diseases that may be caused or worsened by an overactive immune system. Administration may be a subcutaneous injection (SC), intravenous injection (IV), or administered by mouth.

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- Cimzia (certolizumab pegol)
- Etanercept (Enbrel; biosimilars Erelzi, Eticovo)
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	B-lymphocyte depleter	- Rituximab (Rituxan Hycela, Rituxan; biosimilars Riabni, Ruxience, Truxima) [a]	
	IL-1	- Kineret (anakinra) [a] - Ilaris (canakinumab) [a]	
JAK Inhibitors	JAK1/2/3	- Cibinqo (abrocitinib) - Litfulo (ritlecitinib) - Olumiant (baricitinib) - Tofacitinib (Xeljanz, Xeljanz XR) - Rinvoq (upadacitinib)	
	TYK2	- Sotyktu (deucravacitinib)	
PDE-4 Inhibitors		- Otezla (apremilast)	
S1P receptor modulator		- Velsipity (etrasimod) - Zeposia (ozanimod)	
Conventional synthetic DMARDs (csDMARD) (also referred to as conventional immunomodulators)		- Azathioprine (generic, Imuran) - 6-mercaptopurine (generic, 6-MP) - Methotrexate (generic, MTX) - Hydroxychloroquine (HCQ; generic, Plaquenil) - Leflunomide (generic, Arava) - Mycophenolate (MMF; generic, CellCept, Myfortic)	- Cyclosporine (CSA; Gengraf, Neoral, Sandimmune) - Tacrolimus (generic, Prograf) - 5 ASAs [sulfasalazine (generic, SSZ), mesalamine, balsalazide] - Acitretin (generic, Accutane)

[a] See "Cross References" for associated policy for this medication

Policy/Criteria

Most contracts require prior authorization approval of medications used to treat chronic inflammatory diseases prior to coverage.

I. Continuation of therapy (COT): Medications in this policy may be considered medically necessary for COT when criteria A, B, and C below are met.

A. One of the following (1, 2, or 3):

1. For diagnoses NOT listed in the coverage criteria below, full policy criteria must be met for coverage.

OR

2. For diagnoses listed in the coverage criteria below, criteria a and b must be met:

a. The patient was established on therapy prior to current health plan membership AND attestation that the medication was covered by another health plan.

AND

b. There is documentation of clinical benefit, such as disease stability as detailed in the reauthorization criteria.

OR

3. With exception of Olumiant (baricitinib) use for coronavirus-19 (COVID-19), the medication was initiated for acute disease management, as part of an acute unscheduled, inpatient hospital admission.

AND

B. **For Provider-administered drugs only (as applicable):** Site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].

AND

C. **"Administration of Contract" is met.**

***Please note**: Medications obtained as samples, coupons, or promotions, paying cash for a prescription ("out-of-pocket") as an eligible patient, or any other method of obtaining medications outside of an established health plan benefit (from your insurance) does NOT necessarily establish medical necessity. Medication policy criteria apply for coverage, per the terms of the member contract with the health plan.*

II. New starts (treatment-naïve patients): Medications in this policy may be considered medically necessary when the criteria below are met.

A. Acute Graft Versus Host Disease (aGVHD), Prophylaxis
Orencia (abatacept) IV may be considered medically necessary when there is clinical documentation (including, but not limited to chart notes) that criteria 1, 2, and 3 below are met. **1.** Abatacept will be used for **prophylaxis of acute graft versus host disease (aGVHD)**. **AND** **2.** Patient will undergo a hematopoietic cell transplant (HCT) from an unrelated donor (either 8/8 HLA matched or 7/8 HLA mismatch). **AND** **3.** Abatacept will be used in combination with methotrexate and a calcineurin inhibitor (cyclosporine or tacrolimus).

B. Alopecia areata (AA)

Note: medications for cosmetic purposes, including, but not limited to the stimulation of hair growth is dictated by benefit contract language.

1. **Diagnostic Criteria:** The diagnosis of alopecia areata (AA) has been established by or in conjunction with a specialist in dermatology.
2. **Severity Criteria:** Criteria a, b, and c below are met.
   a. Severe AA as indicated by a severity of alopecia tool (SALT) score of ≥ 50 or ≥ 50% scalp hair loss.

   AND

   b. No evidence of terminal hair regrowth within 6 months.

   AND

   c. Both the following have been ineffective or not tolerated, unless all are contraindicated:
      i. At least 6 months of a conventional oral immunosuppressant (methotrexate, cyclosporine, or azathioprine)

      AND

      ii. Either A or B below:

      A. At least 6 weeks of topical or oral corticosteroid therapy.

      OR

      B. At least 6 months of topically immunotherapy (diphenylcyclopropenone [DPCP] or squaric acid dibutyl ester [SADBE]).

Product Group	Products	Criteria Requirements
Level 1	- Leqselvi (deuruxolitinib) - Litfulo (ritlecitinib) - Olumiant (baricitinib)	**1.** Diagnostic Criteria **2.** Severity Criteria

C. Ankylosing Spondylitis (AS) – Self-administered Products		
1. <u>Diagnostic Criteria</u>: A diagnosis of **axial SpA**, including **ankylosing spondylitis** (AS), when established by or in consultation with a specialist in rheumatology.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cosentyx (secukinumab) - Enbrel (etanercept) - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk)	**1.** Diagnostic Criteria
Level 2	- Rinvoq (upadacitinib) - Xeljanz/Xeljanz XR (tofacitinib)	**1.** Diagnostic Criteria **2.** There is clinical documentation that treatment with **at least ONE Level 1** TNF-inhibitor was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Level 3	- Cimzia (certolizumab pegol) syringes - Simponi (golimumab) SC - Taltz (ixekizumab) - Bimzelx (bimekizumab)	**1.** Diagnostic Criteria **2.** There is clinical documentation that treatment with **at least TWO Level 1 or Level 2** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**
Non-Preferred Etanercept Products	- Etanercept biosimilars (Erelzi, Eticovo)	**1.** Diagnostic Criteria **2.** There is a documented intolerance or contraindication to **Enbrel (etanercept)**.

D. Ankylosing Spondylitis (AS) – Provider-administered Products		
1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408]. **2.** **Diagnostic Criteria:** A diagnosis of **axial SpA**, including **ankylosing spondylitis** (AS), when established by or in consultation with a specialist in rheumatology.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cosentyx (secukinumab) IV - Simponi Aria (golimumab) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Level 2	- Cimzia (certolizumab pegol) vials	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** There is clinical documentation that treatment with **at least TWO Level 1** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620

E. Antibody Mediated Rejection (AMR) of Transplant (Solid Organ)

Tocilizumab IV may be considered medically necessary when criteria 1 and 2 below are met.

1. **Diagnostic Criteria:** Criterion a or b below are met.
   a. **Prevention of antibody (Ab)-mediated rejection:** Prior to solid organ transplant and in the peri-operative period, for patients at high risk for Ab-mediated rejection, including highly sensitized patients, and those receiving an ABO-incompatible organ.

   OR

   b. **Treatment of antibody-mediated rejection** (a.k.a. vascular rejection, humoral rejection): Following solid organ transplant and confirmed by either biopsy or presence of panel reactive antibodies (PRAs).

AND

2. **Severity Criteria:** Treatment with immunoglobulin (IVIG), plasma exchange/pheresis (PLEX), and rituximab has been ineffective or is contraindicated.

Product Group	Products	Criteria Requirements
Level 1	- Tyenne (tocilizumab-aazg) IV	**1.** Diagnostic Criteria **2.** Severity Criteria
Non-Preferred Tocilizumab Products	- Actemra (tocilizumab) IV - Tofidence IV (tocilizumab-bavi)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **all Level 1** therapies.

F. Atopic Dermatitis (AD) – Self-administered Products

1. **Diagnostic Criteria:** The medication is being prescribed by or in conjunction with a specialist in dermatology, allergy, or pulmonology.
2. **Severity Criteria:** All the following criteria a, b, and c below are met.
   a. **For Rinvoq (upadacitinib) or Cibinqo (abrocitinib) only:** the patient is age 12 or older.

   AND

   b. The patient has a diagnosis of moderate to severe atopic dermatitis.

   AND

   c. Both the following (i and ii) have been ineffective or not tolerated, unless all are contraindicated:
      i. A medium to very high-potency corticosteroid (see *Appendix 1*), for at least 14 days.

      AND

      ii. Topical tacrolimus, for at least 28 days, unless one of the following apply (criterion a or b below):
         a. Atopic dermatitis affects a body surface area (BSA) greater than or equal to 10% or involvement of a hairy area of the body (such as the scalp) such that use of topical tacrolimus is not feasible.

         OR

         b. Systemic immunosuppressants (such as oral cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, or a biologic) for at least two months have been ineffective, not tolerated, or all are contraindicated.

PLEASE NOTE: Ineffectiveness for topical agents is defined as failure to achieve and maintain remission or a low disease activity state despite treatment with a daily regimen, applied for ≥ 28 days or for the maximum duration recommended by the product prescribing information (e.g., 14 days for high or very-high potency topical corticosteroids).

Product Group	Products	Criteria Requirements
Level 1	- Cibinqo (abrocitinib) - Rinvoq (upadacitinib)	**1.** Diagnostic Criteria **2.** Severity Criteria
	- Adbry (tralokinumab) - Dupixent (dupilumab)	Refer to Medication Policy Manual, Monoclonal antibodies for skin and other inflammatory conditions, dru493

G. Non-Radiographic Axial Spondyloarthritis (Nr-axSpA) – Self-administered Products		
1. **<u>Diagnostic Criteria</u>:** A diagnosis of **non-radiographic axial spondyloarthritis** (Nr-axSpA) when established by or in consultation with a specialist in rheumatology.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cimzia (certolizumab pegol) syringes - Cosentyx (secukinumab)	**1.** Diagnostic Criteria
Level 2	- Rinvoq (upadacitinib)	**1.** Diagnostic criteria **2.** There is clinical documentation that treatment with **at least ONE level 1 TNF** inhibitor was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Level 3	- Taltz (ixekizumab) - Bimzelx (bimekizumab)	**1.** Diagnostic Criteria **2.** There is clinical documentation that treatment with **at least TWO Level 1 or Level 2** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.

H. Non-Radiographic Axial Spondyloarthritis (Nr-axSpA) – Provider-administered Products		
1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408]. **2.** **Diagnostic Criteria:** A diagnosis of **non-radiographic axial spondyloarthritis** (Nr-axSpA) established by or in consultation with a specialist in rheumatology.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cimzia (certolizumab pegol) vials - Cosentyx (secukinumab) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria

I. Behçet's Disease (BD)		
1. **<u>Diagnostic Criteria</u>:** The diagnosis of **Behçet's Disease** (BD) has been established by or in conjunction with a specialist in rheumatology, dermatology, or immunology. **2.** **<u>Severity Criteria</u>:** All the following criteria a, b, and c below are met. **a.** There is documentation of mucocutaneous ulcers (including, but not limited to, oral, genital, or cutaneous ulcers). **AND** **b.** Documentation confirming functional impairment due to BD, which may include, but is not limited to, limitation of activities of daily living (ADLs), such as infections, severe pain, or sleep disturbances. **AND** **c.** Treatment with colchicine, azathioprine, cyclosporine, methotrexate, a topical corticosteroid (e.g., triamcinolone dental paste), or other immunomodulator (see *Appendix 3*) for at least four weeks has been ineffective or not tolerated, unless all are contraindicated.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Otezla (apremilast)	**1.** Diagnostic Criteria **2.** Severity Criteria

J. Chronic Plaque Psoriasis (PsO) – Self-administered Products

1. **Diagnostic Criteria:** A diagnosis of **chronic plaque psoriasis** (PsO) when established by or in consultation with a specialist in dermatology or rheumatology.
2. **Severity Criteria:** At least one of the following criterion a, b, or c below is met.
   - **a.** There is involvement of ≥ 10% of the body surface (BSA) area OR there is significant functional disability due to PsO.

   OR

   - **b.** Treatment with phototherapy (for example, UVB) or photochemotherapy was not effective, not tolerated, or is contraindicated (such as lesions on the face, scalp, hands, feet, nailbeds, or groin area; see *Appendix 2*).

   OR

   - **c.** Treatment with at least one oral/topical conventional medication therapy was not effective after 12 weeks, not tolerated, or all are contraindicated. Conventional medication therapies for the treatment of PsO include: acitretin, anthralin, calcipotriene, calcitriol, coal tar products, cyclosporine, methotrexate, pimecrolimus, tacrolimus, tazarotene, or a topical corticosteroid.

Product Group	Products	Criteria Requirements
Level 1	- Cosentyx (secukinumab) - Enbrel (etanercept) - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Otezla (apremilast) - Simlandi (adalimumab-ryvk) - Skyrizi (risankizumab) - Sotyktu (deucravacitinib) - Stelara (ustekinumab) - Tremfya (guselkumab)	**1.** Diagnostic Criteria **2.** Severity Criteria
Level 2	- Cimzia (certolizumab pegol) syringes	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is clinical documentation that treatment with **at least TWO Level 1 therapies** was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.

J. Chronic Plaque Psoriasis (PsO) – Self-administered Products		
Product Group	**Products**	**Criteria Requirements**
Level 3	- Bimzelx (bimekizumab-bkzx) - Siliq (brodalumab) - Taltz (ixekizumab)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is clinical documentation that treatment with **at least THREE Level 1** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**
Non-Preferred Etanercept Products	- Etanercept biosimilars (Erelzi, Eticovo)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Enbrel (etanercept)**.
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Stelara (ustekinumab).**

K. Chronic Plaque Psoriasis (PsO) – Provider-administered Products

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **chronic plaque psoriasis** (PsO) when established by or in consultation with a specialist in dermatology or rheumatology.
3. **Severity Criteria:** At least one of the following criterion a, b, or c below is met.
   - **a.** There is involvement of ≥ 10% of the body surface (BSA) area OR there is significant functional disability due to PsO.

   OR

   - **b.** Treatment with phototherapy (for example, UVB) or photochemotherapy was not effective, not tolerated, or is contraindicated (such as lesions on the face, scalp, hands, feet, nailbeds, or groin area; see *Appendix 2*).

   OR

   - **c.** Treatment with at least one oral/topical conventional medication therapy was not effective after 12 weeks, not tolerated, or all are contraindicated. Conventional medication therapies for the treatment of PsO include: acitretin, anthralin, calcipotriene, calcitriol, coal tar products, cyclosporine, methotrexate, pimecrolimus, tacrolimus, tazarotene, or a topical corticosteroid.

Product Group	Products	Criteria Requirements
Level 1	- Stelara (ustekinumab)	**1.** Diagnostic Criteria **2.** Severity Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Level 2	- Cimzia (certolizumab pegol) vials - Ilumya (tildrakizumab-asmn)	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** There is clinical documentation that treatment with **at least TWO Level 1** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Stelara (ustekinumab).**

L. Crohn's Disease (CD) – Self-administered Products

1. **Diagnostic Criteria:** A diagnosis of **Crohn's disease** (CD) established by or in consultation with a specialist in gastroenterology.
2. **Severity Criteria:** Either criterion a or b below are met.
   - **a.** At least one of the following criterion (i through vi) below is met.
     - **i.** Fistulizing Crohn's disease.
     - **ii.** Previous hospitalization for Crohn's disease.
     - **iii.** Extensive anatomic involvement.
     - **iv.** Deep ulcers.
     - **v.** Prior surgical resection.
     - **vi.** Stricturing and/or penetrating behavior.

   OR

   - **b.** Acute treatment of an exacerbation when at least one of criterion (i, ii, or iii) below is met.
     - **i.** Treatment with an adequate course of corticosteroids (for example, prednisone 40 to 60 mg/day, oral budesonide 9 mg/day, or budesonide rectal for 7 to 14 days) has been ineffective or is contraindicated.

     OR

     - **ii.** The patient has been unable to taper an adequate course of corticosteroids without experiencing worsening of disease.

     OR

     - **iii.** The patient is experiencing breakthrough disease (e.g., active disease flares) while stabilized for at least 8 weeks on a conventional immunomodulator. Conventional immunomodulators for CD include azathioprine, mercaptopurine, methotrexate, balsalazide, mesalamine, cyclosporine, and sulfasalazine.

Product Group	Products	Criteria Requirements
Level 1	- Entyvio (vedolizumab) SC - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk) - Skyrizi (risankizumab-rzaa) - Stelara (ustekinumab)	**1.** Diagnostic Criteria **2.** Severity Criteria
Level 2	- Upadacitinib (Rinvoq)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with adalimumab was not effective after at least a 12-week treatment course unless not tolerated or contraindicated.

L. Crohn's Disease (CD) – Self-administered Products		
Product Group	**Products**	**Criteria Requirements**
Level 3	- Cimzia (certolizumab pegol) syringes	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with the following (a and b) were not effective after at least 12 weeks of treatment each, unless not tolerated or contraindicated. a. Adalimumab **AND** b. At least one other Level 1 or Level 2 therapy
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**
Non-Preferred Infliximab Products	- Infliximab products (Zymfentra)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Stelara (ustekinumab)**

M. Crohn's Disease (CD) – Provider-administered Products

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **Crohn's disease** (CD) established by or in consultation with a specialist in gastroenterology.
3. **Severity Criteria:** Either criterion a or b below is met.
   - **a.** At least one of the following criteria (I through vi) below is met.
     - **i.** Fistulizing Crohn's disease.
     - **ii.** Previous hospitalization for Crohn's disease.
     - **iii.** Extensive anatomic involvement.
     - **iv.** Deep ulcers.
     - **v.** Prior surgical resection.
     - **vi.** Stricturing and/or penetrating behavior.

   OR

   - **b.** Acute treatment of an exacerbation when at least one of criterion (i, ii, or iii) below, is met.
     - **i.** Treatment with an adequate course of corticosteroids (for example, prednisone 40 to 60 mg/day, oral budesonide 9 mg/day, or budesonide rectal for 7 to 14 days) has been ineffective or is contraindicated.

     OR

     - **ii.** The patient has been unable to taper an adequate course of corticosteroids without experiencing worsening of disease.

     OR

     - **iii.** The patient is experiencing breakthrough disease (e.g., active disease flares) while stabilized for at least 8 weeks on a conventional immunomodulator. Conventional immunomodulators for CD include azathioprine, mercaptopurine, methotrexate, balsalazide, mesalamine, cyclosporine, and sulfasalazine.

Product Group	Products	Criteria Requirements
Level 1	- Entyvio (vedolizumab) - Skyrizi (risankizumab-rzaa) - Stelara (ustekinumab)	**1.** Site of Care Requirements *(Entyvio only)* **2.** Diagnostic Criteria **3.** Severity Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Level 2	- Cimzia (certolizumab pegol) vials	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** Treatment with **at least TWO Level 1** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.

M. Crohn's Disease (CD) – Provider-administered Products		
Product Group	**Products**	**Criteria Requirements**
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Stelara (ustekinumab)**

N. Cytokine-release Syndrome (CRS)		
Tocilizumab IV may be considered medically necessary when there is clinical documentation (including, but not limited to chart notes) that criterion 1 below is met. **1. Product will be used for cytokine release syndrome** (CRS)**.**		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Tyenne (tocilizumab-aazg) IV	**1.** Diagnostic Criteria
Non-Preferred Tocilizumab Products	- Actemra (tocilizumab) IV - Tofidence IV (tocilizumab-bavi)	**1.** Diagnostic Criteria **2.** There is a documented intolerance or contraindication to **all Level 1** therapies.

O. Enthesitis-related Arthritis (ERA)		
1. <u>Diagnostic Criteria</u>: A diagnosis of enthesitis-related arthritis (ERA) when established by or in consultation with a specialist in rheumatology.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cosentyx (secukinumab) - Enbrel (etanercept) - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk)	**1.** Diagnostic Criteria
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**
Non-Preferred Etanercept Products	- Etanercept biosimilars (Erelzi, Eticovo)	**1.** Diagnostic Criteria **2.** There is a documented intolerance or contraindication to **Enbrel (etanercept)**.

P. Generalized Pustular Psoriasis (GPP) – Self-administered Products

Spevigo (spesolimab-sbzo) SC may be considered medically necessary when criteria 1 and 2 below are met.

1. **Diagnostic Criteria:** A diagnosis of **generalized pustular psoriasis (GPP)** when established by or in consultation with a specialist in dermatology.
2. **Severity Criteria: Maintenance treatment for GPP (SC formulation only)** when criteria a, b, and c below are met.
   - **a.** History of at least two moderate-to-severe flares with at least one associated with fever, elevated C-reactive protein level, elevated white blood cell count, asthenia, or myalgia.

   AND

   - **b.** Currently not experiencing a flare.

   AND

   - **c.** Treatment with acitretin and methotrexate for at least eight weeks has been ineffective or not tolerated, unless both are contraindicated.

Product Group	Products	Criteria Requirements
Level 1	- Spevigo (spesolimab-sbzo)	**1.** Diagnostic criteria. **2.** Severity criteria.

Q. Generalized Pustular Psoriasis (GPP) – Provider-administered Products

Spevigo (spesolimab-sbzo) IV or SC may be considered medically necessary when criteria 1 and 2 below are met.

1. **Diagnostic Criteria:** A diagnosis of **generalized pustular psoriasis (GPP)** when established by or in consultation with a specialist in dermatology.
2. **Severity Criteria:** Criterion a or b below are met.
   - **a. Treatment of GPP flare (IV formulation only)** when all of the following are met:
     - **i.** Documentation of disease progression despite usual treatment with cyclosporine OR infliximab unless not tolerated, or both are contraindicated.
     - **ii.** There is involvement of ≥ 5% of body surface area (BSA) with erythema and the presence of pustules.

   OR

   - **b. Maintenance treatment for GPP (SC formulation for loading dose only)** when all of the following are met:
     - **i.** History of at least two moderate-to-severe flares, with at least one associated with fever, elevated C-reactive protein level, elevated white blood cell count, asthenia, or myalgia
     - **ii.** Currently not experiencing a flare
     - **iii.** Treatment with acitretin and methotrexate for at least eight weeks has been ineffective or not tolerated, unless both are contraindicated.

Product Group	Products	Criteria Requirements
Level 1	- Spevigo (spesolimab-sbzo)	**1.** Diagnostic criteria. **2.** Severity criteria.
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620

R. Giant Cell Arteritis (GCA)

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **giant cell arteritis** (GCA) when established by or in consultation with a specialist in rheumatology (see *Appendix 6*).
3. **Severity Criteria:** Requested medication will be given in combination with high-dose corticosteroids (prednisone 20 to 60 mg per day or equivalent) unless contraindicated or not tolerated.

Product Group	Products	Criteria Requirements
Preferred Self-administered Products	- Tyenne (tocilizumab-aazg) SC -	**1.** Diagnostic Criteria **2.** Severity Criteria
Preferred Provider-administered Products	- Tyenne (tocilizumab-aazg) IV	**1.** Site of Care Requirements **2.** Diagnostic criteria **3.** Severity Criteria
Non-Preferred Self-administered Products	- Actemra (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is documented intolerance or contraindication to all preferred self-administered therapies.
Non-Preferred Provider-administered Products	- Actemra (tocilizumab) IV - Tofidence IV (tocilizumab-bavi)	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** There is a documented intolerance or contraindication to all preferred provider-administered therapies.

S. Hidradenitis Suppurativa (HS) – Self-administered Products		
1. **<u>Diagnostic Criteria</u>:** A diagnosis of **hidradenitis suppurativa** (HS) established by or in consultation with a specialist in dermatology. **2.** **<u>Severity Criteria</u>:** Treatment with at least one conventional agent was not effective after 12 weeks, not tolerated, or all are contraindicated. Conventional agents for the treatment of HS include topical antibiotics, systemic antibiotics (e.g., oral tetracyclines, clindamycin, rifampin, moxifloxacin, metronidazole), intralesional corticosteroids (e.g., triamcinolone), hormonal therapies (e.g., oral contraceptives, spironolactone), cyclosporine, finasteride, metformin, or oral retinoids.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cosentyx (secukinumab) - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**

T. Hidradenitis Suppurativa (HS) – Provider-administered Products		
1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408]. 2. **Diagnostic Criteria:** A diagnosis of **hidradenitis suppurativa** (HS) established by or in consultation with a specialist in dermatology. 3. **Severity Criteria:** Treatment with at least one conventional agent was not effective after 12 weeks, not tolerated, or all are contraindicated. Conventional agents for the treatment of HS include topical antibiotics, systemic antibiotics (e.g., oral tetracyclines, clindamycin, rifampin, moxifloxacin, metronidazole), intralesional corticosteroids (e.g., triamcinolone), hormonal therapies (e.g., oral contraceptives, spironolactone), cyclosporine, finasteride, metformin, or oral retinoids.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620

U. Immune-Mediated Colitis		
1. **Diagnostic Criteria:** A diagnosis of **colitis** due to Yervoy (ipilimumab) or an anti-PD1/PD-L1 agent [such as Tecentriq (atezolizumab), Bavencio (avelumab), Libtayo (cemiplimab), Imfinzi (durvalumab), Opdivo (nivolumab), or Keytruda (pembrolizumab)]. **2.** **Severity Criteria:** Treatment with an adequate course of corticosteroids (for example, prednisone 40 to 60 mg/day, oral budesonide 9 mg/day, or budesonide rectal for 7 days) has been ineffective or is contraindicated.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Entyvio (vedolizumab)	**1.** Diagnostic Criteria **2.** Severity Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620

V. Polyarticular Juvenile Idiopathic Arthritis (PJIA) – Self-administered Products		
1. **<u>Diagnostic Criteria</u>:** A diagnosis of **polyarticular juvenile idiopathic arthritis** (PJIA) established by or in consultation with a specialist in rheumatology. **2.** **<u>Severity Criteria</u>:** Treatment with a csDMARD (such as leflunomide, methotrexate, or sulfasalazine) was ineffective after at least 6 weeks, unless not tolerated or all are contraindicated.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Enbrel (etanercept) - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria
Level 2	- upadacitinib (Rinvoq, Rinvoq LQ) - Xeljanz (tofacitinib)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **ONE Level 1 TNF inhibitor** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated.
	- Tyenne (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **adalimumab** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated.
Level 3	- Orencia (abatacept) SC - Cimzia (certolizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is clinical documentation that treatment with at least TWO Level 1 or Level 2 therapies were not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated. **4.** **For Cimzia with patient weight <40kg only:** Dose must be ≥200 mg. **Note:** doses less than 200 mg require administration by a health care professional using the vial kit.
	- Kevzara (sarilumab)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is clinical documentation that treatment with at least THREE Level 1 or Level 2 therapies were not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated. **4.** Patient weight is ≥ 63 kg

Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**
Non-Preferred Etanercept Products	- Etanercept biosimilars (Erelzi, Eticovo)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Enbrel (etanercept)**.
Non-Preferred Tocilizumab Products	- Actemra (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **adalimumab** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated. **4.** There is documented intolerance or contraindication to **Tyenne (tocilizumab) SC.**

W. Polyarticular Juvenile Idiopathic Arthritis (PJIA) – Provider-administered Products

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **polyarticular juvenile idiopathic arthritis** (PJIA) established by or in consultation with a specialist in rheumatology.
3. **Severity Criteria:** Treatment with a csDMARD (such as leflunomide, methotrexate, or sulfasalazine) was ineffective after at least 6 weeks, unless not tolerated or all are contraindicated.

Product Group	Products	Criteria Requirements
Level 1	- Orencia (abatacept) IV - Simponi Aria (golimumab) IV - Tyenne (tocilizumab-aazg) IV - Cimzia (certolizumab pegol) vials	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Tocilizumab Products	- Actemra (tocilizumab) IV - Tofidence (tocilizumab-bavi) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** There is a documented intolerance or contraindication to Tyenne (tocilizumab-aazg) IV.

X. Polymyalgia Rheumatica (PMR)
Kevzara (sarilumab) may be considered medically necessary when there is clinical documentation (including, but not limited to chart notes) that criteria 1 and 2 below are met. **1.** Kevzara (sarilumab) will be used for treatment of **polymyalgia rheumatica** (PMR) when established by or in consultation with a specialist in rheumatology. **AND** **2.** One of the following criteria (a or b) is met: **a.** Treatment with an adequate course of corticosteroids (prednisone 15 to 25 mg /day or equivalent) over 4- 6 weeks has been ineffective or is contraindicated. **OR** **b.** The patient has been unable to taper an adequate course of corticosteroids without experiencing worsening of disease.

Y. Psoriatic Arthritis (PsA) – Self-administered Products		
1. **Diagnostic Criteria:** A diagnosis of **psoriatic arthritis** (PsA) established by or in consultation with a specialist in dermatology or rheumatology.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cosentyx (secukinumab) - Enbrel (etanercept) - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Otezla (apremilast) - Simlandi (adalimumab-ryvk) - Skyrizi (risankizumab-rzaa) - Stelara (ustekinumab) - Tremfya (guselkumab)	**1.** Diagnostic Criteria
Level 2	- Tofacitinib (Xeljanz/Xeljanz XR) - Upadacitinib (Rinvoq, Rinvoq LQ)	**1.** Diagnostic Criteria **2.** Treatment with **ONE Level 1 TNF inhibitor** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated.
Level 3	- Cimzia (certolizumab pegol) syringes - Orencia (abatacept) SC - Simponi (golimumab) SC - Taltz (ixekizumab) - Bimzelx (bimekizumab)	**1.** Diagnostic Criteria **2.** There is clinical documentation that treatment with **at least TWO Level 1 or Level 2** self-administered therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic criteria **2.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**
Non-Preferred Etanercept Products	- Etanercept biosimilars (Erelzi, Eticovo)	**1.** Diagnostic criteria **2.** There is a documented intolerance or contraindication to **Enbrel (etanercept)**.
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic criteria. **2.** There is a documented intolerance or contraindication to **Stelara (ustekinumab).**

Z. Psoriatic Arthritis (PsA) – Provider-administered Products		
1. **<u>Site of Care Requirements</u>:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408]. **2.** **<u>Diagnostic Criteria</u>:** A diagnosis of **psoriatic arthritis** (PsA) established by or in consultation with a specialist in dermatology or rheumatology.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Cosentyx (secukinumab) IV - Simponi Aria (golimumab) IV - Stelara (ustekinumab)	**1.** Site of Care Requirements *(Cosentyx and Simponi Aria only)* **2.** Diagnostic Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Level 2	- Cimzia (certolizumab pegol) vials - Orencia (abatacept) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** There is clinical documentation that treatment with **at least TWO Level 1** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic Criteria **2.** There is a documented intolerance or contraindication to Stelara (ustekinumab)

AA.	Rheumatoid Arthritis (RA) – Self-administered Products	
1. **Diagnostic Criteria:** A diagnosis of **rheumatoid arthritis** (RA) when established by or in consultation with a specialist in rheumatology (see *Appendix 4*). **2.** **Severity Criteria:** Treatment with a conventional synthetic DMARD (csDMARD) for at least 6 to 12 weeks was ineffective, not tolerated, or all csDMARDs are contraindicated. csDMARDs for RA include hydroxychloroquine, leflunomide, methotrexate, and sulfasalazine.		
Product Group	**Products**	**Criteria Requirements**
Level 1	- Enbrel (etanercept) - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria
Level 2	- Rinvoq (upadacitinib) - Tofacitinib (Xeljanz/Xeljanz XR)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **ONE Level 1 TNF inhibitor** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated.
Level 3	- Tyenne (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **adalimumab** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated.
Level 4	- Cimzia (certolizumab pegol) syringes - Kevzara (sarilumab) - Olumiant (baricitinib) - Orencia (abatacept) SC - Simponi (golimumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is clinical documentation that treatment with **at least TWO Level 1 or 2** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
	- Kineret (anakinra)	Refer to Medication Policy Manual, Interleukin-1 Antagonists, dru677
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**

Non-Preferred Etanercept Products	- Etanercept biosimilars (Erelzi, Eticovo)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Enbrel (etanercept)**.
Non-Preferred Tocilizumab Products	- Actemra (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **adalimumab** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated. **4.** There is documented intolerance or contraindication to **Tyenne (tocilizumab).**

BB. Rheumatoid Arthritis (RA) – Provider-administered Products

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **rheumatoid arthritis** (RA) when established by or in consultation with a specialist in rheumatology (see *Appendix 4*).
3. **Severity Criteria:** Treatment with a conventional synthetic DMARD (csDMARD) for at least 6 to 12 weeks was ineffective, not tolerated, or all csDMARDs are contraindicated. csDMARDs for RA include hydroxychloroquine, leflunomide, methotrexate, and sulfasalazine.

Product Group	Products	Criteria Requirements
Level 1	- Simponi Aria (golimumab) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Level 2	- Cimzia (certolizumab pegol) vials - Orencia (abatacept) IV - Tyenne (tocilizumab) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** There is clinical documentation that treatment with **at least TWO Level 1** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated.
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Tocilizumab Products	- Actemra (tocilizumab) IV - Tofidence (tocilizumab-bavi) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** There is clinical documentation that treatment with **at least TWO Level 1** therapies was not effective after at least a 12-week treatment course unless all were not tolerated or are contraindicated. **5.** There is a documented intolerance or contraindication to Tyenne (tocilizumab) IV.

CC. Systemic Juvenile Idiopathic Arthritis (SJIA; Still's disease)

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **systemic juvenile idiopathic arthritis** (SJIA; Still's disease) when established by or in consultation with a specialist in rheumatology.
3. **Severity Criteria:** Both criteria a and b below are met.
   - **a.** There is disease activity greater than 6 weeks.

   AND
   - **b.** One of the following is met (i or ii):
     - **i.** Treatment with at least one oral conventional agent was not effective after 12 weeks, not tolerated, or is contraindicated. Conventional agents for the treatment of SJIA include azathioprine, cyclosporine, leflunomide, methotrexate, systemic corticosteroids, or tacrolimus.

     OR
     - **ii.** Treatment with at least one NSAID (such as ibuprofen, celecoxib) was not effective after 4 weeks, not tolerated, or all are contraindicated.

Product Group	Products	Criteria Requirements
Preferred Provider-administered products	- Tyenne (tocilizumab-aazg) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria
Non-Preferred Provider-Administered Products	- Actemra (tocilizumab) IV - Tofidence IV (tocilizumab-bavi)	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** There is a documented intolerance or contraindication to all preferred provider-administered therapies.
Preferred Self-administered Products	- Tyenne (tocilizumab-aazg) SC	**1.** Diagnostic Criteria **2.** Severity Criteria
	- Kineret (anakinra)	Refer to Medication Policy Manual, Interleukin-1 Antagonists, dru677
Non-Preferred Self-administered Products	- Actemra (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to Tyenne (tocilizumab-aazg)

DD. Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

1. **Diagnostic Criteria:**
   - **a.** The diagnosis has been established by or in consultation with a pulmonologist or rheumatologist.

   AND

   - **b.** Documentation of fibrosis of at least 10% of the lungs on high-resolution computed tomographic scan (HRCT).
2. **Severity Criteria:** Documentation of disease progression despite usual treatment, including both of the following criteria a and b below are met.
   - **a.** At least one immunomodulator/anti-inflammatory used chronically for ILD (such as azathioprine, cyclosporine, tacrolimus, rituximab, cyclophosphamide, mycophenolate mofetil, and/or glucocorticoids) was ineffective, not tolerated, or all are contraindicated.

   AND

   - **b.** Documented disease progression (including but not limited to) one of the following: a decline in forced vital capacity (FVC) of at least 10% in one year, worsening respiratory symptoms, decreased exercise capacity, decline in diffusing capacity of the lungs for carbon monoxide (DLCO) of >15% in one year, worsening on high-resolution computed tomography (HRCT), increased in acute medical care, such as hospitalization, and/or need for supplemental oxygen.

Product Group	Products	Criteria Requirements
Preferred Self-administered Products	- Tyenne (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria
Non-Preferred Self-administered Products	- Actemra (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to preferred self-administered therapies.

EE. Takayasu Arteritis

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** The diagnosis of **Takayasu arteritis** has been established by or in consultation with a specialist in rheumatology or immunology.
3. **Severity Criteria:** One of following criterion a or b below is met.
   - **a.** The patient has been unable to taper corticosteroids without experiencing worsening of disease (e.g., unable to achieve doses of 15 to 20 mg per day or less of prednisone or equivalent after 8 weeks).

   OR

   - **b.** The patient is experiencing breakthrough disease (for example, relapses or active disease flares) while stabilized on a csDMARD (such as methotrexate, leflunomide, mycophenolate mofetil, azathioprine or cyclophosphamide) for at least 8 weeks.

Product Group	Products	Criteria Requirements
Preferred Provider-administered products	- Tyenne (tocilizumab-aazg) IV	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Provider-Administered Products	- Actemra (tocilizumab) IV - Tofidence IV (tocilizumab-bavi)	**1.** Site of Care Requirements **2.** Diagnostic Criteria **3.** Severity Criteria **4.** There is a documented intolerance or contraindication to Tyenne (tocilizumab-aazg) IV.
Non-Preferred infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Preferred Self-administered Products	- Tyenne (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria
Non-Preferred Self-administered Products	- Actemra (tocilizumab) SC	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to Tyenne (tocilizumab).

FF. Transplant (Solid Organ), antibody-mediated rejection (AMR)

Tocilizumab IV may be considered medically necessary when criteria 1 and 2 below are met.

1. **Diagnostic Criteria:** When either criterion a or b below is met.
   a. **Prevention of antibody (Ab)-mediated rejection:** Prior to solid organ transplant and in the peri-operative period, for patients at high risk for Ab-mediated rejection, including highly sensitized patients, and those receiving an ABO-incompatible organ

   OR

   b. **Treatment of antibody-mediated rejection** (a.k.a. vascular rejection, humoral rejection): following solid organ transplant and confirmed by either biopsy or presence of panel reactive antibodies (PRAs).

AND

2. **Severity Criteria:** Treatment with immunoglobulin (IVIG), plasma exchange/pheresis (PLEX), and rituximab has been ineffective or is contraindicated.

Product Group	Products	Criteria Requirements
Level 1	- Tyenne (tocilizumab-aazg) IV	**1.** Diagnostic Criteria **2.** Severity Criteria
Non-Preferred Tocilizumab Products	- Actemra (tocilizumab) IV - Tofidence IV (tocilizumab-bavi)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **all Level 1** therapies.

GG. Ulcerative Colitis (UC) – Self-administered Products

1. **Diagnostic Criteria:** A diagnosis of **ulcerative colitis** (UC) when established by or in consultation with a specialist in gastroenterology.
2. **Severity Criteria:** At least one of the below criterion a, b, or c is met.
   - **a.** Treatment with an adequate course of corticosteroids (for example, prednisone 40 to 60 mg/day, oral budesonide 9 mg/day, or budesonide rectal for 7 to 14 days) was ineffective or is contraindicated.

   OR

   - **b.** The patient has been unable to taper an adequate course of corticosteroids without experiencing worsening of disease.

   OR

   - **c.** The patient is experiencing breakthrough disease (for example, active disease flares) while stabilized on a conventional immunomodulators, for at least 8 weeks. Conventional immunomodulators for UC include azathioprine, balsalazide, cyclosporine, mercaptopurine, mesalamine, and sulfasalazine.

Product Group	Products	Criteria Requirements
Level 1	- Entyvio (vedolizumab) SC - Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk) - Skyrizi (risankizumab) - Stelara (ustekinumab) - Tremfya (guselkumab)	**1.** Diagnostic Criteria **2.** Severity Criteria
Level 2	- Simponi (golimumab) SC - Rinvoq (upadacitinib) - Tofacitinib (Xeljanz/Xeljanz XR)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **adalimumab** was not effective after at least a 12-week treatment course unless not tolerated or contraindicated.
	- Omvoh (mirikizumab-mrkz)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with **ONE** of the following therapies was not effective after at least a 12-week treatment course unless not tolerated or contraindicated. a. Level 1 Therapy **OR** b. Rinvoq (upadacitinib), Tofacitinib (Xeljanz/Xeljanz XR)
Level 3	- Zeposia (ozanimod)	Refer to Medication Policy Manual, Zeposia, ozanimod, dru753

	- Velsipity (etrasimod)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** Treatment with at least **THREE** of the following therapies (i.e., any options listed in a or b below) was not effective after at least a 12-week treatment course unless not tolerated or contraindicated: **a.** Level 1 therapies **OR** b. Rinvoq (upadacitinib), tofacitinib (Xeljanz/Xeljanz)
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**
Non-Preferred Infliximab Products	- Infliximab products (Zymfentra)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic Criteria **2.** Severity Criteria **3.** There is a documented intolerance or contraindication to **Stelara (ustekinumab)**

HH. Ulcerative Colitis (UC) – Provider-administered Products

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **ulcerative colitis** (UC) when established by or in consultation with a specialist in gastroenterology.
3. **Severity Criteria:** At least one of the below criterion a, b, or c is met.
   - **a.** Treatment with an adequate course of corticosteroids (for example, prednisone 40 to 60 mg/day, oral budesonide 9 mg/day, or budesonide rectal for 7 to 14 days) was ineffective or is contraindicated.

   OR

   - **b.** The patient has been unable to taper an adequate course of corticosteroids without experiencing worsening of disease.

   OR

   - **c.** The patient is experiencing breakthrough disease (for example, active disease flares) while stabilized on a conventional immunomodulators, for at least two months. Conventional immunomodulators for UC include azathioprine, balsalazide, cyclosporine, mercaptopurine, mesalamine, and sulfasalazine.

Product Group	Products	Criteria Requirements
Level 1	- Entyvio (vedolizumab) - Skyrizi (risankizumab) - Stelara (ustekinumab) - Tremfya (guselkumab)	**1.** Site of Care Requirements *(Entyvio only)* **2.** Diagnostic Criteria **3.** Severity Criteria
	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Level 2	- Omvoh (mirikizumab-mrkz)	Refer to coverage criteria for ulcerative colitis (UC) – self-administered products
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Ustekinumab Products	- Ustekinumab biosimilars (Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	**1.** Diagnostic Criteria **2.** There is a documented intolerance or contraindication to **Stelara (ustekinumab)**

II. Uveitis – Self-administered Products

1. **Diagnostic Criteria:** A diagnosis of **uveitis** when established by or in consultation with a specialist in ophthalmology.
2. **Corticosteroid Criteria:** Treatment with corticosteroids (oral, periocular, or intravitreal injections) has been:
   a. Ineffective after two weeks of therapy.
   OR
   b. Unable to be tapered following an adequate course without worsening of disease.
   OR
   c. Not tolerated or all are contraindicated.
3. **Severity Criteria:** Treatment with at least one conventional immunomodulator was not effective after a 6-week treatment course, not tolerated, or all are contraindicated. Conventional immunomodulators for treatment of uveitis include azathioprine, cyclosporine, methotrexate, mycophenolate, or tacrolimus.

Product Group	Products	Criteria Requirements
Level 1	- Hadlima (adalimumab-bwwd) - Humira (adalimumab) - Simlandi (adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Corticosteroid Criteria **3.** Severity Criteria
Non-Preferred Adalimumab Products	- Adalimumab biosimilars (Abrilada, Amjevita, Cyltezo, Hulio, Hyrimoz, Idacio, Yuflyma, Yusimry, unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	**1.** Diagnostic Criteria **2.** Corticosteroid Criteria **3.** Severity Criteria **4.** There is a documented intolerance or contraindication to **Humira (adalimumab), Hadlima (adalimumab-bwwd), and Simlandi (adalimumab-ryvk).**

JJ. Uveitis – Provider-Administered Products

1. **Site of Care Requirements:** For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408].
2. **Diagnostic Criteria:** A diagnosis of **uveitis** when established by or in consultation with a specialist in ophthalmology.
3. **Corticosteroid Criteria:** Treatment with corticosteroids (oral, periocular, or intravitreal injections) has been:
   a. Ineffective after two weeks of therapy.

   OR

   b. Unable to be tapered following an adequate course without worsening of disease.

   OR

   c. Not tolerated or all are contraindicated.
4. **Severity Criteria:** Treatment with at least one conventional immunomodulator was not effective after a 6-week treatment course, not tolerated, or all are contraindicated. Conventional immunomodulators for treatment of uveitis include azathioprine, cyclosporine, methotrexate, mycophenolate, or tacrolimus.

Product Group	Products	Criteria Requirements
Level 1	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred Infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620

KK. Other Immunologic Conditions: Pyoderma gangrenosum, Sarcoidosis		
1. <u>Site of Care Requirements</u>: For provider-administered therapies, site of care administration requirements are met [refer to Medication Policy Manual, Site of Care Review, dru408]. **2. <u>Diagnostic Criteria</u>:** The diagnosis has been established by or in consultation with a specialist in pulmonology, rheumatology, immunology, or other specialist for the disease state. **3. <u>Severity Criteria</u>:** Treatment with a conventional immunomodulator (such as methotrexate, azathioprine, cyclosporine, hydroxychloroquine, leflunomide, or mycophenolate; see *Appendix 3*) was not effective or not tolerated.		
Product Group	**Products**	**Criteria Requirements**
Provider-administered products	- Avsola, Inflectra (infliximab)	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620
Non-Preferred infliximab Products	- Infliximab biosimilars (Renflexis, Ixifi) - Remicade (infliximab) - Unbranded Janssen infliximab product	Refer to Medication Policy Manual, Products with Therapeutically Equivalent Biosimilars/Reference Products, dru620

III. Administration, Quantity Limitations, and Authorization Periods

A. Regence Pharmacy Services considers medications in this policy to be self-administered, provider-administered, or either, as listed in **Table 1.**

B. When prior authorization is approved, each drug will be covered in the following quantities and for the following authorization periods outlined in **Table 2.**

C. Unless specifically noted in Table 2, authorization **may** be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective, with documented disease stability or improvement.

Table 1. Administration

Drug	Route	Pharmacy Services considers to be:
Oral administered medications	Oral (PO)	Coverable only under the pharmacy benefit (as a self-administered medication).
Intravenously (IV) administered medications	IV	Coverable only under the medical benefit (as a provider-administered medication).
Subcutaneously (SC) administered medications *(except for those listed below)*	SC	Coverable only under the pharmacy benefit (as a self-administered medication).
Exceptions for the following SC medications:		
Cimzia (certolizumab pegol) lyophilized powder vials	SC	Coverable only under the medical benefit (as a provider-administered medication).
Cimzia (certolizumab pegol) prefilled syringes and pens	SC	Coverable only under the pharmacy benefit (as a self-administered medication).
Cosentyx (secukinumab) prefilled syringes and pens	SC	Coverable only under the pharmacy benefit (as a self-administered medication).
Ilumya (tildrakizumab-asmn)	SC	Coverable only under the medical benefit (as a provider-administered medication).
Skyrizi (risankizumab-rzaa)	SC	Coverable under the pharmacy benefit (as a self-administered medication) OR coverable under the medical benefit (as a provider-administered medication).
Spevigo (spesolimab-sbzo)	SC	Coverable only under the medical benefit (as a provider-administered medication) for GPP **loading dose only** OR coverable under the pharmacy benefit (as a self-administered medication) for GPP **maintenance only.**
Ustekinumab (Stelara; biosimilars Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	SC	Coverable under the pharmacy benefit (as a self-administered medication) OR coverable under the medical benefit (as a provider-administered medication).

Table 2. Authorization Limits

Product	Route	Authorization Limit
Tocilizumab (Actemra; biosimilars Tofidence, Tyenne)	IV	- **AMR/Transplant (solid-organ):** Up to 7 infusions (up to 8 mg/kg with an 800 mg per infusion maximum) in a 6-month period based on a recommended infusion interval of every 4 weeks. Authorization shall be reviewed at least every 6 months to confirm that current medical necessity criteria are met, and the medication is effective. - **CRS:** Up to 4 infusions (up to 12 mg/kg). No additional doses will be authorized. - **PJIA:** Up to 13 infusions (up to 10 mg/kg) in a 12-month period based on a recommended infusion interval of every 4 weeks. - **GCA:** Up to 13 infusions (up to 6 mg/kg) in a 12-month period based on a recommended infusion interval of every 4 weeks. - **RA and Takayasu Arteritis:** Up to 13 infusions (up to 8 mg/kg) in a 12-month period based on a recommended infusion interval of every 4 weeks. - **SJIA:** Up to 26 infusions (up to 12 mg/kg) in a 12-month period based on a recommended infusion interval of every 2 weeks.
	SC	- **GCA and Takayasu Arteritis:** Up to 52 syringes in a 1-year period based on a recommended injection interval of 162 mg every week. - **PJIA:** Up to 26 syringes in a 1-year period based on a recommended injection interval of up to 162 mg every two weeks. - **RA:** Up to 52 syringes in a 1-year period based on a recommended injection interval of 162 mg once weekly or every other week. - **SJIA:** Up to 52 syringes in a 1-year period based on a recommended injection interval of 162 mg once weekly. - **SSc-ILD:** Up to 52 syringes in a 1-year period based on a recommended injection interval of 162 mg once weekly.

Product	Route	Authorization Limit
Adalimumab (Humira, biosimilars: Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz, Idacio, Simlandi, Yuflyma, Yusimry), unbranded: adalimumab-adaz, adalimumab-adbm, adalimumab-ryvk)	SC	- **AS, ERA, PJIA, PsA, RA:** Up to 40 mg every 2 weeks (up to 26 doses in a one-year period). - **HS:** Up to eight 40 mg syringes in the first month based on an initial dose of 160 mg followed by 80 mg on day 15 then 40 mg every week beginning on day 29 (54 syringes in the first 12-month period followed by up to 52 syringes per 12-month period, thereafter). Initial authorization shall be reviewed at 12 weeks to confirm that medication is effective. Thereafter, authorization may be reviewed annually to confirm that current medical necessity criteria are met, and that the medication is effective. - **PsO and Uveitis:** Up to 160 mg (four 40 mg syringes) in the first month based on an initial dose of 80 mg followed by 40 mg every other week (30 syringes in the first 12-month period followed by up to 26 syringes per 12-month period, thereafter). - **CD:** ▪ Up to 12 of the 40 mg syringes in the initial 3-month period; based on a dose of up to 160 mg on day 1, followed by 80 mg on day 15, then 40 mg every other week (31 syringes in the first 12-month period followed by up to 26 syringes per 12-month period, thereafter). ▪ *CD Dose Escalation*: Up to 40 mg every week may be considered medically necessary when there is clinical documentation that current treatment with adalimumab 40 mg every 2 weeks has had an inadequate response after at least a 12-week treatment course (up to 52 syringes per 12-month period). - **UC:** Up to 12 of the 40 mg vials in the initial 3-month period (induction period, per manufacturer labeling), then 40 mg every 2 weeks thereafter (31 syringes in the first 12-month period followed by up to 26 syringes per 12-month period, thereafter). - **Pediatric UC (Patients 5 to 17 years):** Up to 18 of the 40 mg syringes in the initial 3-month period; based on an initial dose of 160 mg on day 1, followed by 80 mg on days 8 and 15, then 80 mg every other week or 40 mg every week beginning on day 29 (58 syringes in the first 12-month period followed by up to 52 syringes per 12-month period, thereafter).
Bimzelx (bimekizumab)	SC	- **PsO:** Up to 320mg (two 160mg syringes/autoinjectors) at weeks 0, 4, 8, 12, and 16, then every 8 weeks thereafter (up to 20 syringes in the first 12-month period followed by up to 14 syringes/autoinjectors per 12-month period thereafter). For patients weighing 120kg or more: up to 320mg (two 160mg syringes/autoinjectors) at weeks 0, 4, 8, 12, and 16, then *every 4 weeks* (up to 28 syringes in the first 12-month period followed by up to 26 syringes/autoinjectors per 12-month period thereafter).[1] - **PsA, AS, NR-axSpA:** Up to 160 mg (one 160 mg syringe/autoinjector) per 28 days based on a dose of 160 mg every 4 weeks (12 syringes/autoinjectors per 12-month period).
Cibinqo (abrocitinib)	PO	**AD:** Up to 30 tablets per 30 days.

Product	Route	Authorization Limit
Cimzia (certolizumab pegol)	SC	- **CD, RA, PsA, AS, NR-axSpA:** Up to 3 doses (six 200 mg syringes/vials) in the first month based on an initial dose of 400 mg SC at weeks 0, 2, and 4 followed by 200 mg every two weeks or 400 mg every four weeks for maintenance (27 doses in the first 12-month period followed by up to 26 doses per 12-month period, thereafter). - **PJIA: (≥20 kg weight)** Up to 3 doses (six 200 mg syringes/vials) in the first month based on an initial dose of 200 or 400 mg at weeks 0, 2, and 4 followed by 200 mg every two weeks (27 doses in the first 12-month period followed by up to 26 doses per 12-month period, thereafter). **Note:** there is no dosage form for Cimzia that allows for patient self-administration for doses below 200 mg. - **PJIA: (10 kg to 20 kg weight)** Up to 3 vials in the first month based on an initial dose of 100 mg at weeks 0, 2, and 4 followed by 50 mg every two weeks (27 doses in the first 12-month period followed by up to 26 doses per 12-month period, thereafter). **Note:** doses less than 200 mg require administration by a health care professional using the vial kit. - **PsO:** Up to 400 mg (two 200 mg syringes/vials) every other week (up to 26 doses per 12-month period).
Cosentyx (secukinumab)	IV	- **AS, NR-axSpA, and PsA:** Up to 13 infusions (with loading dose: 6 mg/kg at week 0, followed by 1.75 mg/kg every 4 weeks thereafter; without loading dose: 1.75 mg/kg every 4 weeks; both dosing regimens with a maximum maintenance dose 300 mg per infusion).

Product	Route	Authorization Limit
	SC	- **AS:** Up to 5 doses (five 150 mg syringes or pens) in the first 4 weeks based on a loading dose of 150 mg at weeks 0, 1, 2, 3, and 4, followed by up to 300 mg every 4 weeks thereafter (16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter). - **Nr-axSpA:** Up to 5 doses (five 150 mg syringes or pens) in the first 4 weeks based on a loading dose of 150 mg at weeks 0, 1, 2, 3, and 4, followed by up to 150 mg every 4 weeks thereafter (16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter). - **ERA:** Up to 5 doses (five 150 mg syringes or pens for patients > 50 kg or five 75 mg syringes for patients < 50 kg) in the first four weeks based on dose given at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter (150 mg/ dose for patients > 50 kg or 75 mg /dose for patients < 50 kg; 16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter). - **HS:** Up to 5 doses (five 300 mg syringes or pens) in the first 4 weeks based on a loading dose of 300 mg at weeks 0, 1, 2, 3, and 4, followed by up to 300 mg every 4 weeks thereafter (16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter). A dosing interval of every 2 weeks (up to 26 doses per 12-month period) may be considered medically necessary in patients who have had an inadequate response to every 4-week dosing. - **PsA:** ▪ Up to 5 doses (five 150 mg syringes or pens) in the first four weeks based on a loading dose of 150 mg at weeks 0, 1, 2, 3, and 4, then 150 to 300 mg every 4 weeks thereafter (16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter). ▪ Pediatric PsA (Patients 2 to 17 years): Up to 5 doses (five 150 mg syringes or pens for patients > 50 kg or five 75 mg syringes for patients < 50 kg) in the first four weeks based on dose given at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter (150 mg/ dose for patients > 50 kg or 75 mg /dose for patients < 50 kg; 16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter). ▪ For patients with both PsA and PsO, dosing for PsO should be used. - **PsO:** ▪ Up to 5 doses (ten 150 mg syringes or pens) in the first four-week period based on dosing of 300 mg at weeks 0, 1, 2, 3, and 4, then up to 300 mg every 4 weeks thereafter (16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter). ▪ Pediatric PsO (Patients 6 to 17 years): Up to 5 doses (five 150 mg syringes or pens for patients > 50 kg or five 75 mg syringes for patients < 50 kg) in the first four weeks based on dose given at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter (150 mg/ dose for patients > 50 kg or 75 mg /dose for patients < 50 kg; 16 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter).

Product	Route	Authorization Limit
Entyvio (vedolizumab)	IV induction followed by IV maintenance	- **CD and UC:** ▪ Up to 6 doses (six 300 mg infusions) in a 6-month period based on a recommended starting interval of 300 mg infusions at zero, two and six weeks, then every eight weeks thereafter (9 infusions in the first 12-month period followed by up to 7 infusions per 12-month period, thereafter). ▪ Dose escalation: A dosing interval of every 4 weeks (up to 13 infusions per 12-month period) may be considered medically necessary in patients who have had an inadequate response to every 8-week dosing given for at least 24 weeks. Dosing more frequent than every 4 weeks is considered investigational (Table 5 *Investigational Uses: Dosing or Dose Escalation* for more information). ▪ Authorization may be reviewed at least annually and clinical documentation indicating that there is disease stability or improvement must be provided. - **Immune-Mediated Colitis:** Up to 6 doses (six 300 mg infusions) in a 6-month period based on a recommended starting interval of 300 mg infusions at zero, two and six weeks, then every eight weeks thereafter.
	IV induction followed by SC maintenance	- **CD and UC:** Up to 2 doses (two 300 mg infusions) in a 2-month period based on a recommended starting interval of 300 mg infusions at zero and two weeks, then up to 26 doses (twenty-six 108 mg injections) per 12-month period based on maintenance dosing of 108 mg SC every 2 weeks.
	SC maintenance	- **CD and UC:** Up to 26 doses (twenty-six 108 mg injections) per 12-month period based on maintenance dosing of 108 mg SC every 2 weeks.
Etanercept (Enbrel, biosimilars)	SC	- **AS, ERA, PJIA, PsA, RA:** Up to 50 mg per week given as a single 50 mg dose weekly or 25 mg twice weekly. - **PsO:** Up to 50 mg twice per week for the first 3 months (per manufacturer labeling), then 50 mg per week thereafter given as a single 50 mg dose weekly or 25 mg twice weekly.
Ilumya (tildrakizumab-asmn)	SC	**PsO:** Up to two doses (two 100 mg syringes) in the initial four-week period followed by one dose (one 100 mg syringes) every 12 weeks thereafter based on an initial dose of 100 mg at weeks 0 and 4 followed by maintenance dosing of 100 mg every 12 weeks (up to five 100 mg syringes in the first 12-month period followed by four 100 mg syringes per 12-month period thereafter).
Kevzara (sarilumab)	SC	**PMR, RA, PJIA:** Up to twenty-six 200 mg syringes in a one-year period based on a dose of 200 mg subcutaneously every two weeks.
Leqselvi (deuruxolitinib)	PO	**AA:** Up to sixty tablets per 30 days.
Litfulo (ritlecitinib)	PO	**AA:** Up to twenty-eight capsules per 28 days.
Olumiant	PO	**AA, RA:** Up to thirty 2 mg tablets per 30 days.

Product	Route	Authorization Limit
(baricitinib)		- *AA Dose Escalation*: Up to 4 mg daily may be considered medically necessary when there is clinical documentation that current treatment with baricitinib 2 mg daily has had an inadequate response (defined as not achieving a SALT score of ≤20 or at least 80% scalp hair coverage) after at least a 9-month treatment course.
Omvoh (mirikizumab-mrkz)	IV	**UC:** Up to 3 doses (three 300 mg infusions) in the first 8-week period based on a recommended starting interval of 300 mg infusions at zero, four, and 8 weeks, then up to 12 doses (twenty-four 100 mg SC injections) in the first 12-month period based on a maintenance dose of 200 mg SC given at week 12 and every 4 weeks thereafter.
	SC	**UC:** Up to 13 doses (twenty-six 100 mg injections) per 12- month period based on maintenance dosing of 200 mg SC every 4 weeks.
Orencia (abatacept)	IV	- **aGVHD:** Up to 4 infusions (up to 10 mg/kg) in a 4-week period based on a dose of 10 mg/kg/ dose given on days −1, +5, +14, and +28 post-transplant. - **RA, PJIA PsA:** Up to 3 infusions (up to 1000 mg) in the first 4-week period, based on weight-based loading doses at weeks 0, 2 and 4, followed by maintenance dosing of up to 13 infusions in a 12-month period, based on a dose of one infusion (up to 1000 mg) every 4 weeks (14 infusions in the first 12-month period followed by up to 13 infusions per 12-month period, thereafter).
	SC	- **PJIA:** Up to 52 doses (52 syringes) in a 12-month period, based on a weight-based dose of 50 mg to 125 mg every week. - **PsA:** Up to 52 doses (52 syringes) in a 12-month period, based on a dose of 125 mg every week. - **RA:** Up to 52 doses (52 syringes) in a 12-month period, based on a dose of 125 mg every week. A single IV loading dose (up to 1000 mg) may be authorized, if required.
Otezla (apremilast)	PO	**PsO, PsA, BD:** Up to 60 tablets per 30 days.
Siliq (brodalumab)	SC	**PsO:** Up to 3 doses (210 mg syringes) in the first month based on an initial dose of 210 mg subcutaneously at weeks 0, 1, and 2 followed by 210 mg every 2 weeks thereafter (27 doses in the first 12-month period followed by up to 26 doses per 12-month period, thereafter).
Simponi (golimumab)	SC	- **AS, PsA, RA:** Up to 12 doses (twelve 50 mg syringes) in a 1-year period based on a recommended injection interval of once monthly. - **UC:** Up to 2 doses in the initial four-week period based on a dose of 200 mg at week 0 and 100 mg at week 2, followed by maintenance therapy of 100 mg every four weeks (14 doses in the first 12-month period followed by up to 13 doses per 12-month period, thereafter).

Product	Route	Authorization Limit
Simponi Aria (golimumab)	IV	- **AS, PsA, RA:** Up to 2 infusions (up to 2 mg/kg) in the first 4-week period, based on weight-based loading doses at weeks 0 and 4, followed by maintenance dosing of up to 7 infusions in a 12-month period, based on a dose of one infusion (up to 2 mg/kg) every 8 weeks (8 infusions in the first 12-month period followed by up to 7 infusions per 12-month period, thereafter). - **PJIA:** Up to 2 infusions (up to 80 mg/m2) in the first 4-week period, based on body-surface-area-based loading doses at weeks 0 and 4, followed by maintenance dosing of up to 7 infusions in a 12-month period, based on a dose of one infusion (up to 80 mg/m2) every 8 weeks (8 infusions in the first 12-month period followed by up to 7 infusions per 12-month period, thereafter). - **Dose escalation:** Dosing interval of up to every 6 weeks may be considered medically necessary in patients who have had an inadequate response to every 8-week dosing given for at least 24 weeks. - Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met, and the medication is effective.
Skyrizi (risankizumab-rzaa)	SC (PsA, PsO)	**PsA, PsO:** Up to 2 doses (four 75 mg syringes or two 150 mg syringes) in the initial four-week period followed by 150 mg (two 75 mg syringes or one 150 mg syringe) every 12 weeks based on dosing of 150 mg SC at weeks 0 and 4 followed by maintenance dosing of 150 mg every 12 weeks (up to twelve 75 mg syringes or six 150 mg syringes in the first 12-month period followed by up to ten 75 mg syringes or five 150 mg syringes per 12-month period, thereafter).
	IV Induction (CD, UC)	**CD:** Up to 3 doses (three 600 mg infusions) in the first 8-week period based on a recommended starting interval of 600 mg infusions at zero, four, and 8 weeks, then up to 6 (six 180 mg or 360 mg cartridges) in the first 12-month period based on a maintenance dose of 180 mg or 360 mg given at week 12 and every 8 weeks thereafter. **UC:** Up to 3 doses (1,200 mg infusions) in the first 8-week period based on a recommended starting interval of 1200 mg infusions at zero, four, and 8 weeks, then up to 6 (six 180 mg or 360 mg cartridges) in the first 12-month period based on a maintenance dose of 180 mg or 360 mg given at week 12 and every 8 weeks thereafter).
	SC Maintenance dosing (CD, UC)	- **CD, UC:** Up to 7 doses (seven 180 mg or 360 mg cartridges) per 12- month period based on maintenance dosing of 180 mg or 360 mg SC every 8 weeks. - Authorization **may** be reviewed at least annually to confirm that current medical necessity criteria are met, and the medication is effective.
Sotyktu (deucravacitinib)	PO	**PsO:** Up to thirty tablets per 30 days based on a recommended dose of 6 mg daily.

<table>
<tr><th>Product</th><th>Route</th><th>Authorization Limit</th></tr>
<tr><td rowspan="2">Spevigo (spesolimab-sbzo)</td><td>IV</td><td>- GPP flare: Up to two 900 mg infusions given within a 4-week approval period, based on a single dose of 900 mg. A second additional 900 mg dose, given one week after the initial dose, may be given once if symptoms persist, within the 4-week approval period. NOTE: No more than two doses are coverable for any one flare.
- For consideration of treatment of a new flare (after at least 4 weeks): Authorization shall be reviewed to confirm that current medical necessity criteria are met, including flare criteria, and that the medication was effective for the previously treated flare. Each additional flare authorization is for a maximum of two 900 mg doses over a 4-week approval period.</td></tr>
<tr><td>SC</td><td>- GPP maintenance when not experiencing a flare: One 600 mg dose (four pre-filled 150 mg syringes) in the initial four-week period followed by 300 mg (two pre-filled 150 mg syringes) every four weeks thereafter.
- GPP maintenance after IV treatment of a flare: Four weeks after treatment with IV Spevigo (spesolimab), up to one 300 mg dose (two 150 mg prefilled syringes) every four weeks thereafter.
- Authorization may be reviewed at least every 6 months to confirm that current medical necessity criteria are met, and the medication is effective.</td></tr>
<tr><td rowspan="2">Ustekinumab (Stelara; biosimilars Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)</td><td>SC (PsO, PsA)</td><td>PsO and PsA:
- For all patients regardless of weight, up to five doses (five 45 mg syringes or vials) in a 48-week period based on dosing of 45 mg at week 0 and 4, then 45 mg every 12 weeks thereafter (up to five 45 mg syringes or vials in the first 12-month period followed by four 45 mg syringes or vials per 12-month period thereafter).
- Dose escalation: For patients in whom the 45 mg dose has shown benefit, but who have not achieved clinical remission after at least a 12-week trial, doses of up to 90 mg every 12 weeks may be considered medically necessary. Dosing more frequent than 90 mg every 12 weeks is considered investigational (see Table 5 Investigational Uses: Dosing or Dose Escalation for more information).</td></tr>
<tr><td>IV Induction (CD, UC)</td><td>- CD and UC Only: A single, weight-based IV infusion initially (vials, see chart below for details), then up to 6 doses (six 90 mg syringes or twelve 45 mg vials) based on maintenance dosing of 90 mg SC every 8 weeks. Initial IV dosing is as follows:
<table>
<tr><th>Weight</th><th>Dose</th></tr>
<tr><td>55 kg or less</td><td>260 mg (2 x 130 mg vial)</td></tr>
<tr><td>More than 55 kg to 85 kg</td><td>390 mg (3 x 130 mg vial)</td></tr>
<tr><td>More than 85 kg</td><td>520 mg (4 x 130 mg vial)</td></tr>
</table>
- Additional IV induction courses doses may be considered medically necessary in patients who have previously had an inadequate response to every 8-week dosing given for at least 24 weeks or who have had a break in therapy.</td></tr>
</table>

Product	Route	Authorization Limit
	SC Maintenance dosing (CD, UC)	- **CD and UC:** ▪ Up to 7 doses (seven 90 mg syringes or fourteen vials) in a one-year based on maintenance dosing of 90 mg SC every 8 weeks. ▪ Dose escalation/Re-induction: A dosing interval of up to every 4 weeks be or additional IV doses may be considered medically necessary in patients who have had an inadequate response to every 8-week dosing given for at least 24 weeks. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met, and the medication is effective.
Taltz (ixekizumab)	SC	- **PsO:** Up to 7 doses (eight 80 mg syringes) in the initial 12-week period based on a dose of 160 mg initially at week 0, followed by 80 mg at weeks 2,4, 6, 8, 10, and 12, followed by maintenance dosing of 80 mg every four weeks (up to eighteen 80 mg syringes in the first 12-month period followed by up to thirteen 80 mg syringes per 12-month period, thereafter). - **AS, PsA:** ▪ Up to 13 doses (fifteen 80 mg syringes) in a one-year period based on 160 mg initially at week 0, followed by maintenance dosing of 80 mg every 4 weeks (up to fifteen 80 mg infusions in the first 12-month period followed by up to thirteen 80 mg syringes per 12-month period, thereafter). ▪ For patients with both PsA and PsO, dosing for PsO should be used. - **NR-axSpA:** Up to 13 doses (thirteen 80 mg syringes) in a one-year period a dose 80 mg every 4 weeks.
Tofacitinib (Xeljanz, Xeljanz XR)	PO	- **AS, PsA, RA:** ▪ Xeljanz: Up to sixty 5 mg tablets per 30 days, based on a recommended dose of 5 mg twice daily. ▪ Xeljanz XR: Up to thirty 11 mg tablets per 30 days, based on a recommended dose of 11 mg once daily. - **PJIA:** ▪ Xeljanz Oral Solution: Up to 300 mL of 1 mg/mL oral solution per 30 days, based on a recommended dose of up to 5 mg (5 mL of oral solution) twice daily. ▪ Xeljanz: Up to sixty 5 mg tablets per 30 days, based on a recommended dose of 5 mg twice daily. - **UC:** ▪ Xeljanz: Up to sixty 5 mg or 10 mg tablets per 30 days based on a recommended dose of 5-10 mg twice daily. ▪ Xeljanz XR: Up to thirty 22 mg tablets per 30 days, based on a recommended dose of 22 mg once daily.
Tremfya (guselkumab)	SC (PsO and PsA)	**PsA, PsO:** Up to 2 doses (two 100 mg syringes/pens) in the first 4-week period based on an initial dose of 100 mg SC at weeks 0 and 4, followed by maintenance dosing of 100 mg every 8 weeks (up to eight doses in the first 12-month period followed by up to seven doses every 12 months thereafter).
	IV Induction (UC Only)	**UC:** Up to 3 doses (200mg infusions) within an 8-week period based on a recommended starting interval of 200mg at week 0, 4, and 8. Induction to be followed by the recommended SC maintenance dosing.

Product	Route	Authorization Limit
	SC Maintenance dosing for UC	**UC:** Up to 100 mg SC at Week 16, and every 8 weeks thereafter (up to five 100 mg syringes/autoinjectors in the first 12-month period followed by up to seven syringes/pens every 12 months thereafter), OR 200 mg SC at Week 12, and every 4 weeks thereafter (up to eleven 200 mg pens/syringes in the first 12-month period followed by up to thirteen 200 mg pens/syringes every 12 months thereafter).
Upadacitinib (Rinvoq, Rinvoq LQ))	PO	- **PsA, RA, AS, PJIA, NR-axSpA:** Up to thirty 15 mg tablets per 30 days, based on a recommended dose of 15 mg once daily. - **PsA/PJIA** oral solution 1 mg/mL: up to 360ml per 30 days (based on up to 6 mg twice daily). - **AD:** Up to 30 mg daily per 30 days, based on a recommended dose of up to 30 mg once daily. - **CD:** Up to 45 mg daily per 30 days for 12 weeks, then up to 30 mg daily, based on a recommended dose of up to 30 mg once daily for maintenance. - **UC:** Up to 45 mg daily per 30 days for 8 weeks then up to 30 mg daily, based on a recommended dose of up to 30 mg once daily for maintenance.
Velsipity (etrasimod)	PO	**UC:** Up to 30 tablets per 30 days.

Key: aGVHD: acute graft versus host disease; AD: atopic dermatitis; AMR: antibody mediated rejection; AS: ankylosing spondyloarthritis; BD: Behçet's disease; CD: Crohn's disease; CRS: cytokine-release syndrome; ERA: enthesitis-related arthritis; GCA: giant cell arteritis; GPP: generalized pustular psoriasis; HS: hidradenitis suppurativa; PJIA: polyarticular juvenile idiopathic arthritis; PMR: polymyalgia rheumatica; NR-axSpA: non-radiographic axial spondyloarthritis; PsA: psoriatic arthritis; PsO: plaque psoriasis; RA: rheumatoid arthritis; SJIA: systemic juvenile idiopathic arthritis; SpA: spondyloarthritis; SSc-ILD: systemic sclerosis-associated interstitial lung disease; UC: ulcerative colitis

IV. Not Medically Necessary Uses

Medications included in this policy are not considered medically necessary when used according to Table 3.

Table 3. Not medically Necessary Uses

Adalimumab	Maintenance doses > 40 mg every 2 weeks for RA	Adalimumab is considered not medically necessary when used in maintenance doses exceeding 40 mg every 2 weeks for rheumatoid arthritis (RA). The benefit of increasing the dose of adalimumab for the treatment of RA from 40 mg every other week to 40 mg weekly as monotherapy is uncertain. [2] - One study reported a modest improvement in ACR50; however, there were not significant improvements in ACR20 or ACR70. - Because the study was not designed to evaluate the comparative effectiveness of higher doses, the comparison between weekly and every other week dosing is exploratory. - As the added benefit of increasing the dose of adalimumab is uncertain, the use of 40 mg weekly is considered not medically necessary.
Unbranded adalimumab-adbm, adalimumab-adaz, adalimumab-ryvk	All uses	The unbranded biosimilars adalimumab-adbm and adalimumab-ryvk manufactured by Quallent Pharmaceuticals and adalimumab-adaz manufactured by Cordavis are considered not medically necessary for all uses.
Etanercept	Maintenance doses > 50 mg per week	Etanercept is considered not medically necessary when used in maintenance doses exceeding 50 mg per week. - There is no data available establishing that therapy with etanercept at a dose of 50 mg twice weekly (beyond 3 months of initial therapy) offers a significant advantage over continued therapy with 50 mg of etanercept weekly. [3 4]
Ilumya (tildrakizumab-asmn)	Doses > 100 mg every 12 weeks	Ilumya (tildrakizumab-asmn) is considered not medically necessary when used in doses exceeding 100 mg every 12 weeks. - Ilumya (tildrakizumab-asmn) is FDA approved for PsO at a dose of 100 mg every 12 weeks. While clinical trials of in PsO evaluated doses 100 mg and 200 mg every 12 weeks, both doses appeared to have similar efficacy. Therefore, the use of doses higher than 100 mg every 12 weeks is considered not medically necessary. [5]

Ustekinumab (Stelara; biosimilars Imuldosa, Otulfi, Pyzchiva, Selarsdi, Wezlana)	Initial doses of 90 mg for PsO/PsA	Ustekinumab is considered not medically necessary at initial doses of 90 mg per every 12 weeks, regardless of weight. - Given that more than half of all patients respond to the 45 mg dose, and the significantly higher cost of 90 mg dosing, a trial of 45 mg for all patients, regardless of weight, represents the best treatment value for PsO/PsA. - When treatment with 45 mg has resulted in some benefit but has not a clinical remission after at least a 12-week trial, up to 90 mg every 12 weeks may be considered medically necessary. - Dosing was established through a post-hoc analysis of the results of the Phoenix 1 and Phoenix 2 trials. The recommended weight-based dosing scheme was not studied in a prospective manner. [6 7] Patients greater than 100 kg were found to have, on average, a better response to treatment when receiving a dose of 90 mg every 12 weeks compared with 45 mg every 12 weeks. ▪ In Phoenix 1, 68.5% and 54.0% of patients greater than 100 kg achieved PASI75 in the 90 mg and 45 mg groups, respectively. ▪ In Phoenix 2, 71.1% and 49.1% of patients greater than 100 kg achieved PASI75 in the 90 mg and 45 mg groups, respectively. - There is no evidence to support the need for re-induction when the dose is escalated from 45 mg to 90 mg is made.
Olumiant (baricitinib)	Doses > 2 mg daily in rheumatoid arthritis (RA)	Olumiant (baricitinib) is considered not medically necessary when used in doses exceeding 2 mg daily for RA. - Olumiant (baricitinib) is FDA approved for 2 mg daily in RA. - While doses of 4 mg have been shown to be effective, a signal of thromboembolic risk was identified, and the dose was not approved in RA. Further controlled-studies, including a comparative study between the 2 mg and 4 mg, are needed to clarify the risk-benefit profile of the higher dose in RA. [8]
	COVID-19, outpatient use	Olumiant (baricitinib) is considered not medically necessary when used for COVID-19 in the *outpatient* setting. - Olumiant (baricitinib) is FDA approved for the treatment of COVID-19 in *hospitalized* adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) - When used to treat COVID-19, dosing is limited to 14 days or until hospital discharge, whichever occurs first.[9] - There is no available safety and efficacy data supporting the use of baricitinib for COVID-19 in the outpatient setting.

V. Investigational Uses

A. Combination use of targeted DMARDs.

B. Unless otherwise specified in the coverage criteria above, medications included in this policy are considered investigational when used for all other conditions, due to lack of published data, lack of high-quality data, or lack of positive data. Details of select 'Investigational Uses' are listed below in tables 4 and 5.

C. Unless specified in the Administration, Quantity Limitations, and Authorization Periods or as 'Not Medically Necessary Uses' above, all dose escalations above the quantity limit are considered investigational (Additional details are in Table 5).

Table 4: Investigational Uses: Indications

Blau's Syndrome	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of Blau's syndrome. - No randomized, controlled trials have been published evaluating the use of adalimumab in patients with Blau's syndrome.
Extraintestinal complications of IBD: Arthritis (IBD-associated arthropathy)	- Arthritis is a common extraintestinal complication of IBD (either UC or CD). However, there is no reliable evidence to establish the efficacy or safety of targeted DMARDs in patients with arthritis associated with IBD who do not otherwise require targeted therapy. - The evidence is limited to small, short-term, open-label trials and case studies with infliximab. Given the lack of blinding and lack of control arm, the incremental benefit of infliximab therapy is uncertain. [10] - There are no reliable published clinical trials with any other biologic DMARDs for treatment of arthritis associated with IBD (in the absence of active bowel disease). - Of note: patients with IBD and a confirmed diagnosis of CD or UC with active bowel disease may be covered per the coverage criteria for management of IBD symptoms (active bowel disease). However, the isolated arthritis symptoms (in the absence of active bowel disease) are not coverable.
Graft Versus Host Disease (GVHD)	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of GVHD. - In one open-label clinical trial (n=62) incidences of GVHD-related mortality, non-relapse mortality, and overall survival were not different between patients treated with infliximab or placebo. [11]
Granuloma Annulare	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of granuloma annulare. - While case reports have been published describing the treatment of granuloma annulare with etanercept, other reports have been published describing no effect, or an association with the formation of granuloma annulare and treatment with TNF-alfa inhibitors, including etanercept. Additional information is necessary to the benefit of etanercept in this population. [12]
Guttate Psoriasis	- Guttate psoriasis is a type of cutaneous psoriasis. It is characterized by the presence of small, erythematous papules whereas plaque psoriasis is characterized itchy, red, scaly, raised lesions on the skin. Guttate psoriasis is typically managed with topical agents or UV light therapy. - There is no evidence to establish the efficacy or safety of targeted DMARDs in the treatment of guttate psoriasis.
Immune-mediated reactions (other than colitis or CRS with CAR-T cell therapy) due to immunotherapy	- There is no reliable evidence to establish the efficacy of safety of targeted DMARDs in the treatment of immune-mediated reactions, including but not limited to pneumonitis, hepatitis, or arthritis, due to PD-1, PDL-1, or CTLA4 inhibitors. - PD-1, PDL-1, and CTLA4 inhibitors contain warnings for immune-mediated hepatitis. In clinical trials, patients who experienced immune-mediated hepatitis were managed with systemic corticosteroids and mycophenolate. - For immune-mediated hepatitis, NCCN guidelines state that mycophenolate is recommended instead of infliximab due to the concern for hepatotoxicity with infliximab.

Reactive Arthritis/Reiter's Syndrome	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of reactive arthritis/Reiter's Syndrome.
Sciatica	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of sciatica. - Evidence for infliximab in the treatment of sciatica is limited to a randomized controlled trial in 40 patients. At 52 weeks, 67% of patients who received infliximab reported no pain compared with 63% of patients who received placebo (p = 0.72). This difference was not statistically significant. [13 14] - There are no randomized controlled trials that evaluate the efficacy and safety of a commercially available formulation of etanercept in the treatment of sciatica. - Evidence for adalimumab in the treatment of sciatica in limited to a small randomized, controlled trial evaluated adalimumab in 61 patients. There was a modest improvement in pain as measured by a 10-point visual analog scale and at three years, the need for back surgery was reduced in adalimumab-treated patients; however, larger clinical trials are needed to confirm the benefit of adalimumab in this population. [15 16]
Scleroderma	- There is insufficient evidence to support the use of tocilizumab for scleroderma. The evidence is limited to one small, placebo-controlled, phase 2 trial using subcutaneous tocilizumab (n=88). The trial found a change in modified Rodan skin score, but no significant difference in skin thickening, disability, fatigue, itching, or patient or clinician global disease severity. Larger Phase 3 trials are needed to establish the safety and efficacy of tocilizumab for scleroderma. [17]
Sjögren's Syndrome	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of Sjögren's syndrome. - Evidence for etanercept in Sjögren's syndrome is limited a small trial, in which there were no significant differences in the subjective measures of disease severity. [18]
Systemic Lupus Erythematous (SLE)	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of SLE. - A small uncontrolled clinical trial reported modest efficacy with infliximab in patients with systemic lupus erythematosus, though larger, better designed trials are needed to confirm these results. [19] - A small preliminary study assessing the use of tocilizumab in patients with SLE found promising signs of response, but larger, controlled studies will be needed to establish the efficacy and safety in this population. [20] - One small randomized, placebo-controlled trial evaluated the use of abatacept in patients with non–life-threatening SLE and polyarthritis. The primary endpoint (proportion of patients with a new flare of SLE) was not met but was suggestive of a positive effect in certain exploratory measures. Further study is needed to establish the safety and efficacy of abatacept in SLE. [21] - One 24-week, phase 2 study evaluated the use of baricitinib in patients with SLE. Results demonstrated that baricitinib 4 mg once may reduce SLE disease activity; however, results for the 2 mg dose were not significant. Larger, longer-term studies are needed to clarify the benefit of baricitinib in SLE. [22]

Wegener's Granulomatosis	- There is no reliable evidence to establish the efficacy or safety of targeted DMARDs in the treatment of Wegener's Granulomatosis. - Evidence for infliximab is limited to one small clinical trial in 17 patients. Both infliximab and rituximab appeared to provide benefit in achieving complete or partial response; however, there was a trend favoring rituximab. Additionally, rituximab was better able to maintain remission during the long-term follow-up.

Table 5: Investigational Uses: Dosing or Dose Escalation

Combination use of targeted immunomodulators	- The use of combination (more than one) targeted DMARD therapy, such as Humira (adalimumab), Otezla (apremilast), tofacitinib (Xeljanz/Xeljanz XR), Sotyktu (deucravacitinib), or Entyvio (vedolizumab), is considered investigational (includes all medications included in this policy). *Combination use of apremilast and other targeted immunomodulators:* - There is no reliable evidence to establish the efficacy or safety of the combined use of apremilast and other targeted DMARDs (such as biologics) in the treatment of PsO or PsA. - There are no randomized, controlled trials evaluating the combined use of apremilast and any other targeted DMARD. The evidence is limited to retrospective studies in small numbers of patients. Additional studies are needed to establish long-term efficacy and the overall risk-benefit profile of combination use.
Secukinumab – Maintenance doses higher than 300 mg every 4 weeks for PsA or PsO	- There is insufficient evidence to support the use of secukinumab at maintenance doses higher than 300 mg every 4 weeks for PsO. - Phase 3 clinical trials of secukinumab for PsA and PsO evaluated maintenance dosing regimens of 150 mg or 300 mg every 4 weeks. Higher or more frequent doses have not been evaluated. It is uncertain if there is any additional benefit with increased dosing and the safety profile has not been evaluated.
Secukinumab – Maintenance doses higher than 150 mg every 4 weeks for AS	- There is insufficient evidence to support the use of secukinumab at maintenance doses higher than 150 mg every 4 weeks for AS. - Phase 3 clinical trials of secukinumab for AS evaluated maintenance dosing regimens of 150 mg every 4 weeks. Higher or more frequent doses have not been evaluated. It is uncertain if there is any additional benefit with increased dosing and the safety profile has not been evaluated.
Ustekinumab – Doses higher than 90 mg every 12 weeks for PsO or PsA	- There is insufficient evidence to support the use of ustekinumab at maintenance doses higher than 90 mg every 12 weeks for PsO or PsA. - There are no randomized, controlled trials to support doses higher than 90 mg every 12 weeks in PsO or PsA.
Vedolizumab - Doses higher than 300 mg every 4 weeks	- There is insufficient evidence to support the use of vedolizumab at maintenance doses higher than 300 mg every 4 weeks for CD and UC. - In phase 3 clinical studies of vedolizumab in CD and UC the highest dose of vedolizumab used was 300 mg every four weeks. Higher or more frequent doses have not been evaluated.

Position Statement

- There are many treatments for chronic inflammatory conditions that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines.
- The intent of this policy is to allow coverage of each medication in settings where it has been safe and effective, with coverage after use of lower cost standard of care therapies, including preferred targeted DMARD options.
- Non-medical therapies, such as prescribed exercise therapy, physical therapy, weight loss, and smoking cessation are important treatment plan components for patients suffering from many chronic inflammatory conditions.
- When a systemic medication therapy is needed to manage a chronic inflammatory condition, generic oral therapies usually offer the best value.
- When non-medical therapies and oral medications are inadequate, a targeted DMARD or immunomodulator [conventional synthetic DMARD (csDMARD)] may be appropriate and use is supported by guidelines. Targeted DMARDs include non-biologics and biologics. Biologics include both anti-TNF and non-anti-TNF options.
- When there is no demonstrated difference in safety or efficacy among the studied targeted DMARDs, the medication with the lowest cost often provides the best value for members.
- Individual responses and tolerability of targeted DMARDs, including biologics, are unpredictable and may vary between patients. If one targeted DMARD provides an inadequate response, another targeted DMARD may yet be effective.
- Due to the potential for development of antibodies with anti-TNF therapies which may result in loss of efficacy, clinical practice guidelines generally recommend a trial with one to two anti-TNF therapies. [23-27] For those who have an inadequate response or intolerance to a TNF inhibitor, it is reasonable to consider a targeted treatment with an alternative mechanism of action and proven efficacy for the patient's diagnosis.
- All DMARDs, conventional and targeted, are immunosuppressants and carry a risk of increased infection. Risk and infection type varies by mechanism of action and medication.
- 2021 JAK1/2/3 inhibitors label updates placed their usage after other systemic therapies for the indications in which they have FDA approval due to safety concerns (which include major cardiovascular events and mortality among other concerns).
- There is significant variation in recommended dosing across indications for individual medications, particularly with targeted agents; therefore, when multiple dosage forms of a targeted agent are available, coverage can be provided for those indications where the dosage form has been evaluated in randomized controlled trials, the dosage form has been proven safe and effective, and for which the dosage form has an established dose. For all other indications, the specific dosage form will be considered investigational.
- The medications in this policy, including loading doses, are coverable for the lowest effective doses, aligned with how they were studied in clinical trials, including use of loading doses.

Evidence summary:

Rheumatic Conditions – Background

- Treatments for rheumatic conditions may include non-medical therapies, medications for the management of symptoms, medications that modify the disease course such as conventional synthetic or targeted disease modifying anti-rheumatic drugs (DMARDs).
- Medications to control inflammation such as nonsteroidal anti-inflammatory medications (NSAIDs, e.g., ibuprofen, indomethacin, and naproxen) and glucocorticoids (oral or injected into the joint) are effective for the management of symptoms, particularly during the early stages of disease.
- Generic, conventional synthetic DMARDs (csDMARDs), including methotrexate (MTX), hydroxychloroquine, leflunomide, and sulfasalazine are effective for decreasing symptoms and slowing disease progression, and are recommended by current guidelines.
  * MTX is generally the initial csDMARD for rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA).
  * csDMARDs have known risks. The management of these risks is well established.
- Targeted DMARDs can also decrease symptoms, help preserve joint functioning, and slow the progression of the disease.
- In RA, the best response is seen when targeted DMARDs are used in combination with MTX. ACR Guidelines for the treatment of RA recommend that biologic therapy should be used in combination with methotrexate, when possible, due to increased efficacy over biologic monotherapy. Infliximab and golimumab have been shown to be effective only when used with MTX.
- In JIA, combination therapy with a csDMARD is strongly recommended for infliximab to reduce the risk of anti-drug antibodies against infliximab. [28]

Rheumatic Conditions – Axial Spondyloarthritis (SpA)

- Axial spondylarthritis (SpA) is a form of inflammatory arthritis that includes ankylosing spondylitis (AS) and non-radiographic axial spondylarthritis (nr-axSpA).
- Several targeted DMARDs (as listed in the coverage criteria) have been shown to be effective in the treatment of AS or nr-axSpA.
- There is moderate quality evidence to support the use of targeted DMARDs, particularly TNF inhibitors, in SpA. Clinical trials have consistently shown that treatment with TNF inhibitors reduced disease activity in this population.
- 2019 ACR guidelines for both AS and nr-axSpA recommend TNF inhibitors as the first-line targeted agent. They do not recommend any one TNF inhibitor over another except in patients who also have inflammatory bowel disease or iritis in which case adalimumab or infliximab would be recommended over etanercept. [29]
- Because of similar efficacy among the studied targeted DMARDs, non-preferred/non-formulary options are coverable when preferred/formulary options are ineffective, as detailed in the coverage criteria.

Rheumatic Conditions – Enthesitis-related Arthritis (ERA)

- ERA is a type of juvenile idiopathic arthritis (JIA) that causes swelling or inflammation of the entheses (tendon-to-bone insertion sites).
- 2019 ACR guidelines for Juvenile Idiopathic Arthritis recommend NSAIDs as initial therapy for patients with ERA followed by TNF inhibitors. Methotrexate or sulfasalazine may be used if TNF inhibitors are contraindicated. ACR guidelines have not been updated to include secukinumab.[28]
- There is little comparative evidence to distinguish among the biologic options for ERA due to the lack of head-to-head comparisons.
- The evidence for secukinumab in ERA is based on one small placebo-controlled phase III withdrawal trial that demonstrated a reduced time to disease flare for people on secukinumab versus placebo.[30]

Rheumatic Conditions – Polyarticular Juvenile Idiopathic Arthritis (PJIA); Juvenile Rheumatoid Arthritis (JRA)

- Several targeted DMARDs (as listed in the coverage criteria) have been shown to be effective in the treatment of JIA.
- 2019 ACR guidelines for JIA recommend methotrexate, leflunomide, or sulfasalazine as initial therapy for patients with JIA. Methotrexate is recommended over leflunomide and sulfasalazine due to a larger body of evidence. Biologic agents are recommended in patients who have disease activity despite treatment with methotrexate, sulfasalazine, or leflunomide or in patients with high disease activity or have disease in high-risk joints. [28]
- Combination therapy with a biologic and a csDMARD is recommended to prevent the formation of anti-drug antibodies.
- There is little comparative evidence to distinguish among the targeted options for JIA. Guidelines state that there are mostly equivalent data for safety and efficacy between the biologics and there are lack of head-to-head comparisons between them.
- In patients who have had an inadequate response to a TNF inhibitor, switching to a non-TNF biologic is preferred over a second TNF inhibitor. However, a second TNF inhibitor may be appropriate if patients had a good response to the initial TNF inhibitor. [28]

Rheumatic Conditions – Polymyalgia Rheumatica (PMR)

- The ACR/EULAR guidelines for treatment of PMR recommend treatment with corticosteroids for flare with a long, slow taper. Prior trials in anti TNFI's have been unsuccessful, and trials with treatment with conventional DMARDs have yielded mixed results.
- Sarilumab has demonstrated modest improvement in the ability of patients to maintain sustained remission at one year compared to placebo with a steroid taper.

Rheumatic Conditions – Psoriatic Arthritis (PsA)

- Several targeted DMARDs (as listed in the coverage criteria) have been shown to be effective in the treatment of PsA.
- ACR Guidelines recommend TNF inhibitors as the first-line treatment for PsA. However, other mechanisms can be used in patients with contraindications to TNF inhibitors. The guidelines do not specify the use of any one TNF inhibitor over another. [31]

- In patients who have failed a TNF inhibitor, a second TNF inhibitor is recommend over switching to a different mechanism of action (e.g., an IL-12/23 inhibitor, biologic, IL-17 inhibitors, abatacept, or JAK inhibitor). However, a different mechanism of action may be used in cases of primary TNF inhibitor failure (no response) or a serious adverse event due to a TNF inhibitor. [31]
- Because of similar efficacy among the studied targeted DMARDs, non-preferred/non-formulary options are coverable when preferred/formulary options are ineffective, as detailed in the coverage criteria.

Rheumatic Conditions – Rheumatoid Arthritis (RA)

- Several targeted DMARDs (as listed in the coverage criteria, as well as rituximab) have been shown to be effective in the treatment of RA.
- The efficacy of these targeted DMARDs in the treatment of RA is similar. Guidelines do not recommend one specific targeted DMARD. The initial choice of therapy includes biologic DMARDs (TNF inhibitors or a non-TNF biologic) or targeted synthetic DMARDs (e.g., JAK inhibitors). However, 2021 ACR guidelines have not accounted for recent drug safety communications regarding the risk of serious heart-related events with JAK inhibitors. [32 33]
- In patients who have had an inadequate response to targeted therapy, guidelines recommend switching to a targeted DMARD of a different class rather a different DMARD of the same class. [32]
- Guidelines have recommendations for specific patient populations including non-TNF inhibitors over TNF inhibitors for patients with New York Heart Association (NYHA) class III or IV heart failure. This recommendation is based on the risk of worsening heart failure observed in RCTs of TNF inhibitors in patients with heart failure. [32]
- Because of similar efficacy among the studied targeted DMARDs, non-preferred/non-formulary options are coverable when preferred/formulary options are ineffective, as detailed in the coverage criteria.

Rheumatic Conditions – Systemic Juvenile Idiopathic Arthritis (SJIA)

- Systemic JIA is a subtype of juvenile idiopathic arthritis that is associated with systemic inflammation. [34]
- Systemic JIA is defined as arthritis in at least one joint for at least 6 weeks in patients less than 16 years of age that is accompanied for other systemic manifestation such as erythematous rash, lymphadenopathy, hepatomegaly, or splenomegaly, and serositis. [34]
- Several targeted agents (as listed in the coverage criteria) have been shown to be effective or are recommended by clinical practice guidelines in the treatment of SJIA. [24]
- Due to lack of high-quality data, the comparative efficacy for these agents in the treatment of SJIA is uncertain.
- The efficacy of these targeted DMARDs (as listed in the coverage criteria) in the treatment of SJIA is similar. However, there is a significant difference in the cost between these treatment options. Therefore, the costlier treatment options are coverable only when the less costly options are ineffective.

Rheumatic Conditions – Giant Cell Arteritis (GCA)

- Data evaluating the use of biologic agents in the treatment of GCA is limited; however, there are few treatment options for this condition, which can result in serious complications.
- Subcutaneous tocilizumab in combination with prednisone has been shown to improve remission rates compared to prednisone alone in patients with *newly diagnosed or relapsing* GCA. [35]
- Intravenous tocilizumab is approved for the treatment of GCA; evidence is based primarily on pharmacokinetic exposure data and extrapolation to the efficacy established for subcutaneous tocilizumab in patients with GCA.[36]
- Evidence for the use of TNF inhibitors is lacking, as several small trials have not shown benefit in the treatment of GCA.

Rheumatic Conditions – Behçet's disease

- Evidence for efficacy of apremilast for Behçet's disease (BD) was based on one phase 3, randomized, controlled trial. [37 38] The study included patients who were previously treated with at least one non-biologic therapy and were candidates for systemic therapy. Patients had to have at least two oral ulcers at screening and at least two oral ulcers at randomization. Patients with active major organ involvement were excluded and concomitant treatment for Behçet's disease was not allowed (such as with oral csDMARDs).
- Endpoints were the number of oral ulcer and pain from oral ulcers (rated from 0 to 100).
- At week 12, apremilast significantly improved the daily average number of oral ulcers and reduced pain from oral ulcers. Additionally, higher rates of patients who received apremilast were oral ulcer-free at 12 weeks compared to placebo (53% vs. 22%).

Skin conditions - Atopic Dermatitis (AD)

- AD is a chronic, pruritic inflammatory skin disease. It is often associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and asthma.
- Treatment guidelines recommend the use of topical corticosteroids and topical calcineurin inhibitors in a step-wise approach, as well as systemic immunosuppressants, such as oral cyclosporine, including when topical therapies are insufficient.
- Clinical studies with systemic biologics were conducted in patients with atopic dermatitis who were not adequately controlled with topical medications.[39-41]
- Based on a recent long-term safety study with tofacitinib there is concern that increases in cardiovascular events, venous thromboembolism, and cancer may be class effects of all JAK inhibitors. Additional long-term controlled safety studies are needed to evaluate these concerns further.
- In comparative trials versus Dupixent (dupilumab), Rinvoq (upadacitinib) showed modest improvements in itchiness and skin clearance[42] but the benefit may be outweighed by potential long-term safety concerns.
- While there are two topical calcineurin inhibitors currently available, topical tacrolimus is indicated for moderate to severe AD whereas Elidel (pimecrolimus) is indicated for mild to moderate disease.

- Goals of treatment include clearance of skin lesions, control of itch, prevention of adverse events and triggers associated with various treatment modalities and preventing future exacerbations.

Skin Conditions – Chronic Plaque Psoriasis (PsO)

- There are many treatments for chronic plaque psoriasis (PsO) that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines.
- Light therapy, including UVB and PUVA, is effective and safe, and PUVA may result in long-term remission. When patients are not able to receive office-administered light therapy, light units for home use may be an appropriate alternative (see Appendix 2 for absolute and relative contraindications for phototherapy/photochemotherapy).
- AAD guidelines (2014) recommend phototherapy after failure of first-line treatment (emollients, topical steroids, and topical calcineurin inhibitors). Most patients with mild-to-moderate psoriasis can achieve adequate control with topical medications or phototherapy.
- When systemic therapy is needed to manage psoriasis, csDMARDs often provide the best value. [43]
    * Conventional synthetic DMARDS (csDMARDs), including MTX, cyclosporine, and Soriatane (acitretin), have a proven track record and have been the standard of care for many years.
    * csDMARDs typically take effect with 6 weeks though some patients may require 12 weeks to have full effect. Among these options, cyclosporine is known to work rapidly.
    * Like all immunosuppressants, including targeted DMARDs, the csDMARDs have known risks. The management of these risks is well established.
- Targeted DMARD may be appropriate for patients with moderate to severe psoriasis (e.g., at least 10% BSA and/or significant pain or functional impairment due to the PsO or when conventional topical or oral therapies, or phototherapy have been inadequate).
- Several targeted DMARDs (as listed in the coverage criteria) have been shown to be effective in the treatment of moderate to severe PsO.
- Within each drug class, efficacy among drugs is similar. In general, when comparing different classes, agents directed against both IL-17A and IL-17F (bimekizumab), IL-17A (ixekizumab and secukinumab) and IL-23 (risankizumab) are more effective at producing skin clearance than TNF inhibitors and other mechanisms of action (PDE-4 inhibitors and tyrosine kinase inhibitors). [43] However, safety is also considered. Despite bimekizumab's head-to-head superiority data compared to ustekinumab, secukinumab and adalimumab, there are concerns for potential for suicidal ideation and behavior and long-term data is lacking. There are several other agents with good efficacy and established safety.

Skin conditions – Generalized Pustular Psoriasis[44-47]

- GPP is a rare subtype of psoriasis. Flares are characterized by an abrupt onset of widespread painful pustules which can coalesce into larger, "lakes of pus" overlying painful erythema. Significant flares are often accompanied by systemic symptoms, notably fever,

general malaise, and extracutaneous manifestations such as arthritis, uveitis, and neutrophilic cholangitis, and may be associated with life-threatening complications,

- Acute flares may be idiopathic or may be triggered by infection, withdrawal, or administration of certain medications (including those used in the treatment of GPP such as corticosteroids, methotrexate, or tumor necrosis factor [TNF] inhibitors), pregnancy, or stress.
- Treatment guidelines recommend the identification and management of potential triggers.
- Choice of therapy depends on disease acuity. Acitretin and methotrexate are the preferred initial treatments for adults with relatively stable GPP due to their relatively slow onset of action. They can be used for long-term maintenance treatment.
- Cyclosporine and infliximab are used for more severe, acute GPP. Cyclosporine or infliximab are often considered first line for severe GPP due to their rapid onset of action. Once control of acute disease is achieved, patients may be maintained on fast-acting therapies or transitioned to acitretin or methotrexate for long-term treatment. There is no comparative data regarding relative efficacies of agents used for GPP.

Skin Conditions – Hidradenitis Suppurativa

- High-quality data evaluating the use of targeted DMARDs in the treatment of hidradenitis suppurativa (HS) are limited; however, there are relatively few treatment options for this condition.
- Although adalimumab is FDA approved for the treatment of HS, infliximab also has data to support use in this indication. [48]
    * A high-quality systematic review showed that weekly-dosed adalimumab improved quality of life in HS compared to placebo; although, the effect size was approximately equal to what is considered a minimally clinically important difference.
    * In the same systematic review, infliximab also improved quality of life compared to placebo, with an effect size well above the threshold for a minimally clinically important difference.
- Trials of adalimumab and secukinumab in HS only included patients with more severe disease, defined as Hurley Stage II or III disease and with at least three abscesses or inflammatory nodules.
- Trials showed that adalimumab significantly improved the hidradenitis suppurativa response rate after 12 weeks of treatment; however, efficacy and safety beyond 12-weeks of treatment has not been established. [49 50]
- Trials showed that secukinumab significantly improved the hidradenitis suppurativa response rate by 16 weeks of treatment.[30]
- Additional long-term randomized controlled trials are needed to understand relative efficacy of other treatments, the safety associated with weekly-dosed adalimumab, and role of oral, non-biologic/non-targeted DMARD treatments for HS.
- Evidence-based guidelines for hidradenitis suppurativa are not available, primarily due to lack of data. However, standard of care therapy reviews suggest the following:
    * Patients may benefit from non-pharmacologic interventions such as good personal hygiene, smoking cessation, and weight-loss.

* For mild to moderate HS, topical clindamycin and tetracyclines have a proven track record of safety and have been the standard of care.
* When systemic therapy is needed to manage refractory hidradenitis suppurativa, oral therapies often provide the best value. Options include systemic antibiotics (e.g., oral tetracyclines, clindamycin, rifampin, moxifloxacin, metronidazole), hormonal therapies (e.g., oral contraceptives, spironolactone), cyclosporine, finasteride, metformin, or oral retinoids.

Gastrointestinal conditions –Crohn's Disease (CD) and Ulcerative Colitis (UC)

- There are many treatments for Crohn's disease (CD) and ulcerative colitis (UC) that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines. [51 52]
- Several targeted DMARDs (as listed in the coverage criteria) have been shown to be effective in the treatment of CD and/or UC, for inducing and maintaining remission compared to placebo.
- Due to a lack of head-to head comparative studies, the overall comparative efficacy for these targeted DMARDs in the treatment of CD is uncertain. There is also a lack of comparative evidence for treatment of UC. Therefore, non-preferred/non-formulary options are coverable when preferred/formulary options are ineffective, as detailed in the coverage criteria.
- Although studied in UC, there are no controlled trials of golimumab in CD. Likewise, although studied in CD, there are no controlled trials of certolizumab pegol or natalizumab in UC.
- Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) is routinely performed in patients with UC who undergo colectomy. Idiopathic inflammation of the pouch — referred to as pouchitis — is the most common long-term complication of IPAA. Retrospective, uncontrolled studies suggest that TNF antagonists, vedolizumab, or ustekinumab may be effective in the treatment of pouchitis that is refractory to antibiotics.[52]
- Safety considerations:
  * Due to an increased risk of mortality and thrombosis with JAK inhibitors, JAK inhibitors only indicated for patients who have previously had an inadequate response or intolerance to TNF inhibitors.
  * Use of JAK inhibitors should be limited to the shortest duration, with consideration of the benefits and risks for the individual patient. The prescribing information states that the lowest effective dose needed to maintain response should be used.[39 53]

Guidelines: [51] [52 54]

- Lifestyle interventions, such as smoking cessation and diet modification, are important components of a comprehensive treatment plan for patients suffering from CD.
- When medication therapy is needed to manage CD and UC, oral and topical (administered rectally) therapies often provide the best value.

- First-line therapies to induce remission for CD/UC vary, based on severity and anatomic distribution, but may include:
  * Oral corticosteroids, “topical” steroids (enteric-coated budesonide), oral aminosalicylates (5ASAs, such as sulfasalazine or mesalamine). Steroids are used over csDMARDs for induction of remission in moderate to severe UC. Several product formulations are specific to anatomic location of the disease, such as enteric-coated (EC) budesonide or EC mesalamine, or rectal 5ASAs.
  * In addition, topical mesalamine may be used for UC, depending on the extent and location of disease.
  * The use of conventional corticosteroids, such as prednisone, is generally reserved for patients with moderate-to-severe CD/UC refractory to first-line therapies, given the adverse events. Use is generally limited to one to two weeks.
  * Corticosteroids, such as prednisone (40 - 60 mg/day or 1 mg/kg/day), are effective for induction of remission for CD and UC.
- Once remission is induced with corticosteroids, maintenance csDMARD therapy should be initiated. Choice of therapy varies between CD and UC, as well as response to induction therapy(s). Antimetabolite csDMARDs [such as methotrexate (MTX), 6-mercaptopurine (6MP), azathioprine] are slow acting and can take 8 to 12 weeks to have full effect. They are also used to decrease immunogenicity in combination with targeted DMARDs.
- First-line therapies to maintain remission include:
  * CD: 6-mercaptopurine, azathioprine, and methotrexate.
  * UC: oral 5ASAs (e.g., sulfasalazine), topical mesalamine or corticosteroids, or oral corticosteroids, depending on the extent and location of disease.
- When non-medical therapies and oral/topical medications (steroids or aminosalicylates) are inadequate, a targeted DMARD may be appropriate for induction and/or maintenance of disease remission.
- Guidelines for CD list multiple targeted DMARDs as effective treatment options. [51]
  * TNF inhibitors, including infliximab and adalimumab, are recommended in patients who are resistant to corticosteroids or whose disease is refractory to csDMARDs such as azathioprine or 6-mercaptopurine.
  * Ustekinumab is an option for moderate-to-severe CD patients who failed previous treatment with corticosteroids, thiopurines, methotrexate, or anti-TNF inhibitors or who have had no prior exposure to anti-TNF inhibitors.
  * Vedolizumab is also listed as an effective option for the induction and maintenance of remission in CD.
  * Due to the risk of progressive multifocal leukoencephalopathy (PML), a serious (sometimes fatal) adverse event, natalizumab is only recommended after other treatment options have failed.
  * Patients with fistulizing disease and severely active disease may be candidates for initial targeted DMARD. Definitions for severe disease include the following previous hospitalization for Crohn’s disease, extensive anatomic involvement, deep ulcers, prior surgical resection, stricturing and/or penetrating behavior.

- Clinical practice guidelines for the treatment of UC indicate that for patients who initially respond to infliximab but lose response, an increase in dose or shortening of the interval between infusions may improve the likelihood of successful treatment. These guidelines acknowledge that these strategies have not been evaluated in a controlled manner.
- Lack of response and loss of response to TNF inhibitors is common in both CD and UC. The choice of subsequent agent after failure of a TNF inhibitor is typically guided by serum levels. ACG guidelines state that, in patients with adequate serum levels of anti-TNF antibodies switching to another TNF is unlikely to be of benefit.

Gastrointestinal conditions – Immune-mediated Colitis

- Serious or steroid-refractory colitis is a known adverse event associated with checkpoint inhibitors such as ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, cemiplimab, and durvalumab. NCCN guidelines recommend prednisone or methylprednisolone as the first-line treatment for moderate colitis. Infliximab or vedolizumab may be considered if there has been no improvement within 2-3 days of initiating glucocorticoids. [55]
- NCCN guidelines state that the duration of therapy with TNF-inhibitors is not clearly defined but is usually a single dose though a second dose may be required. [55]
- There is not an FDA approved dose for vedolizumab when used for immune-mediate colitis. However, a retrospective analysis identified that most patients required between one and four doses to achieve resolution. [56 57]

Gastrointestinal conditions – Collagenous Colitis

- The European Guidelines on Microscopic Colitis (including lymphocytic colitis and collagenous colitis) recommend budesonide as front line for both induction as well as maintenance in some cases. Evidence for use of second-line therapies in patients with microscopic colitis is scarce and based primarily on case reports. Guidelines support the use of TNF inhibitors and vedolizumab for refractory microscopic colitis. TNF inhibitors, including infliximab and adalimumab, have been reported to induce remission. Vedolizumab has been associated with clinical remission based on case reports; almost all patients were refractory to prior TNF inhibitors; however, no randomized control trials have been published to date.[58]

Other Immunologic Conditions

Acute Graft Versus Host Disease (aGVHD)[59]

- Graft versus host disease (GVHD) is a common complication of allogeneic hematopoietic cell transplant (HCT) that occurs when the graft (donor) cells identify the transplant recipient cells (host) as foreign and initiates an immune reaction that may lead to organ damage or death.
- The risk for GVHD is higher when receiving a HCT from an unrelated donor.

- There are no standard guidelines for prophylaxis of acute GVHD, protocols vary by transplant center. The choice of therapy may depend on the underlying disease, degree of HLA disparity, conditioning regimen, and patient characteristics. Several regimens include a calcineurin inhibitors (tacrolimus, cyclosporine) given with either methotrexate or mycophenolate mofetil. Post-transplantation with cyclophosphamide or T-cell depletion is also used.
- At 6 months post-transplant, abatacept was shown to increase acute GVHD free survival as well as improve overall survival when used for patients with 8/8 HLA matched or 7/8 HLA mismatched unrelated donor HCT when used in combination with a calcineurin inhibitor plus methotrexate.[60]

Alopecia areata (AA)

- Alopecia areata (AA) is a chronic, autoimmune disorder that targets hair follicles, leading to nonscarring hair loss; it causes both hair shedding and inhibition of hair regrowth. The condition most commonly presents on the scalp but may also occur in other hair-bearing areas, such as the eyebrows, eyelashes, beard, and extremities.[61]
- The evidence for baricitinib in AA is based on two double-blind, randomized, placebo-controlled trials in patients with at least 50% scalp hair loss for more than 6 months. In both trials, the proportion of patients who achieved at least 80% scalp hair coverage at week 36 (the primary endpoint) in the baricitinib arms were significantly more than the placebo arms.[9]
- The efficacy of deuruxolitinib in AA was demonstrated in two randomized, double-blind, placebo-controlled trial. In both trials, a greater proportion of patients achieved the primary endpoint of at least 80% scalp coverage at week 24. [62 63]
- The evidence for ritlecitinib in AA is based on one randomized, double-blind, placebo-controlled trial. Only patients with at least 50% scalp hair loss with no signs of terminal hair regrowth within 6 months were included in the trial. The proportion of patients who achieved at least 80% scale hair coverage at week 24 (primary endpoint) was significantly more in the ritlecitinib arm than placebo arm.[64]
- The Alopecia Areata Consensus Expert guidelines support the use of corticosteroids, topical immunotherapy and conventional (which may include diphenylcyclopropenone [DPCP] or squaric acid dibutyl ester [SADBE]), or oral immunosuppressants (methotrexate, azathioprine, cyclosporine), noting time to effect may take several weeks to months.[65]
- Coverage for stimulation of hair growth is defined by contract language.

Antibody Mediated Rejection of Transplant (solid-organ)[66 67]

- Acute allograft (organ) rejection may be cellular (T-cell mediated) or humoral (antibody-mediated) (AHR, AMR).
- Pre-treatment (desensitization) may reduce the risk of AMR in highly sensitized renal transplant patients.
- Acute humoral rejection (AHR) is also an AMR and can occur outside of the peri-operative period, but most commonly within 6 months after transplant. The diagnosis is confirmed by a renal biopsy.
- The goal of therapy is early antibody elimination with IVIG, pheresis, or a combination of modalities. However, evidence for therapies used in AMR are generally of low quality and protocols vary between transplant centers. PLEX and IVIG are generally regarded as a

standard of care for acute active AMR. Rituximab has also been suggested as a treatment option by KDIGO guidelines.[66]

- One study assessed the use of tocilizumab as rescue therapy in 36 kidney transplant patients with chronic AMR who failed standard-of-care treatment with IVIG and rituximab, with or without plasma exchange. Tocilizumab was administered as 8 mg/kg monthly, with a maximal dose of 800 mg for 6 to 25 months. Graft- and patient- survival rates were 80% and 91% at six years post treatment, respectively.[68]
- In a small pilot study (N=10), patients who did not respond to desensitization with IVIG and rituximab (+/- plasma exchange) who were given tocilizumab 8 mg/kg on day 15 then monthly for 6 months with IVIG had a decrease in donor specific antibodies.[69]

Coronavirus-19 (COVID-19)[70 71]

- Baricitinib is FDA-approved for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) when used to treat COVID-19. Dosing is limited to 14 days or until hospital discharge, whichever occurs first.[9]
- The evidence for baricitinib in COVID-19 is based primarily on two, large, randomized control trials in hospitalized COVID-19 patients requiring oxygen support. Although the compositive endpoint of progression and mortality was no different between baricitinib or placebo when added to standard of care, there was a statistically significant difference in mortality between groups. When compared to remdesivir alone, baricitinib plus remdesivir reduced the time to recovery as well as composite endpoint of progression or death. However, applicability is limited as patients were not on standard of care corticosteroids. Patients in the trial stopped baricitinib upon discharge or after 14 days, whichever occurred first.
- There is no available safety and efficacy data supporting the use of baricitinib in COVID-19 in the outpatient setting.

Cytokine Release Syndrome (CRS)

- Tocilizumab IV is FDA-approved for the treatment of cytokine release syndrome associated with the use of chimeric antigen receptor (CAR) T cell therapy, such as Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel). It is given as a one-time weight-based dose but up to three additional doses may be administered if there is no clinical improvement.
- Subcutaneous tocilizumab and sarilumab, another IL-6 inhibitor, have not been studied in cytokine release syndrome.

Pyoderma Gangrenosum [72 73]

- Pyoderma gangrenosum (PG) is a rare ulcerative skin condition that is often associated with underlying systemic disease.
- First-line options for PG typically are systemic corticosteroids, cyclosporine, or tacrolimus. Infliximab is considered a second-line option when there has been an inadequate response to first-line therapy.
- Infliximab or other targeted DMARD therapy may be used when there is an underlying co-diagnosis of an inflammatory condition, such as ulcerative colitis.

Sarcoidosis

- Sarcoidosis is a multisystem granulomatous disorder characterized by the presence of granulomas in involved organs. It most commonly impacts the lungs and lymph nodes but may manifest in other organs. [74]
- Corticosteroid therapy is used as the primary treatment. Second-line medication options are considered for patients with corticosteroid-refractory disease, and include csDMARDs such as azathioprine, methotrexate, and leflunomide. Targeted DMARD therapy with infliximab is reserved for patients who have not responded to prior csDMARDs. [74 75]

Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

- SSc-ILD is an autoimmune condition characterized by immune dysregulation, vasculopathy, and overproduction of collagen. This leads to leading to skin and internal organ fibrosis and thickening of the pulmonary interstitium.
- Establishing an accurate diagnosis of ILD is very important, since misdiagnosis can lead to inappropriate therapy. In general, the diagnosis of interstitial lung disease (idiopathic or due to underlying lung disease) can be made with a high degree of confidence in patients with a compatible clinical presentation and typical high-resolution computed tomography (HRCT) findings.
- Cyclophosphamide, mycophenolate, and other immunomodulators are recommended as initial therapy. Mycophenolate mofetil is often preferred in practice as it has comparable benefit to cyclophosphamide but has a better toxicity profile. Escalation of therapy to biologic or targeted therapy is recommended if there is an inadequate treatment response to initial therapies.[76 77]
- Actemra (tocilizumab) has been shown to slow the rate of decline in pulmonary function in patients with SSc-ILD. While promising, additional data on survival, hospitalization, and quality of life is needed.[36]
- Intravenous administration of Actemra (tocilizumab) is not approved for SSc-ILD. [36]

Takayasu arteritis

- Takayasu arteritis is a rare type of vasculitis where inflammation damages the aorta. Takayasu arteritis is complex and requires specialist management to accurately diagnosis and manage the condition.
- High dose corticosteroids in combination with csDMARDs are recommend as the initial treatment. Targeted DMARD therapy with tocilizumab or infliximab is recommended as second-line options in patients with persistent symptoms despite combination therapy of corticosteroids with a csDMARD, as well as for patients who are unable to taper off corticosteroids. [78]
- Tocilizumab has been evaluated at doses of 8 mg/kg intravenously every 4 weeks or 162 mg subcutaneously weekly. There is limited information on the efficacy of higher doses. [78-81]

Uveitis [82]

- Corticosteroids are the mainstay of therapy in uveitis. Guidelines recommend a high dose course (prednisone 1 mg/kg/day or up to 60-80 mg per day) for up to one month.

- A csDMARD is recommended if there is no response, or worsening, after two to four weeks of steroids. American Academy of Ophthalmology (AAO) guidelines recommend mycophenolate mofetil, azathioprine, methotrexate, cyclosporine, or tacrolimus. There is insufficient comparative evidence to conclude superiority of one csDMARD over another.
- Targeted DMARDs are recommended in patients who have had an inadequate response to corticosteroids and csDMARDs.
    * Adalimumab is FDA approved for uveitis and recommended as a treatment option in AAO guidelines. Adalimumab has been shown to lower flare rates and loss of visual acuity in two phase 3 RCTs in patients with active uveitis despite high-dose corticosteroids.
    * Infliximab is also a recommended treatment option for uveitis based on evidence from several comparative, open-label trials.

Safety Considerations

- In general, the overall safety profiles of targeted DMARDs for chronic inflammatory diseases is favorable. However, several have warnings related to infection risk and hypersensitivity reactions. [51 83-85] All are immunosuppressants and increase the risk of infection, though some drugs may increase the risk more than others.
- Certain products have unique safety concerns that should be factored into the overall risk-benefit profile.
- Oral JAK1/2/3 inhibitors (tofacitinib, upadacitinib, baricitinib, deuruxolitinib, ritlecitinib, and abrocitinib) contain a boxed warning for increased risk of serious infections, mortality, malignancies, major adverse cardiovascular events, and thrombosis. In a post-marketing safety study, tofacitinib did not meet its primary endpoint of non-inferiority for risk of cardiovascular events and malignancy. Results showed that patients who received tofacitinib at either 5 mg or 10 mg twice daily had a higher rate of cardiovascular events and malignancy compared to patients who received a TNF inhibitor. Though the study only evaluated tofacitinib the warning has been extended to other JAK1/2/3 inhibitors used in the treatment of RA and other inflammatory diseases. [33 53 86-88]
    * The boxed warning is based on a safety study designed to evaluate the safety of tofacitinib relative to TNF inhibitors. The study included patients aged 50 or older with at least one CV risk factor and all patients received background MTX. Patients were randomized to one of three groups: tofacitinib 5 mg twice daily, tofacitinib 10 mg twice daily, or a TNF inhibitor.
    * The study failed to meet its pre-specified safety endpoint of non-inferiority to TNF inhibitors for risk of cardiovascular events and malignancy.
    * The prescribing information for each JAK1/2/3 inhibitor has been updated to clarify that each JAK1/2/3 inhibitor is only indicated for to certain patients who have not responded or cannot tolerate one or more TNF blockers.[53]
    * The FDA continues to investigate these safety concerns and will provide updates as additional information becomes is available.
    * The risks and benefits of JAK1/2/3 inhibitors in patients at risk for venous thromboembolism should be carefully considered when choosing treatment strategies.

- JAK1/2/3 inhibitors have boxed warnings describing an increased risk of thrombosis. Due to this risk, the use of JAK1/2/3 inhibitors is limited to patients who have failed prior treatment options. There are several alternative targeted agents for the treatment of RA that do not carry a risk for VTE and have longer records of safety experience with comparable or better efficacy than baricitinib. [33]
- While newer agents such as IL-23 inhibitors and IL-17 inhibitors, have demonstrated favorable risk-benefit profiles in clinical studies there is limited long-term safety experience. Additionally, there is limited evidence directly comparing to existing standards of care. [51 83-85]
- New or worsening heart failure is listed as a warning and precaution for TNF inhibitors. A clinical trial evaluating etanercept for the treatment of heart failure was terminated early due to lack of efficacy and suggested higher morality in etanercept-treated patients compared to placebo. Post-market, new or worsening heart failure have been reported with TNF inhibitors.

Dose Escalation

- There are no randomized, controlled trials to support dose escalation of ustekinumab from every 8 to 12 weeks to every four-week dosing in any condition. It is uncertain if there is any additional benefit with increased dosing and there is limited long-term safety data.
    * The evidence supporting the use of every four-week dosing in CD is limited to retrospective, observational studies. [89 90] While some patients experienced disease remission, high-quality, prospective studies are needed to identify the ideal population and clarify the risk-benefit profile. Due to limited evidence supporting use, more frequent dosing of ustekinumab for CD is limited to patients who have had an inadequate response to every 8-week dosing.
    * There are no high-quality studies evaluating the use of every 4-week dosing of ustekinumab in PsO.
    * Additional studies are also needed to clarify the role of dose escalation versus standard dosing or other mechanisms of action.
- Guidelines do not currently support the use of therapeutic drug monitoring of ustekinumab to guide dose escalation.
    * There is very limited evidence on the efficacy of different maintenance troughs for ustekinumab. [91 92]
    * While therapeutic drug monitoring may play a role in the management of TNF inhibitors, the same concepts may not apply to ustekinumab due to its different mechanism of action and pharmacokinetic properties.
- Phase 3 clinical trials of vedolizumab for UC and CD included maintenance dosing intervals of every 4 weeks and every 8 weeks (with a dose of 300 mg). The results demonstrated that the two maintenance doses produce similar response rates. In long-term extension studies some patients who had an inadequate response to every 8-week dosing were able to achieve a response or regain response after increasing to every 4-week dosing. Therefore, the use of every 4-week dosing is limited to patients who have lost response or have had an inadequate response to every 8-week dosing.
- In PsO, there was no statistically significant difference in response for patients who were dose escalated to secukinumab 300 mg every 2 weeks vs every 4 weeks in patients who had suboptimal response to standard dosing at 16 weeks. After 16 weeks, most patients who continued with a 4-week dosing interval were able achieve response.[93]

- Pharmacokinetic and exposure-response modeling suggest shortening the dosing interval for golimumab IV to every 6 weeks may ameliorate waning efficacy toward the end of the standard 8-week dosing interval experienced by a small proportion of patients.[94]

Appendix 1: Relative Potencies of Topical Corticosteroids [95]

Class	Drug	Dosage Form	Strength (%)
Very High Potency	Augmented betamethasone dipropionate	Ointment	0.05
	Clobetasol propionate	Cream, foam, ointment	0.05
	Diflorasone diacetate	Ointment	0.05
	Halobetasol propionate	Cream, ointment	0.05
High Potency	Amcinonide	Cream, lotion, ointment	0.1
	Augmented betamethasone dipropionate	Cream	0.05
	Betamethasone dipropionate	Cream, foam, ointment, solution	0.05
	Desoximetasone	Cream, ointment	0.25
	Desoximetasone	Gel	0.05
	Diflorasone diacetate	Cream	0.05
	Fluocinonide	Cream, gel, ointment, solution	0.05
	Halcinonide	Cream, ointment	0.1
	Mometasone furoate	Ointment	0.1
	Triamcinolone acetonide	Cream, ointment	0.5
Medium Potency	Betamethasone valerate	Cream, foam, lotion, ointment	0.1
	Clocortolone pivalate	Cream	0.1
	Desoximetasone	Cream	0.05
	Fluocinolone acetonide	Cream, ointment	0.025
	Flurandrenolide	Cream, ointment	0.05
	Fluticasone propionate	Cream	0.05
	Fluticasone propionate	Ointment	0.005
	Mometasone furoate	Cream	0.1
	Triamcinolone acetonide	Cream, ointment	0.1
Lower Medium Potency	Hydrocortisone butyrate	Cream, ointment, solution	0.1
	Hydrocortisone probutate	Cream	0.1
	Hydrocortisone valerate	Cream, ointment	0.2
	Prednicarbate	Cream	0.1
Low Potency	Alclometasone dipropionate	Cream, ointment	0.05
	Desonide	Cream, gel, foam, ointment	0.05
	Fluocinolone acetonide	Cream, solution	0.01
Lowest Potency	Dexamethasone	Cream	0.1
	Hydrocortisone	Cream, lotion, ointment, solution	0.25, 0.5, 1
	Hydrocortisone acetate	Cream, ointment	0.5-1

Appendix 2: Absolute and Relative Contraindications for Phototherapy/Photochemotherapy

History of melanoma or squamous-cell carcinoma
History of photosensitivity
Increased risk of photosensitivity due to concomitant disease state (e.g., porphyria, systemic lupus erythematosus) or chronic medication use (e.g., tetracycline or sulfonamide antibiotics)
Physical inability to stand for the required exposure time
Presence of premalignant lesions (e.g., actinic keratosis)
Presence of psoriatic arthritis
Treatment of facial or scalp lesions
Treatment of lesions in the groin area
Treatment of lesions on the palms of the hands or soles of the feet, or on nail beds
Type 1 or type 2 skin

Appendix 3: Select List of Conventional Synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs)

csDMARDS for Rheumatic, Skin Conditions, and Uveitis	
Azathioprine (AZA; Imuran)	Methotrexate (oral, injectable)*
Cyclosporine (CSA; Gengraf, Neoral, Sandimmune)*	Mycophenolate (MMF; CellCept, Myfortic)
Hydroxychloroquine (HCQ; Plaquenil)	Sulfasalazine (SSZ; Azulfidine)
Arava (leflunomide)	Soriatane (acitretin) *
csDMARDs for Gastrointestinal conditions	
Azathioprine (AZA; Imuran)	Mercaptopurine (6-MP; Purinethol)
Balsalazide (Colazal, Giazo)	Mesalamine (Apriso, Asacol HD, Delzicol, Lialda, Pentasa)
Cyclosporine (CSA; Gengraf, Neoral, Sandimmune)	Sulfasalazine (SSZ; Azulfidine)

*: Medications used in the treatment of dermatologic conditions

Appendix 4: American College of Rheumatology (ACR) Classification Criteria for Establishing the Diagnosis of Rheumatoid Arthritis (RA) [96 97]

Diagnosis of RA requires the presence of at least 4 of 7 criteria below:	
1.	Morning stiffness in and around joints lasting more than 1 hour.
2.	Arthritis in at least 1 area in a wrist or proximal interphalangeal (PIP) joint (hands or fingers) for > 6 weeks.
3.	Simultaneous swelling or fluid accumulation in 3 or more joints for > 6 weeks.
4.	Symmetric (bilateral joint) involvement for > 6 weeks.
5.	Presence of rheumatoid nodules.
6.	Positive serum rheumatoid factor.
7.	Radiographic changes typical of RA (erosion or unequivocal bony decalcification in or adjacent to the involved joint) on hand and wrist present.

Appendix 5: American College of Rheumatology (ACR) Assessment Components for Improvement in Rheumatoid Arthritis (RA) [98]

-	Tender joint count.
-	Swollen joint count.
-	Patient's assessment of pain.
-	Patient's global assessment of disease activity.
-	Physician's global assessment of disease activity.
-	Patient's assessment of physical function.
-	Acute phase reactant measures (erythrocyte sedimentation rate or C-reactive protein levels).

Appendix 6: American College of Rheumatology (ACR) Classification Criteria for Establishing the Diagnosis of Giant Cell Arteritis (GCA)

Diagnosis of GCA requires the presence of at least 3 of 5 criteria below:	
1.	Morning stiffness in and around joints lasting more than 1 hour.
2.	New onset of localized headache.
3.	Temporal artery tenderness or decreased temporal artery pulse.
4.	Erythrocyte sedimentation rate of 50 mm per hour or greater.
5.	Abnormal temporal artery biopsy.

Cross References
BlueCross BlueShield Association Medical Policy, 5.01.15 - Off Label Use of Infliximab. [April 2023]
Immune Globulin Replacement Therapy (IVIG, SCIG), Medication Policy Manual, Policy No. dru020
Medications for multiple sclerosis, Medication Policy Manual, Policy No. dru753
Site of Care Review, Medication Policy Manual, Policy No. dru408
Monoclonal antibodies for skin and other inflammatory conditions, Medication Policy Manual, Policy No. dru493
Chimeric Antigen Receptor (CAR) T-cell Therapies, Medication Policy Manual, Policy No. dru523
Interleukin-1 Antagonists, Medication Policy Manual, Policy No. 677
Products with Therapeutically Equivalent Biosimilars/Reference Products, Medication Policy Manual, Policy No. dru620

Codes	Number	Description
HCPCS	J3262	Injection, tocilizumab (Actemra IV), 1 mg
HCPCS	J0717	Injection, certolizumab pegol (Cimzia lyophilized powder vials), 1 mg
HCPCS	J3380	Injection, vedolizumab (Entyvio), 1 mg
HCPCS	J3245	Injection, tildrakizumab (Ilumya), 1 mg
HCPCS	J0129	Injection, abatacept (Orencia), 10 mg
HCPCS	J1602	Injection, golimumab (Simponi Aria), 1 mg, for intravenous use
HCPCS	J2327	Injection, risankizumab-rzaa (Skyrizi), intravenous, 1 mg
HCPCS	J1747	Injection, spesolimab-sbzo (Spevigo), 1 mg
HCPCS	J3358	Ustekinumab (Stelara), for intravenous injection, 1 mg
HCPCS	J3357	Ustekinumab (Stelara), for subcutaneous injection, 1 mg
HCPCS	Q5133	Injection, tocilizumab-bavi (tofidence), biosimilar, 1 mg
HCPCS	Q5135	Injection, tocilizumab-aazg (tyenne), biosimilar, 1 mg
HCPCS	Q5137	Injection, ustekinumab-auub (wezlana), biosimilar, subcutaneous, 1 mg
HCPCS	Q5138	Injection, ustekinumab-auub (wezlana), biosimilar, intravenous, 1 mg

References

1. 1Bimzelx [Prescribing Information]. Smyrna, GA 30080: UCB, Inc; October, 2023
2. van de Putte LB, Atkins C, Malaise M, et al. Efficacy and safety of adalimumab as monotherapy in patients with rheumatoid arthritis for whom previous disease modifying antirheumatic drug treatment has failed. *Ann Rheum Dis.* 2004;63:508-16. PMID: 15082480
3. Klareskog L, van der Heijde D, de Jager JP, et al. Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial. *Lancet.* 2004;363:675-81. PMID: 15001324
4. Johnsen AK, Schiff MH, Mease PJ, et al. Comparison of 2 doses of etanercept (50 vs 100 mg) in active rheumatoid arthritis: a randomized double blind study. *J Rheumatol.* 2006;33:659-64. PMID: 16482646
5. Reich K, Papp KA, Blauvelt A, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. *Lancet.* 2017;390(10091):276-88. PMID: 28596043
6. 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;371:1665-74. PMID: 18486739
7. 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;371:1675-84. PMID: 18486740
8. Food and Drug Administration, Final Summary Minutes of the Arthritis Advisory Committee Meeting: Baricitinib: https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM610770.pdf. Accessed: 7/18/2018
9. Olumiant (baricitinib) [Prescribing Information]. Indianapolis, IN: Eli Lilly; June 2022.
10. Inman RD. Treatment of arthritis associated with inflammatory bowel disease. Last updated January 2022. . In: Sieper J, ed. Waltham, MA: UpToDate, 2016.
11. Couriel DR, Saliba R, de Lima M, et al. A phase III study of infliximab and corticosteroids for the initial treatment of acute graft-versus-host disease. *Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation.* 2009;15(12):1555-62. PMID: 19896079
12. R. B. Granuloma annulare: Management. Last updated September 2021. In: Stratman E, ed. Waltham, MA: UpToDate, 2016.
13. Korhonen T, Karppinen J, Paimela L, et al. The treatment of disc-herniation-induced sciatica with infliximab: one-year follow-up results of FIRST II, a randomized controlled trial. *Spine.* 2006;31(24):2759-66. PMID: 17108825
14. Korhonen T, Karppinen J, Paimela L, et al. The treatment of disc herniation-induced sciatica with infliximab: results of a randomized, controlled, 3-month follow-up study. *Spine.* 2005;30(24):2724-8. PMID: 16371894
15. Genevay S, Viatte S, Finckh A, et al. Adalimumab in severe and acute sciatica: a multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis and rheumatism.* 2010;62(8):2339-46. PMID: 20506391
16. Genevay S, Finckh A, Zufferey P, et al. Adalimumab in acute sciatica reduces the long-term need for surgery: a 3-year follow-up of a randomised double-blind placebo-controlled trial. *Ann Rheum Dis.* 2012;71(4):560-2. PMID: 21998121

17. Khanna D, Denton CP, Jahreis A, et al. Safety and efficacy of subcutaneous tocilizumab in adults with systemic sclerosis (faSScinate): a phase 2, randomised, controlled trial. *Lancet.* 2016;387(10038):2630-40. PMID: 27156934

18. Moutsopoulos NM, Katsifis GE, Angelov N, et al. Lack of efficacy of etanercept in Sjogren syndrome correlates with failed suppression of tumour necrosis factor alpha and systemic immune activation. *Ann Rheum Dis.* 2008;67(10):1437-43. PMID: 18198195

19. Uppal SS, Hayat SJ,Raghupathy R. Efficacy and safety of infliximab in active SLE: a pilot study. *Lupus.* 2009;18(8):690-7. PMID: 19502264

20. Illei GG, Shirota Y, Yarboro CH, et al. Tocilizumab in systemic lupus erythematosus: data on safety, preliminary efficacy, and impact on circulating plasma cells from an open-label phase I dosage-escalation study. *Arthritis and rheumatism.* 2010;62(2):542-52. PMID: 20112381

21. Merrill JT, Burgos-Vargas R, Westhovens R, et al. The efficacy and safety of abatacept in patients with non-life-threatening manifestations of systemic lupus erythematosus: results of a twelve-month, multicenter, exploratory, phase IIb, randomized, double-blind, placebo-controlled trial. *Arthritis and rheumatism.* 2010;62(10):3077-87. PMID: 20533545

22. Wallace DJ, Furie RA, Tanaka Y, et al. Baricitinib for systemic lupus erythematosus: a double-blind, randomised, placebo-controlled, phase 2 trial. *Lancet.* 2018;392(10143):222-31. PMID: 30043749

23. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Secondary 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis [cited 10/30/2013]. 'Available from:' http://ard.bmj.com/content/70/6/896.full.

24. 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Initiation and Safety Monitoring of Therapeutic Agents for the Treatment of Arthritis and Systemic Features. Secondary 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Initiation and Safety Monitoring of Therapeutic Agents for the Treatment of Arthritis and Systemic Features [cited 09/13/2013]. 'Available from:' http://www.rheumatology.org/Practice/Clinical/Guidelines/Clinical_Practice_Guidelines/.

25. European League Against Rheumatism recommendations for the management of psoriatic arthritis with pharmacological therapies. Secondary European League Against Rheumatism recommendations for the management of psoriatic arthritis with pharmacological therapies [cited 09/13/2013]. 'Available from:' http://ard.bmj.com/content/71/1/4.abstract.

26. 2012 Update of the 2008 American College of Rheumatology Recommendations for the Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis. Secondary 2012 Update of the 2008 American College of Rheumatology Recommendations for the Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis [cited 09/13/2013]. 'Available from:' http://www.rheumatology.org/Practice/Clinical/Guidelines/Clinical_Practice_Guidelines/.

27. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. Secondary EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs [cited 09/13/2013]. 'Available from:' http://ard.bmj.com/content/early/2010/05/04/ard.2009.126532.abstract.

28. Angeles-Han ST, Ringold S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis-Associated Uveitis. *Arthritis care & research.* 2019;71(6):703-16. PMID: 31021540

29. Ward MM DA, Gensler LS, Dubreuil M, Yu D, Khan MA, Haroon N, Borenstein D, Wang R, Biehl A, Fang MA, Louie G, Majithia V, Ng B, Bigham R, Pianin M, Shah AA, Sullivan N, Turgunbaev M, Oristaglio J, Turner A, Maksymowych WP, Caplan L. Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis care & research.* 2019;71(10):1285-99. PMID:

30. Cosentyx (secukinumab) [Prescribing Information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2021.

31. Singh JA, Guyatt G, Ogdie A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheumatol.* 2019;71(1):5-32. PMID: 30499246

32. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis care & research.* 2021;73(7):924-39. PMID: 34101387

33. FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions. Secondary FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions [cited 9/9/2021]. 'Available from:' https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-related-events-cancer-blood-clots-and-death?utm_medium=email&utm_source=govdelivery.

34. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis and rheumatism.* 2013;65(10):2499-512. PMID: 24092554

35. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of Tocilizumab in Giant-Cell Arteritis. *The New England journal of medicine.* 2017;377(4):317-28. PMID: 28745999

36. 36Actemra [Prescribing Information]. South San Francisco, CA: Genentech, Inc; March 2021

37. 37Otezla [Prescribing Information]. Summit, NJ: Celgene Corporation; July 2019

38. Otezla AMCP Dossier. Summit, NJ; July 2019. Celgene Corp. 2019.

39. Rinvoq (upadacitinib) [Prescribing Information]. North Chicago, IL: AbbVie Inc.; January 2022.

40. Reich K, Teixeira HD, de Bruin-Weller M, et al. Safety and efficacy of upadacitinib in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis (AD Up): results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* 2021;397(10290):2169-81. PMID: 34023009

41. Guttman-Yassky E, Teixeira HD, Simpson EL, et al. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. *Lancet.* 2021;397(10290):2151-68. PMID: 34023008

42. Fleischmann R, Pangan AL, Song IH, et al. Upadacitinib Versus Placebo or Adalimumab in Patients With Rheumatoid Arthritis and an Inadequate Response to Methotrexate: Results of a Phase III, Double-Blind, Randomized Controlled Trial. *Arthritis Rheumatol.* 2019;71(11):1788-800. PMID: 31287230

43. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *Journal of the American Academy of Dermatology.* 2019;80(4):1029-72. PMID: 30772098

44. 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(4):1029-72. PMID: 30772098.

45. American Academy of Dermatology Association. Pustular Psoriasis: Treatment Options. Accessed 9/30/2022. Available at: https://www.aad.org/public/diseases/psoriasis/treatment/genitals/pustular.

46. Kalb, R.E. (2022). Pustular psoriasis: pathogenesis, clinical manifestations, and diagnosis (literature review current through August 2022).

UpToDate. Waltham, MA, UpToDate.

47. Choon SE, Navarini AA,Pinter A. Clinical Course and Characteristics of Generalized Pustular Psoriasis. Am J Clin Dermatol. 2022;23(Suppl 1):21-29. PMID: 35061227.

48. Ingram JR, Woo PN, Chua SL, et al. Interventions for hidradenitis suppurativa: a Cochrane systematic review incorporating GRADE assessment of evidence quality. *The British journal of dermatology*. 2016. PMID: 26801356

49. Jemec GBE, Okun MM, Forman SB, et al. Adalimumab medium-term dosing strategy in moderate-to-severe hidradenitis suppurativa: integrated results from the phase III randomized placebo-controlled PIONEER trials. Br J Dermatol. 2019 Nov;181(5):967-975. doi: 10.1111/bjd.17919. Epub 2019 Aug 14. PMID: 30916379;.

50. 50Humira® [Prescribing Information]. North Chicago, IL: Abbvie, Inc.; January 2019

51. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113:481-517. PMID: 29610508

52. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020;158(5):1450-61. PMID: 31945371

53. 53Xeljanz [Prescribing Information]. New York, NY: Pfizer; December 2019

54. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol*. 2019;114:384-413. PMID: 30840605

55. NCCN Clinical Practice Guidelines in Oncology: Management of Immunotherapy-Related Toxicities v.2.2019. Secondary NCCN Clinical Practice Guidelines in Oncology: Management of Immunotherapy-Related Toxicities v.2.2019. [cited 6/5/2019]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf.

56. Bergqvist V, Hertervig E, Gedeon P, et al. Vedolizumab treatment for immune checkpoint inhibitor-induced enterocolitis. *Cancer Immunol Immunother*. 2017;66:581-92. PMID: 28204866

57. Abu-Sbeih H, Ali FS, Alsaadi D, et al. Outcomes of vedolizumab therapy in patients with immune checkpoint inhibitor–induced colitis: a multi-center study. *Journal for ImmunoTherapy of Cancer*. 2018;6(1):142. PMID: 30518410

58. Miehlke S, Guagnozzi D, Zabana Y, et al. European guidelines on microscopic colitis: United European Gastroenterology and European Microscopic Colitis Group statements and recommendations. *United European Gastroenterol J*. 2021;9(1):13-37. PMID: 33619914

59. Chao, NJ and Zeiser, R. Prevention of acute graft-versus-host disease. Last updated November 2021. Waltham, MA: UpToDate, 2021.

60. Watkins B, Qayed M, McCracken C, et al. Phase II Trial of Costimulation Blockade With Abatacept for Prevention of Acute GVHD. *J Clin Oncol*. 2021;39(17):1865-77. PMID: 33449816

61. Messenger, AG. Alopecia areata: Clinical manifestations and diagnosis [literature review current though July 2022]. Waltham, MA: UpToDate, 2022.

62. King B, Senna MM, Mesinkovska NA, et al. Efficacy and safety of deuruxolitinib, an oral selective Janus kinase inhibitor, in adults with alopecia areata: Results from the Phase 3 randomized, controlled trial (THRIVE-AA1). *Journal of the American Academy of Dermatology*. 2024. PMID: 39053611

63. Center for Drug Evaluation and Research. Application 217900Orig1S000. Multi-Discipline Review and Evaluation for NDA 217900- Leqselvi (deuruxolitinib). Accessed September 3, 2024. Available at

https://www.accessdata.fda.gov/drugsatfda_docs/nda/2024/217900Orig1s000MultidisciplineR.pdf.

64. King B, Zhang X, Harcha WG, et al. Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomised, double-blind, multicentre, phase 2b-3 trial. *Lancet*. 2023;401(10387):1518-29. PMID: 37062298

65. Meah N, Wall D, York K, et al. The Alopecia Areata Consensus of Experts (ACE) study: Results of an international expert opinion on treatments for alopecia areata. *Journal of the American Academy of Dermatology*. 2020;83(1):123-30. PMID: 32165196

66. Kasiske BL, Zeier MG, Chapman JR, et al. KDIGO clinical practice guideline for the care of kidney transplant recipients: a summary. *Kidney Int*. 2010;77(4):299-311. PMID: 19847156

67. Velidedeoglu E, Cavaille-Coll MW, Bala S, et al. Summary of 2017 FDA Public Workshop: Antibody-mediated Rejection in Kidney Transplantation. *Transplantation*. 2018;102(6):e257-e64. PMID: 29470345

68. Choi J, Aubert O, Vo A, et al. Assessment of Tocilizumab (Anti-Interleukin-6 Receptor Monoclonal) as a Potential Treatment for Chronic Antibody-Mediated Rejection and Transplant Glomerulopathy in HLA-Sensitized Renal Allograft Recipients. *Am J Transplant*. 2017;17(9):2381-89. PMID: 28199785

69. Vo AA, Choi J, Kim I, et al. A Phase I/II Trial of the Interleukin-6 Receptor-Specific Humanized Monoclonal (Tocilizumab) + Intravenous Immunoglobulin in Difficult to Desensitize Patients. *Transplantation*. 2015;99(11):2356-63. PMID: 26018350

70. Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19. *The New England journal of medicine*. 2021;384(9):795-807. PMID: 33306283

71. Marconi VC, Ramanan AV, de Bono S, et al. Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial. *Lancet Respir Med*. 2021;9(12):1407-18. PMID: 34480861

72. Teagle A,Hargest R. Management of pyoderma gangrenosum. *J R Soc Med*. 2014;107:228-36. PMID: 24912791

73. Regueiro M, Valentine J, Plevy S, et al. Infliximab for treatment of pyoderma gangrenosum associated with inflammatory bowel disease. *Am J Gastroenterol*. 2003;98:1821-6. PMID: 12907338

74. Soto-Gomez N, Peters JI,Nambiar AM. Diagnosis and Management of Sarcoidosis. *Am Fam Physician*. 2016;93:840-8. PMID: 27175719

75. Thillai M, Atkins CP, Crawshaw A, et al. BTS Clinical Statement on pulmonary sarcoidosis. *Thorax*. 2021;76:4-20. PMID: 33268456

76. Roofeh D, Jaafar S, Vummidi D, et al. Management of systemic sclerosis-associated interstitial lung disease. *Curr Opin Rheumatol*. 2019;31(3):241-49. PMID: 30870216

77. Hoffmann-Vold AM, Maher TM, Philpot EE, et al. Assessment of recent evidence for the management of patients with systemic sclerosis-associated interstitial lung disease: a systematic review. *ERJ Open Res*. 2021;7(1). PMID: 33644224

78. Hellmich B, Agueda A, Monti S, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis*. 2020;79:19-30. PMID: 31270110

79. Mekinian A, Saadoun D, Vicaut E, et al. Tocilizumab in treatment-naive patients with Takayasu arteritis: TOCITAKA French prospective multicenter open-labeled trial. *Arthritis Res Ther*. 2020;22:218. PMID: 32943098

80. Nakaoka Y, Higuchi K, Arita Y, et al. Tocilizumab for the treatment of patients with refractory Takayasu arteritis. *Int Heart J*. 2013;54:405-11. PMID: 24309452

81. Nakaoka Y, Isobe M, Takei S, et al. Efficacy and safety of tocilizumab in patients with refractory Takayasu arteritis: results from a randomised, double-blind, placebo-controlled, phase 3 trial in Japan (the TAKT study). *Ann Rheum Dis*. 2018;77:348-54. PMID: 29191819

82. Dick AD, Rosenbaum JT, Al-Dhibi HA, et al. Guidance on Noncorticosteroid Systemic Immunomodulatory Therapy in Noninfectious Uveitis: Fundamentals Of Care for UveitiS (FOCUS) Initiative. *Ophthalmology*. 2018;125(5):757-73. PMID: 29310963

83. Smolen JS, Landewe R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;76:960-77. PMID: 28264816

84. Institute for Clinical and Economic Review, Targeted Immunomodulators for the Treatment of Moderate-to-Severe Plaque Psoriasis: Effectiveness and Value: November 4, 2016. https://icer-review.org/wp-content/uploads/2016/08/NE_CEPAC_Psoriasis_Evidence_Report_110416.pdf. Accessed: 11/15/2016

85. Institute for Clinical and Economic Review, Targeted Immune Modulators for Rheumatoid Arthritis: Effectiveness & Value: April 7, 2017. https://icer-review.org/wp-content/uploads/2016/08/NE_CEPAC_RA_Evidence_Report_FINAL_040717.pdf. Accessed: 6/21/17

86. Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz, Xeljanz XR) in rheumatoid arthritis patients; FDA to investigate. Secondary Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz, Xeljanz XR) in rheumatoid arthritis patients; FDA to investigate [cited 03/01/2019]. 'Available from:' https://www.fda.gov/Drugs/DrugSafety/ucm631871.htm.

87. FDA approves Boxed Warning about increased risk of blood clots and death with higher dose of arthritis and ulcerative colitis medicine tofacitinib (Xeljanz, Xeljanz XR). Secondary FDA approves Boxed Warning about increased risk of blood clots and death with higher dose of arthritis and ulcerative colitis medicine tofacitinib (Xeljanz, Xeljanz XR) [cited 7/26/2019]. 'Available from:' https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-boxed-warning-about-increased-risk-blood-clots-and-death-higher-dose-arthritis-and.

88. Pfizer Shares Co-Primary Endpoint Results From Post-Marketing Required Safety Study of XELJANZ® (TOFACITINIB) In Subjects with Rheumatoid Arthritis (RA). Secondary Pfizer Shares Co-Primary Endpoint Results From Post-Marketing Required Safety Study of XELJANZ® (TOFACITINIB) In Subjects with Rheumatoid Arthritis (RA) [cited 3/3/2021]. 'Available from:' https://www.pfizer.com/news/press-release/press-release-detail/pfizer-shares-co-primary-endpoint-results-post-marketing.

89. Greenup AJ, Rosenfeld G,Bressler B. Ustekinumab use in Crohn's disease: a Canadian tertiary care centre experience. *Scandinavian journal of gastroenterology*. 2017;52(12):1354-59. PMID: 28885058

90. Ma C, Fedorak RN, Kaplan GG, et al. Long-term Maintenance of Clinical, Endoscopic, and Radiographic Response to Ustekinumab in Moderate-to-Severe Crohn's Disease: Real-world Experience from a Multicenter Cohort Study. *Inflammatory bowel diseases*. 2017;23(5):833-39. PMID: 28328624

91. Feuerstein JD, Nguyen GC, Kupfer SS, et al. American Gastroenterological Association Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. *Gastroenterology*. 2017;153(3):827-34. PMID: 28780013

92. Vande Casteele N, Herfarth H, Katz J, et al. American Gastroenterological Association Institute Technical Review on the Role of Therapeutic Drug Monitoring in the Management of Inflammatory Bowel Diseases. *Gastroenterology*. 2017;153(3):835-57 e6. PMID: 28774547

93. Reich K, Korber A, Mrowietz U, et al. Secukinumab 2-weekly vs. 4-weekly dosing in patients with plaque-type psoriasis: results from the randomized GAIN study. *The British journal of dermatology*. 2021;184(5):849-56. PMID: 32652528

94. Lee JB, Broadwell A, Fan Y, et al. Population Pharmacokinetic and Exposure-Response Model Simulations: Predicted Exposure and Efficacy

for Maintenance Doses of Intravenous Golimumab Every 6 or 8 Weeks in Patients With Moderately to Severely Active Rheumatoid Arthritis. *Clin Ther*. 2022;44(3):457-64 e2. PMID: 35183373

95. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *Journal of the American Academy of Dermatology*. 2014;71(1):116-32. PMID: 24813302

96. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis and rheumatism*. 1988;31(3):315-24. PMID: 3358796

97. Kay J,Upchurch KS. ACR/EULAR 2010 rheumatoid arthritis classification criteria. *Rheumatology (Oxford)*. 2012;51 Suppl 6:vi5-9. PMID: 23221588

98. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology. Preliminary definition of improvement in rheumatoid arthritis. *Arthritis and rheumatism*. 1995;38(6):727-35. PMID: 7779114

Revision History

Revision Date	Revision Summary
12/12/2024	Effective 3/1/2025 • Added Cimzia (certolizumab) as a Level 3 treatment option for its new indication in polyarticular juvenile idiopathic arthritis (pJIA). • Added Bimzelx (bimekizumab) as a Level 3 treatment option for new indications in active non-radiographic axial spondyloarthritis, active ankylosing spondylitis, and psoriatic arthritis. • Added Leqselvi (deuruxolitinib) to policy as a Level 1 for alopecia areata (AA). • Added new Stelara (ustekinumab) biosimilars (Imuldosa and Otulfi) as non-preferred. • Removed Abry (tralokinumab) from policy (moved to new policy Monoclonal Antibodies for Skin and Other Inflammatory Conditions dru493). • Updated Tremfya (guselkumab) quantity limit to include new 200 mg dosage form and the autoinjector pens.
9/19/2024	Effective 01/01/2025 • Moved Actemra (tocilizumab) IV and SC to non-preferred for all applicable indications. Added Tyenne SC (tocilizumab-aazg) to policy as preferred. • Moved Entyvio SC (vedolizumab) from non-preferred (Level 3) to preferred (Level 1) self-administered option for Crohn's disease and ulcerative colitis. • Moved Omvoh (mirikizumab) from non-preferred (Level 3) to preferred (Level 2) self-administered option for ulcerative colitis. • Moved Sotyktu (deucravacitinib) from a Level 2 to a Level 1 self-administered option for chronic plaque psoriasis. • Added new Stelara (ustekinumab) biosimilars (Pyzchiva, Selarsdi, Wezlana) as non-preferred.
9/19/2024	Effective 12/1/2024 • Added Tremfya (guselkumab) as a Level 1 treatment option for ulcerative colitis, including IV induction. • Added Skyrizi (risankizumab) as a Level 1 treatment option for ulcerative colitis, including IV induction. • Added Kevzara (sarilumab) for as a Level 4 self-administered treatment option for active polyarticular juvenile idiopathic arthritis. • Updated QL for Adbry (tralokinumab) to include new SC autoinjector formulation. • Clarified Cimzia (certolizumab pegol) preferred product criteria for Crohn's disease- now adalimumab and one other Level 1 or Level 2 therapy. • Clarified Velsipity (etrasimod) and Omvoh (mirikizumab) Level 3 product criteria for ulcerative colitis. No change to intent.

Revision Date	Revision Summary
6/20/2024	Effective 10/1/2024 • Added new Spevigo (spesolimab) SC formulation for maintenance treatment of generalized pustular psoriasis (GPP). • Added biosimilar Simlandi (adalimumab-ryvk) to policy as preferred. • Added unbranded products adalimumab-adbm, adalimumab-ryvk (Quallent Pharmaceuticals), and adalimumab-adaz (Cordavis) to policy as not medically necessary. • Added Tofidence IV (tocilizumab-bavi) to policy as non-preferred. • Added Tyenne IV (tocilizumab-aazg) to policy as preferred. • Added Entyvio SC (vedolizumab) to policy as non-preferred (Level 3) self-administered option for Crohn's disease (CD). • Updated Entyvio SC (vedolizumab) criteria for ulcerative colitis (UC) after two Level 1 or 2 alternatives (previously required three Level 1 or 2 alternatives). • Added Rinvoq (upadacitinib) as a Level 2 product for polyarticular juvenile idiopathic arthritis (PJIA), a new FDA indication. • Added Rinvoq LQ (upadacitinib) new oral solution to policy at parity with Rinvoq.
3/21/2024	Effective 7/1/2024 • Changed Amjevita (adalimumab-atto) [all NDCs] from preferred to non-preferred adalimumab product. • Changed Sotyktu (deucravacitinib) from a Level 3 to a Level 2 self-administered option for chronic plaque psoriasis. • Added Omvoh (mirikizumab-mrkz), Velsipity (etrasimod), and Entyvio SC (vedolizumab) to policy as non-preferred (Level 3) self-administered options for ulcerative colitis (UC). The provider-administered loading doses for Omvoh will follow coverage of the self-administered product. • Added Bimzelx (bimekizumab-bkzx) to policy as a non-preferred (Level 4) self-administered option for chronic plaque psoriasis. • Updated to reflect Avsola (infliximab-axxq) as a preferred infliximab product and Zymfentra (infliximab-dyyb) as a non-preferred infliximab product (for Crohn's disease and ulcerative colitis). • Updated background to include pouchitis and collagenous colitis. • Added Cosentyx (secukinumab) for treatment of hidradenitis suppurativa. • Updated Adbry (tralokinumab) atopic dermatitis age restriction from 18 years of age to 12 years of age based on FDA age expansion. • Updated cross references to include Medications for multiple sclerosis, dru753 and removed both Zeposia (ozanimod), dru674 and Tysabri (natalizumab), dru111 which were both moved to dru753.

Revision Date	Revision Summary
12/7/2023	Effective 1/1/2024 • Added Litfulo (ritlecitinib) to policy for alopecia areata (AA). • Modified criteria for Olumiant (baricitinib) to allow coverage for alopecia areata (AA) • Added new Cosentyx (secukinumab) IV formulation to policy criteria and QL for AS, nrSpA, and PsA. • Removed Cosentyx (secukinumab) lyophilized powder vials for subcutaneous administration as these vials were discontinued. • Made Cibinqo (abrocitinib) a Level 1 treatment option for atopic dermatitis at parity with Adbry (tralokinumab-ldrm) and Rinvoq (upadacitinib)
09/14/2023	Effective 12/1/2023: • Added non-preferred biosimilar Yuflyma (adalimumab-aaty) to the policy. • Modified the QL for SC Actemra (tocilizumab) for treatment of SJIA.
6/1/2023	Effective 7/1/2023: • Modified Cibinqo (abrocitinib) coverage in atopic dermatitis to include ages down to 12 years. • Add preferred adalimumab biosimilars: Hadlima (adalimumab-bwwd), and the Amjevita (adalimumab-atto) biosimilars with NDCs beginning with 55513. • Added Kevzara (sarilumab) to policy for polymyalgia rheumatica (PMR) as a level 1 option. • Added Rinvoq (upadacitinib) to policy for Crohn's disease as a level 2 option.
12/9/2022	Effective 1/19/2023: • Added Spevigo (spesolimab-sbzo) to the policy for generalized pustular psoriasis (GPP) as a provider-administered option. • Added Sotyktu (deucravacitinib) to policy for plaque psoriasis (PsO) as a level 3 self-administered option. • Skyrizi (risankizumab-rzaa) quantity limit updated to include new 180 mg maintenance dose for Crohn's Disease (CD). • Rinvoq (upadacitinib) added to policy for non-radiographic axial spondyloarthritis (Nr-axSpA) as a level 2 self-administered option. Taltz (ixekizumab) product group renamed level 3 (previously named level 2) in Nr-axSpA.
8/29/2022	Effective 10/1/2022: • Modified Rinvoq (upadacitinib) and Xeljanz/Xeljanz XR (tofacitinib) for ulcerative colitis (UC) to be level 2 self-administered options. • Added Skyrizi (risankizumab-rzaa) to policy for Crohn's Disease (CD) as a level 1 self-administered and provider-administered option. • Modified step therapy criteria for level 2 self-administered options for Crohn's Disease (CD). • Added Olumiant (baricitinib) to policy for COVID-19 as not medically necessary (NMN) when used in the outpatient setting. • Added Olumiant (baricitinib) to policy for alopecia areata (AA) as a cosmetic contract exclusion.

Revision Date	Revision Summary
5/23/2022	Effective 6/14/2022: • Removed Kineret (anakinra) and infliximab products from Table 2. • Updated policy formatting and added HCPCS codes for provider-administered products. • Added Rinvoq (upadacitinib) to policy for ulcerative colitis (UC) as a level 3 option. • Added Rinvoq (upadacitinib) to policy for ankylosing spondylitis (AS) as a level 2 option. • Added Adbry (tralokinumab-ldrm) to policy for atopic dermatitis (AD) as a level 1 option. • Added Cibinqo (abrocitinib) to policy for atopic dermatitis (AD) as a level 2 option. • Added Actemra (tocilizumab) IV to policy for Giant Cell Arteritis (GCA). • Updated policy to allow dosing escalation of Simponi Aria (golimumab) to every 6 weeks. • Updated Entyvio (vedolizumab) for Crohn's Disease (CD) to a level 1 option.
2/22/2022	Effective 3/13/2022: • Added Rinvoq (upadacitinib) to policy for psoriatic arthritis (PsA) as a level 2 option. • Added Skyrizi (risankizumab-rzaa) to policy for psoriatic arthritis (PsA) as a level 1 option. • Added tofacitinib (Xeljanz/ Xeljanz XR) to policy for ankylosing spondylitis (AS) as a level 2 option. Cimzia (certolizumab pegol) syringes. • Simponi (golimumab) SC, and Taltz (ixekizumab) were moved to level 3. • Added coverage criteria for Rinvoq (upadacitinib) for atopic dermatitis (AD). • Added coverage criteria for Enbrel (etanercept), Humira (adalimumab), Cosentyx (secukinumab), and Simponi (golimumab) for enthesitis-related arthritis (ERA). • Added coverage criteria for intravenous Actemra (tocilizumab) for solid organ transplant, antibody mediated rejection (AMR). • Added criteria to allow coverage of intravenous Orencia (abatacept) for prophylaxis of graft versus host disease (GVHD). • Yusimry (adalimumab-aqvh) added to policy as a non-preferred adalimumab product. • Wording for intravenous Actemra (tocilizumab) criteria for cytokine release syndrome (CRS) was modified to allow for coverage as part of CAR-T treatment plan. • Updated position statement to clarify that non-TNFs may be an option for New York Heart Association (NYHA) class III/IV heart failure (HF) based on guidelines and post-market reports of new or worsening HF with TNF inhibitors.

Revision Date	Revision Summary
10/15/2021	Effective 1/1/2022: • Revised nomenclature for preferred and non-preferred products. • Updated step therapy requirements for Rinvoq (upadacitinib) and Xeljanz (tofacitinib) for rheumatoid arthritis. • Clarified dosing of Cosentyx (secukinumab). • Added coverage criteria for Actemra (tocilizumab) for Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD). • Updated step therapy requirements for Siliq (brodalumab). • Updated preferred infliximab products. • Added Janssen (infliximab) to policy as non-preferred. • Clarified dosing and uses for Cosentyx (secukinumab) vials.
7/19/2021	Effective 10/1/2021: • Moved Kineret (anakinra) from this policy to new combination Interleukin-1 Antagonists policy (dru677). • Simplified severity criteria for rheumatoid arthritis (RA). Removed specific ineffectiveness requirements. • Updated diagnostic requirements for systemic juvenile idiopathic arthritis (SJIA). Now require disease activity for at least 6 weeks instead of 6 months. • Updated Skyrizi (risankizumab-rzaa) quantity limits for newly available 150 mg syringes.
4/21/2021	• Reformatted policy. • Added Otezla (apremilast) to the policy and archived its standalone policy (dru342 Otezla, apremilast). • Added coverage criteria for Kineret (anakinra) for Deficiency of the Interleukin-1–Receptor Antagonist (DIRA). • Added coverage criteria for sarcoidosis and Takayasu Arteritis. • Clarified that combination therapy with any targeted immunomodulator is considered investigational. • Updated investigational uses. • Updated quantity limits for pediatric ulcerative colitis.
1/20/2021	• Added coverage criteria for Xeljanz (tofacitinib) in PJIA. Updated quantity limits to include Xeljanz (tofacitinib). • Added coverage criteria for Entyvio (vedolizumab) in immune-mediated colitis. • Clarified definition of investigational uses. • Remove term “Preferred” in criterion “P” table to limit confusion with trade. • Split “non-preferred” criteria for self-administered UC drugs into separate criterion for Xeljanz and Simponi.

Revision Date	Revision Summary
10/28/2020	Effective 1/1/2021: • Revised step therapy requirements: - Taltz (ixekizumab) no longer requires a trial of Cimzia (certolizumab pegol) for AS. - Tremfya (guselkumab) is now considered a preferred product for PsA. - Actemra (tocilizumab) now requires step therapy with adalimumab for PJIA and RA. - Enbrel (etanercept) is now considered a preferred medication for chronic plaque psoriasis (PsO). - Stelara (ustekinumab) is now considered a preferred product for UC (self-administered and provider-administered). - Entyvio (vedolizumab) is now considered a preferred provider-administered product for UC. • Added Hulio (adalimumab-fkjp) to policy. • Added Simponi Aria as a preferred provider-administered option for polyarticular juvenile idiopathic arthritis (PJIA), a newly approved FDA indication. • Increased authorization limit for infliximab in immune-mediated colitis to two infusions.

8/25/2020	Effective 10/1/2020: • Separated AS, HS, PJIA, and uveitis sections into separate provider-administered and self-administered sections. • Revised clinical documentation requirements. • Updated quantity limits for Cimzia (certolizumab pegol), Taltz (ixekizumab), and Cosentyx (secukinumab) based on newly FDA approved indications. • Removed references to appendix 3 in policy criteria and listed requirements for prior conventional therapies directly in criteria. • Ankylosing spondylitis: - Cimzia and Simponi will continue to require step therapy through two preferred products. - Taltz will now require step therapy through three preferred products. • Non-Radiographic Axial Spondyloarthritis: - New diagnosis category in policy. - Non-preferred products (e.g., Taltz) will require step therapy through two preferred products. • Chronic Plaque Psoriasis: - Non-biologic-step-therapy requirements changed from "BSA ≥ 10% AND phototherapy AND conventional DMARD" to "BSA ≥ 10% OR phototherapy OR conventional agent." - Conventional agent list expanded from just DMARDs to also include treatments such as topical corticosteroids. - Enbrel will no longer be a preferred product and will require step therapy with Humira (unless the patient is under 18 years of age). - Siliq and Cimzia will now only require step therapy with two preferred products. • **Crohn's Disease:** Self-administered Cimzia will require step therapy with Humira specifically. • Hidradenitis Suppurativa - Removed requirement for disease severity. - Removed requirement for functional impairment. - Expanded list of acceptable step therapies from only antibiotics to also include corticosteroids, hormonal therapies, metformin, and retinoids. • Polyarticular Juvenile idiopathic Arthritis - Actemra SC will require step therapy with Humira specifically. - Orencia SC will require step therapy with Humira, Enbrel, and Actemra specifically. • Psoriatic Arthritis: - Xeljanz will now be a preferred product. - Added Tremfya as a non-preferred product. • **Rheumatoid Arthritis:** Actemra and Xeljanz will now be preferred products. • **Systemic juvenile idiopathic arthritis:** Expanded list of acceptable step therapies from only conventional DMARDs to

Revision Date	Revision Summary
	also include NSAIDs. • **Ulcerative Colitis:** Self-administered Stelara will no longer be a preferred product and will require step therapy with Humira. • **Uveitis:** Expanded list of acceptable step therapies from only systemic corticosteroids to also include periocular intravitreal corticosteroids.
4/22/2020	• Added continuation of therapy (COT) criteria. • Added Avsola (infliximab-axxq) and Abrilada (adalimumab-afzb) to policy. • Updated quantity limits for Cosentyx (secukinumab) in axial Spondyloarthritis/ankylosing spondylitis. • Updated dosing for Xeljanz XR (tofacitinib) in ulcerative colitis. • Clarified criteria for preferred provider-administered options for ulcerative colitis.
10/23/2019	• Rinvoq (upadacitinib) has been added as a preferred self-administered option for RA (new FDA approval). • Simponi (golimumab) has been changed to a non-preferred product for AS, PsA, RA, and UC. • Taltz (ixekizumab) has been added as a non-preferred option for axial Spondyloarthritis/ankylosing spondylitis (new FDA indication). • Stelara (ustekinumab) has been added as a preferred option for UC. • Actemra (tocilizumab) subcutaneous and intravenous dosing has been revised to match the prescribing information. • Removed site of care requirements for immune-mediated colitis, as an acute management indication. • Clarified Olumiant (baricitinib) quantity limits to state 30 tablets per 30 days.
7/24/2019	• Dosing and quantity limits have been simplified and reformatted. • Skyrizi (risankizumab-rzaa) has been added as a preferred self-administered option for plaque psoriasis. • Tremfya (guselkumab) is now preferred for psoriasis. • Entyvio (vedolizumab) now requires prior of one preferred option instead of two when used for CD. • Clarified timeframe for an adequate trial of csDMARDs in multiple indications. • Added atopic dermatitis as an investigational use for Olumiant (baricitinib). • Clarified requirements for Humira (adalimumab) and Enbrel (etanercept) biosimilars. • Simplified requirements for Actemra (tocilizumab) in GCA. • Removed requirement that csDMARDs are given with targeted agents for RA. • Reformatted investigational and NMN use sections (no changes to intent).
5/7/2019	Removed Xeljanz (tofacitinib) step therapy for psoriatic arthritis (PsA) and rheumatoid arthritis (RA). Added to list of non-preferred options for PsA and RA.

Revision Date	Revision Summary
11/16/2018	• Clarified investigational dosing for Cosentyx (secukinumab). • Added coverage criteria for Cimzia (certolizumab pegol) as non-preferred, provider-administered option for PsO. • Clarified that any dose escalation above the quantity limit is considered investigational, unless listed in coverage criteria.
8/17/2018	• Updated indications for Cimzia (certolizumab pegol), Taltz (ixekizumab), and tofacitinib (Xeljanz/Xeljanz XR). • Updated Actemra (tocilizumab) dosage forms and indications to match prescribing information. • Added coverage criteria for Ilumya (tildrakizumab-asmn) as a non-preferred, provider-administered option for PsO. • Added coverage criteria for Olumiant (baricitinib) as a non-preferred, self-administered option for RA. • Updated coverage criteria for infliximab biosimilars to state that they must meet all criteria for the reference product and there must be a documented contraindication or intolerance to the reference product. • Added additional criteria for severe CD. • Clarified reauthorization requirements for adalimumab when used for HS. • RA: Clarified that targeted agents must initially be administered with a csDMARD. • UC: Aligned criteria for steroids and csDMARDs for provider-administered and self-administered sections. • Updated nomenclature for each drug class. • Clarified that provider-administered medications may be reviewed for continued authorization. • Added coverage criteria for pyoderma gangrenosum.
3/1/2018	Added Cimzia (certolizumab pegol) to the site of care program.
2/1/2018	• Updated indications for Simponi Aria (golimumab) and Orencia (abatacept). • Revised dosing intervals for Entyvio (vedolizumab). • Added coverage Actemra (tocilizumab) for cytokine release syndrome due to with chimeric antigen receptor T cell therapy. • Clarified that use of Stelara (ustekinumab) every four weeks is considered investigational. • Clarified that the use of multiple courses of Stelara (ustekinumab) IV loading doses for Crohn's disease is considered investigational.
1/1/2018	• Updated preferred and non-preferred products for all indications. • Removed Otezla (apremilast) from policy. • Clarified Cosentyx (secukinumab) dosing.

Revision Date	Revision Summary
8/11/2017	• Added coverage criteria for Kevzara (sarilumab), as a non-preferred self-administered option for RA. • Added coverage criteria for subcutaneous Actemra (tocilizumab) for GCA. • Added coverage criteria for Orencia (abatacept) for PsA and updated JIA coverage criteria to include SC dosing. • Added coverage criteria for Tremfya (guselkumab), as a non-preferred self-administered option for PsO. • Added Renflexis (infliximab-abda) to policy. • UC: revised step therapy requirements for Entyvio (vedolizumab).
5/12/2017	• Added coverage criteria for Siliq (brodalumab), as a non-preferred self-administered option for PsO. • Clarified step therapy for "self-administered UC treatments." • Updated dose and quantity limits for Taltz (ixekizumab) and Cosentyx (secukinumab). • Added the following as investigational uses: - Scleroderma (any branded medication). - Use of Otezla (apremilast) in combination with targeted immunomodulators for any indication.
12/16/2016	• Updated preferred and non-preferred products for all indications. • Added Inflectra (infliximab-dyyb) to policy. • Updated investigational uses. • CD: Added Stelara (ustekinumab) and revised quantity limits for infliximab. • UC: Revised quantity limits for infliximab.
4/8/2016	• AS: added Cosentyx (secukinumab), changed to diagnosis to axial SpA. • PsO: added Taltz (ixekizumab), updated step therapy requirements nonpreferred drugs. • Added criteria for Giant Cell Arteritis and Hidradenitis Suppurativa. • PsA: Updated step therapy requirements for non-preferred drugs, added secukinumab. • Updated language for combination uses with an oral DMARD for infliximab and golimumab (IV). • Added Xeljanz XR to policy. • Updated investigational uses.
1/8/2016	Updated formatting of biologics policies, consolidating into a single policy for chronic inflammatory diseases.

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