LifeWise
Health Plan of Washington

PHARMACY / MEDICAL POLICY – 5.01.550

Pharmacotherapy of Arthropathies

Effective Date: **Jan. 3, 2025***	RELATED MEDICAL POLICIES:
Last Revised: Oct. 1, 2024	5.01.563 Pharmacotherapy of Inflammatory Bowel Disorder
Replaces: N/A	5.01.566 Pharmacotherapy of Thrombocytopenia
	5.01.575 Dupixent (dupilumab)
*This policy has been revised. Click here to view the current policy.	5.01.607 Continuity of Coverage for Maintenance Medications
	5.01.629 Pharmacologic Treatment of Psoriasis
	11.01.523 Site of Service: Infusion Drugs and Biologic Agents

Select a hyperlink below to be directed to that section.

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Arthropathy is another word for arthritis. Arthritis means inflammation of the joint. Arthritis results in pain, swelling, stiffness, and loss of motion in the joints. Autoimmune disorders occur when your own immune cells attack your joints or other organs and cause inflammation. Inflammatory arthropathies are a group of disorders affecting the joints, which share certain common features such as inflammation and changes in immune regulation. Conditions addressed in this policy include ankylosing spondylitis, juvenile idiopathic arthritis, rheumatoid arthritis, and psoriatic arthritis.

Advances in science and drugs (agents) have provided new ways to treat these disorders using special medications called "biologics." This policy discusses when biologics are considered medically necessary for inflammatory conditions. The information is presented in a format that cross-references biologic agents by brand and generic name, target disease, and drug class.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs providers about when a service may be covered.

Policy Coverage Criteria

We will review specific intravenous (IV) and injectable drugs for medical necessity for all ages.

For those age 13 and older, we also will review the site of service for medical necessity. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home. Click **here** to be directed to the site of service review criteria.

Drugs subject to site of service review addressed in this policy are:

- Actemra (tocilizumab) IV
- Avsola (infliximab-axxq)
- Cosentyx (secukinumab) IV
- Inflectra (infliximab-dyyb)
- Infliximab (Janssen – unbranded)
- Orencia (abatacept)
- Remicade (infliximab)
- Renflexis (infliximab-abda)
- Rituxan (rituximab)
- Simponi Aria (golimumab)
- Tofidence (tocilizumab-bavi) IV

Click on the links below to be directed to the related medical necessity criteria:

Ankylosing Spondylitis

Arthropathies: Polyarticular Juvenile Idiopathic Arthritis

Arthropathies: Systemic Juvenile Idiopathic Arthritis

Arthropathies: Rheumatoid Arthritis

Site of Service Administration	Medical Necessity
Medically necessary sites of service • **Physician's office** • **Infusion center** • **Home infusion**	**IV infusion therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site:** • These are the preferred **medically necessary** sites of service for specified drugs.
Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**IV infusion therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site.** **This site is considered medically necessary for the first 90 days for the following:** • The initial course of infusion of a pharmacologic or biologic agent **OR** • Re-initiation of an agent after 6 months or longer following discontinuation of therapy* ***Note:** This does not include when standard dosing between infusions is 6 months or longer **This site is considered medically necessary when there is no outpatient infusion center within 50 miles of the individual's home and there is no contracted home infusion agency that will travel to their home, or a hospital is the only place that offers infusions of this drug.** **This site is considered medically necessary only when the individual has a clinical condition which puts him or her at**

Site of Service Administration	Medical Necessity
	increased risk of complications for infusions, including any ONE of the following: • Known cardiac condition (e.g., symptomatic cardiac arrhythmia) or pulmonary condition (e.g., significant respiratory disease, serious obstructive airway disease, %FVC ≤ 40%) that may increase the risk of an adverse reaction • Unstable renal function which decreases the ability to respond to fluids • Difficult or unstable vascular access • Acute mental status changes or cognitive conditions that impact the safety of infusion therapy • A known history of severe adverse drug reactions and/or anaphylaxis to prior treatment with a related or similar drug
Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**These sites are considered not medically necessary for infusion and injectable therapy services of various medical and biologic agents when the site-of-service criteria in this policy are not met.**

Please note that claims billed for the drugs described in this policy that are administered via an intravenous route (IV) must be processed through a medical benefit only (not pharmacy).

Medications listed in this policy may also be subjected to quantity limits per the US Food and Drug Administration (FDA) labeled dosing.

Step therapy tiers are listed below; please refer to the Policy section for details.

Ankylosing Spondylitis		
First-line Agents		
TNF-α Inhibitors	**IL-17 Inhibitor**	**Janus Kinase Inhibitor**
Inflectra (IV) Infliximab (Janssen – unbranded) (IV) Remicade (IV)	Taltz (SC)	Rinvoq (oral)

<table>
<tr><th colspan="3">Ankylosing Spondylitis</th></tr>
<tr><td>Enbrel (SC)</td><td rowspan="2"></td><td rowspan="2">Xeljanz / XeljanzXR
(oral)</td></tr>
<tr><td>Cyltezo (SC)
Humira (AbbVie) [NDCs starting with 00074] (SC)
Simlandi (adalimumab-ryvk) (SC)
Adalimumab-adaz (Hyrimoz unbranded) (SC)
Adalimumab-adbm (Cyltezo unbranded) (SC)
Adalimumab-ryvk (Simlandi unbranded) (SC)
Simponi Aria (IV)</td></tr>
<tr><th colspan="3">Second-line Agents</th></tr>
<tr><th>TNF-α Inhibitors</th><th colspan="2">IL-17 Inhibitor</th></tr>
<tr><td>Avsola (IV)

Renflexis (IV)</td><td colspan="2" rowspan="12">Cosentyx (IV/SC)</td></tr>
<tr><td>Abrilada (SC)</td></tr>
<tr><td>Humira (Cordavis) [NDCs starting with 83457] (SC)</td></tr>
<tr><td>Adalimumab-aacf (Idacio unbranded) (SC)</td></tr>
<tr><td>Adalimumab-aaty (Yuflyma unbranded) (SC)</td></tr>
<tr><td>Adalimumab-fkjp (Hulio unbranded) (SC)</td></tr>
<tr><td>Amjevita (SC)</td></tr>
<tr><td>Hadlima (SC)</td></tr>
<tr><td>Hulio (SC)</td></tr>
<tr><td>Hyrimoz (SC)</td></tr>
<tr><td>Idacio (SC)</td></tr>
</table>

Ankylosing Spondylitis	
Yuflyma (SC)	
Yusimry (SC)	
Cimzia (SC)	
Simponi (SC)	

Agent	Medical Necessity, Ankylosing Spondylitis
First-line TNF-α Antagonists	

• **Cyltezo (adalimumab-adbm) SC**
• **Humira (adalimumab) (AbbVie) [NDCs starting with 00074] SC**
• **Simlandi (adalimumab-ryvk) SC**
• **Adalimumab-adaz (Hyrimoz unbranded) SC**
• **Adalimumab-adbm (Cyltezo unbranded) SC**
• **Adalimumab-ryvk (Simlandi unbranded) SC**
• **Enbrel (etanercept) SC**
• **Simponi Aria (golimumab) IV**
	Simponi Aria (golimumab) IV is subject to review for site of service administration.
	
	Cyltezo (adalimumab-adbm), Simlandi (adalimumab-ryvk), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Enbrel (etanercept) or Simponi Aria (golimumab) may be considered medically necessary for the treatment of ankylosing spondylitis when:
	• Medication is being prescribed by or in consultation with a rheumatologist
	
	Humira (adalimumab) (AbbVie) [NDCs starting with 00074] may be considered medically necessary for the treatment of ankylosing spondylitis when:
	• Medication is being prescribed by or in consultation with a rheumatologist
	AND
	• The individual has had an inadequate response or intolerance to one of the following drugs:[1]
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded)
	  ○ Taltz (ixekizumab)

Agent	Medical Necessity, Ankylosing Spondylitis
	[1]Note: Only applies to individuals not previously treated with requested therapy
• **Inflectra (infliximab-dyyb) IV** • **Infliximab (Janssen – unbranded) IV** • **Remicade (infliximab) IV**	**Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) are subject to review for site of service administration.** **Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) may be considered medically necessary for the treatment of ankylosing spondylitis when:** • Medication is being prescribed by or in consultation with a rheumatologist
First-line IL-17 Inhibitors	
Taltz (ixekizumab) SC	**Taltz (ixekizumab) may be considered medically necessary for the treatment of ankylosing spondylitis when:** • Medication is being prescribed by or in consultation with a rheumatologist
First-line Janus Kinase Inhibitor	
• **Rinvoq (upadacitinib)** • **Xeljanz (tofacitinib) oral** • **Xeljanz XR (tofacitinib extended-release) oral**	**Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended-release) may be considered medically necessary for the treatment of ankylosing spondylitis when:** • Medication is being prescribed by or in consultation with a rheumatologist **AND** • The individual has had an inadequate response or intolerance to one or more TNF blockers
Second-line TNF-α Antagonists	
• **Abrilada (adalimumab-afzb) SC** • **Adalimumab-aacf (Idacio unbranded) SC** • **Adalimumab-aaty (Yuflyma unbranded) SC** • **Adalimumab-fkjp (Hulio unbranded) SC** • **Amjevita (adalimumab-atto) SC**	**Abrilada (adalimumab-afzb), adalimumab-aacf (Idacio unbranded), adalimumab-aaty (Yuflyma unbranded), adalimumab-fkjp (Hulio unbranded), Amjevita (adalimumab-atto), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), Humira (adalimumab) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz), Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of ankylosing spondylitis when:**

Agent	Medical Necessity, Ankylosing Spondylitis

• **Hadlima (adalimumab-bwwd) SC**
• **Hulio (adalimumab-fkjp) SC**
• **Humira (adalimumab) (Cordavis) [NDCs starting with 83457] SC**
• **Hyrimoz (adalimumab-adaz) SC**
• **Idacio (adalimumab-aacf) SC**
• **Yuflyma (adalimumab-aaty) SC**
• **Yusimry (adalimumab-aqvh) SC**
	• Medication is being prescribed by or in consultation with a rheumatologist
	AND
	• The individual has had an inadequate response or intolerance to ALL the following agents:
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)

• **Cimzia (certolizumab pegol) SC**
• **Simponi (golimumab) SC**
	Cimzia (certolizumab pegol) and Simponi (golimumab) SC may be considered medically necessary for the treatment of ankylosing spondylitis when:
	• Medication is being prescribed by or in consultation with a rheumatologist
	AND
	• The individual has had an inadequate response or intolerance to TWO of the following drugs:
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded)
	  ○ Rinvoq (upadacitinib)
	  ○ Taltz (ixekizumab)
	  ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release)

• **Avsola (infliximab-axxq) IV** • **Renflexis (infliximab-abda) IV**	**Avsola (infliximab-axxq) and Renflexis (infliximab-abda) are subject to review for site of service administration.**

Agent	Medical Necessity, Ankylosing Spondylitis
	Avsola (infliximab-axxq) and Renflexis (infliximab-abda) may be considered medically necessary for the treatment of ankylosing spondylitis when: • Medication is being prescribed by or in consultation with a rheumatologist **AND** • The individual has had a documented trial and treatment failure with Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), or Remicade (infliximab)
Second-line IL-17 Inhibitors	
Cosentyx (secukinumab) IV/SC	**Cosentyx (secukinumab) IV is subject to review for site of service administration.** **Cosentyx (secukinumab) may be considered medically necessary for the treatment of ankylosing spondylitis when:** • The individual has had an inadequate response or intolerance to two of the following drugs: ○ Enbrel (etanercept) ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) ○ Rinvoq (upadacitinib) ○ Taltz (ixekizumab) ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release) **AND** • Medication is being prescribed by or in consultation with a rheumatologist

Step therapy tiers are listed below; please refer to the Policy section for details.

Polyarticular Juvenile Idiopathic Arthritis		
First-line Agents		
TNF-α Inhibitors	**Janus Kinase Inhibitor**	**IL-6 Inhibitor**

Polyarticular Juvenile Idiopathic Arthritis		
Cyltezo (SC) Humira (AbbVie) [NDCs starting with 00074] (SC) Adalimumab-adaz (Hyrimoz unbranded) (SC) Adalimumab-adbm (Cyltezo unbranded) (SC) Adalimumab-ryvk (Simlandi unbranded) (SC) Simponi Aria (IV)	Rinvoq (oral tablet) Rinvoq LQ (oral solution) Xeljanz (oral tablet), Xeljanz (oral solution)	Actemra (IV/SC) Tofidence (IV) Tyenne (IV/SC)
Enbrel (SC)		

Second-line Agents		
TNF-α Inhibitors	**T-Cell Costimulation Modulator**	**IL-6 Inhibitor**
Abrilada (SC)	Orencia (IV/SC)	Kevzara (SC)
Adalimumab-aacf (Idacio unbranded) (SC)		
Adalimumab-aaty (Yuflyma unbranded) (SC)		
Adalimumab-fkjp (Hulio unbranded) (SC)		
Amjevita (SC)		
Hadlima (SC)		
Hulio (SC)		
Humira (Cordavis) [NDCs starting with 83457] (SC)		
Hyrimoz (SC)		
Idacio (SC)		
Yuflyma (SC)		
Yusimry (SC)		

Agent	Medical Necessity, Polyarticular Juvenile Idiopathic Arthritis
First-line TNF-α Antagonists	

Agent	Medical Necessity, Polyarticular Juvenile Idiopathic Arthritis

• **Cyltezo (adalimumab-adbm) SC**
• **Humira (adalimumab) (AbbVie) [NDCs starting with 00074] SC**
• **Simlandi (adalimumab-ryvk) SC**
• **Adalimumab-adaz (Hyrimoz unbranded) SC**
• **Adalimumab-adbm (Cyltezo unbranded) SC**
• **Adalimumab-ryvk (Simlandi unbranded) SC**
• **Enbrel (etanercept) SC**
	Cyltezo (adalimumab-adbm), Simlandi (adalimumab-ryvk), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), or Enbrel (etanercept) may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:
	• The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine
	OR
	• Is being started on Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], Simlandi (adalimumab-ryvk), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), or Enbrel (etanercept) concurrently with leflunomide, methotrexate, or sulfasalazine
	AND
	• Medication is being prescribed by or in consultation with a rheumatologist
	
	Humira (adalimumab) (AbbVie) [NDCs starting with 00074] may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:
	• The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine
	OR
	• Is being started on Humira (adalimumab) (AbbVie) [NDCs starting with 00074] concurrently with leflunomide, methotrexate, or sulfasalazine
	AND
	• Has had an inadequate response or intolerance to one of the following drugs:[1]
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR**

Agent	Medical Necessity, Polyarticular Juvenile Idiopathic Arthritis
	adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) **AND** • Medication is being prescribed by or in consultation with a rheumatologist [1]Note: Only applies to individuals not previously treated with requested therapy
Simponi Aria (golimumab) IV	**Simponi Aria (golimumab) IV is subject to review for site of service administration.** **Simponi Aria (golimumab) IV may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:** • The individual is aged 2 years or older **AND** • Has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine **AND** • Medication is being prescribed by or in consultation with a rheumatologist
First-line Janus Kinase Inhibitor	
• **Rinvoq (upadacitinib) oral** • **Rinvoq LQ (upadacitinib) oral** • **Xeljanz (tofacitinib) oral** • **Xeljanz Oral Solution (tofacitinib) oral**	**Rinvoq (upadacitinib), Rinvoq LQ (upadacitinib), Xeljanz (tofacitinib) and Xeljanz Oral Solution (tofacitinib) may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:** • The individual has had an inadequate response or intolerance to one or more TNF blockers **AND** • Medication is being prescribed by or in consultation with a rheumatologist
First-line IL-6 Inhibitors	
• **Actemra (tocilizumab) IV/SC** • **Tofidence (tocilizumab-bavi) IV**	**Actemra (tocilizumab) IV and Tofidence (tocilizumab-bavi) IV are subject to review for site of service administration.**

Agent	Medical Necessity, Polyarticular Juvenile Idiopathic Arthritis
• **Tyenne (tocilizumab-aazg) IV/SC**	**Actemra (tocilizumab) IV/SC, Tofidence (tocilizumab-bavi) IV, and Tyenne (tocilizumab-aazg) IV/SC may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:** • The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine **AND** • Has had an inadequate response or intolerance to Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) **AND** • Medication is being prescribed by or in consultation with a rheumatologist)
Second-line IL-6 Inhibitors	

Kevzara (sarilumab) SC	**Kevzara (sarilumab) SC may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:**
	• The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine
	AND
	• Has had an inadequate response or intolerance to two of the following drugs:
	  ○ Actemra (tocilizumab) SC **OR** Tyenne (tocilizumab-aazg) SC
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded)
	  ○ Rinvoq (upadacitinib) **OR** Rinvoq LQ (upadacitinib)
	  ○ Xeljanz (tofacitinib) **OR** Xeljanz Oral Solution (tofacitinib)
	AND

Agent	Medical Necessity, Polyarticular Juvenile Idiopathic Arthritis
	• Medication is being prescribed by or in consultation with a rheumatologist
Second-line T-Cell Costimulation Modulators	

Orencia (abatacept) IV/SC	**Orencia (abatacept) IV is subject to review for site of service administration.**
	
	Orencia (abatacept) IV/SC may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:
	• The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine
	AND
	• Has had an inadequate response or intolerance to two of the following drugs:
	  ○ Actemra (tocilizumab) SC **OR** Tyenne (tocilizumab-aazg) SC
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded)
	  ○ Rinvoq (upadacitinib) **OR** Rinvoq LQ (upadacitinib)
	  ○ Xeljanz (tofacitinib) **OR** Xeljanz Oral Solution (tofacitinib)
	AND
	• Medication is being prescribed by or in consultation with a rheumatologist

Second-line TNF-α Antagonists	
• **Abrilada (adalimumab-afzb) SC** • **Adalimumab-aacf (Idacio unbranded)** • **Adalimumab-aaty (Yuflyma unbranded) SC** • **Adalimumab-fkjp (Hulio unbranded) SC**	**Abrilada (adalimumab-afzb), adalimumab-aacf (Idacio unbranded), adalimumab-aaty (Yuflyma unbranded), adalimumab-fkjp (Hulio unbranded), Amjevita (adalimumab-atto), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), Humira (adalimumab) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz), Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh)**

Agent	Medical Necessity, Polyarticular Juvenile Idiopathic Arthritis
• **Amjevita (adalimumab-atto) SC** • **Hadlima (adalimumab-bwwd) SC** • **Hulio (adalimumab-fkjp) SC** • **Humira (adalimumab) (Cordavis) [NDCs starting with 83457] SC** • **Hyrimoz (adalimumab-adaz) SC** • **Idacio (adalimumab-aacf) SC** • **Yuflyma (adalimumab-aaty) SC** • **Yusimry (adalimumab-aqvh) SC**	**may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:** • The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine **AND** • Has had an inadequate response or intolerance to ALL the following agents: ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded) ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074] ○ Adalimumab-adaz (Hyrimoz unbranded) ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded) **AND** • Medication is being prescribed by or in consultation with a rheumatologist

Step therapy tiers are listed below; please refer to the Policy section for details.

Systemic Juvenile Idiopathic Arthritis
First-line Agents
IL-6 Inhibitors
Actemra (IV/SC) Tofidence (IV) Tyenne (IV/SC)

Agent	Medical Necessity, Systemic Juvenile Idiopathic Arthritis
First-line IL-6 Inhibitors	
• **Actemra (tocilizumab) IV/SC** • **Tofidence (tocilizumab-bavi) IV**	**Actemra (tocilizumab) IV and Tofidence (tocilizumab-bavi) IV are subject to review for site of service administration.** **Actemra (tocilizumab) IV/SC, Tofidence (tocilizumab-bavi) IV, and Tyenne (tocilizumab-aazg) IV/SC may be considered**

Agent	Medical Necessity, Systemic Juvenile Idiopathic Arthritis
• **Tyenne (tocilizumab-aazg) IV/SC**	**medically necessary for the treatment of systemic juvenile idiopathic arthritis when:** • The individual has had an inadequate response or intolerance to a corticosteroid, leflunomide, methotrexate, nonsteroidal anti-inflammatory drug (NSAID), or sulfasalazine **AND** • Medication is being prescribed by or in consultation with a rheumatologist

Step therapy tiers are listed below; please refer to the Policy section for details.

Enthesitis-Related Arthritis
First-line Agents
IL-17 Inhibitors
Cosentyx (SC)

Agent	Medical Necessity, Enthesitis-Related Arthritis
First-line IL-17 Inhibitors	
Cosentyx (secukinumab) SC	**Cosentyx (secukinumab) may be considered medically necessary for the treatment of enthesitis-related arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist **Note:** Enthesitis-related arthritis is a category of juvenile idiopathic arthritis (JIA) that includes children with arthritis and enthesitis which is inflammation of the sites where tendons, ligaments, or joint capsule insert into the bone.

Step therapy tiers are listed below; please refer to the Policy section for details.

Rheumatoid Arthritis		
First-line Agents		
TNF-α Inhibitors	**IL-6 Inhibitor**	**Janus Kinase Inhibitor**

<table>
<tr><th colspan="5">Rheumatoid Arthritis</th></tr>
<tr><td>Inflectra (IV)
Infliximab (Janssen – unbranded) (IV)
Remicade (IV)</td><td colspan="2" rowspan="3">Actemra (IV/SC)
Tofidence (IV)
Tyenne (IV/SC)</td><td colspan="2">Xeljanz / Xeljanz XR (oral)</td></tr>
<tr><td>Cyltezo (SC)
Humira (AbbVie) [NDCs starting with 00074] (SC)
Simlandi (adalimumab-ryvk) (SC)
Adalimumab-adaz (Hyrimoz unbranded) (SC)
Adalimumab-adbm (Cyltezo unbranded) (SC)
Adalimumab-ryvk (Simlandi unbranded) (SC)
Simponi Aria (IV)</td><td colspan="2">Rinvoq (oral)</td></tr>
<tr><td>Enbrel (SC)</td><td colspan="2"></td></tr>
<tr><th colspan="5">Second-line Agents</th></tr>
<tr><th>TNF-α Inhibitors</th><th>IL-6 Inhibitor</th><th>IL-1 Inhibitor</th><th>T-Cell Costimulation Modulator</th><th>Janus Kinase Inhibitor</th></tr>
<tr><td>Avsola (IV)
Renflexis (IV)</td><td rowspan="8">Kevzara (SC)</td><td rowspan="8">Kineret (SC)</td><td rowspan="8">Orencia (IV/SC)</td><td rowspan="8">Olumiant (oral)</td></tr>
<tr><td>Cimzia (SC)</td></tr>
<tr><td>Simponi (SC)</td></tr>
<tr><td>Abrilada (SC)</td></tr>
<tr><td>Adalimumab-aacf (Idacio unbranded) (SC)</td></tr>
<tr><td>Adalimumab-aaty (Yuflyma unbranded) (SC)</td></tr>
<tr><td>Adalimumab-fkjp (Hulio unbranded) (SC)</td></tr>
<tr><td>Amjevita (SC)</td></tr>
</table>

Rheumatoid Arthritis				
Hadlima (SC)				
Hulio (SC)				
Humira (Cordavis) [NDCs starting with 83457] (SC)				
Hyrimoz (SC)				
Idacio (SC)				
Yuflyma (SC)				
Yusimry (SC)				

Agent	Medical Necessity, Rheumatoid Arthritis
First-line TNF-α Antagonists	
• **Cyltezo (adalimumab-adbm) SC** • **Humira (adalimumab) (AbbVie) [NDCs starting with 00074] SC** • **Simlandi (adalimumab-ryvk) SC** • **Adalimumab-adaz (Hyrimoz unbranded) SC** • **Adalimumab-adbm (Cyltezo unbranded) SC** • **Adalimumab-ryvk (Simlandi unbranded) SC** • **Enbrel (etanercept) SC** • **Simponi Aria (golimumab) IV**	**Simponi Aria (golimumab) IV is subject to review for site of service administration.** **Cyltezo (adalimumab-adbm), Simlandi (adalimumab-ryvk), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Enbrel (etanercept) or Simponi Aria (golimumab) IV may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **Humira (adalimumab) (AbbVie) [NDCs starting with 00074] may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine

Agent	Medical Necessity, Rheumatoid Arthritis

	AND
	• Has had an inadequate response or intolerance to one of the following drugs:[1]
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded)
	AND
	• Medication is being prescribed by or in consultation with a rheumatologist
	
	[1]Note: Only applies to individuals not previously treated with requested therapy

• **Inflectra (infliximab-dyyb) IV** • **Infliximab (Janssen – unbranded) IV** • **Remicade (infliximab) IV**	**Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) are subject to review for site of service administration.** **Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist
First-line IL-6 Inhibitor	
• **Actemra (tocilizumab) IV/SC** • **Tofidence (tocilizumab-bavi) IV** • **Tyenne (tocilizumab-aazg) IV/SC**	**Actemra (tocilizumab) IV and Tofidence (tocilizumab-bavi) IV are subject to review for site of service administration.** **Actemra (tocilizumab) IV/SC, Tofidence (tocilizumab-bavi) IV, and Tyenne (tocilizumab-aazg) IV/SC may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:**

Agent	Medical Necessity, Rheumatoid Arthritis
	• The individual has had an inadequate response or intolerance to hydroxychloroquine, leflunomide, methotrexate, or sulfasalazine **AND** • Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) **AND** • Medication is being prescribed by or in consultation with a rheumatologist
First-line Janus Kinase Inhibitors	
• **Rinvoq (upadacitinib) oral** • **Xeljanz (tofacitinib) oral** • **Xeljanz XR (tofacitinib extended-release) oral**	**Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended-release) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual is aged 18 years or older **AND** • Has had an inadequate response or intolerance to one or more TNF blockers **AND** • Medication is being prescribed by or in consultation with a rheumatologist **Note:** The use of tofacitinib in the setting of alopecia is considered cosmetic and is not covered by this policy.
Second-line TNF-α Antagonists	
• **Abrilada (adalimumab-afzb) SC** • **Adalimumab-aacf (Idacio unbranded)** • **Adalimumab-aaty (Yuflyma unbranded) SC** • **Adalimumab-fkjp (Hulio unbranded) SC**	**Abrilada (adalimumab-afzb), adalimumab-aacf (Idacio unbranded), adalimumab-aaty (Yuflyma unbranded), adalimumab-fkjp (Hulio unbranded), Amjevita (adalimumab-atto), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), Humira (adalimumab) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz), Idacio (adalimumab- aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh)**

Agent	Medical Necessity, Rheumatoid Arthritis

• **Amjevita (adalimumab-atto) SC**
• **Hadlima (adalimumab-bwwd) SC**
• **Hulio (adalimumab-fkjp) SC**
• **Humira (adalimumab) (Cordavis) [NDCs starting with 83457] SC**
• **Hyrimoz (adalimumab-adaz) SC**
• **Idacio (adalimumab-aacf) SC**
• **Yuflyma (adalimumab-aaty) SC**
• **Yusimry (adalimumab-aqvh) SC**
	may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:
	• The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine
	AND
	• Medication is being prescribed by or in consultation with a rheumatologist
	AND
	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)

• **Cimzia (certolizumab pegol) SC**
• **Simponi (golimumab) SC**
	Cimzia (certolizumab pegol) and Simponi (golimumab) SC may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:
	• The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine
	AND
	• Medication is being prescribed by or in consultation with a rheumatologist
	AND
	• Has had an inadequate response or intolerance to TWO of the following agents:
	  ○ Actemra (tocilizumab) SC **OR** Tyenne (tocilizumab-aazg) SC
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded)
	  ○ Rinvoq (upadacitinib)

Agent	Medical Necessity, Rheumatoid Arthritis
	○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release)
• **Avsola (infliximab-axxq) IV** • **Renflexis (infliximab-abda) IV**	**Avsola (infliximab-axxq) and Renflexis (infliximab-abda) are subject to review for site of service administration.** **Avsola (infliximab-axxq) and Renflexis (infliximab-abda) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **AND** • Has had a documented trial and treatment failure with Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), or Remicade (infliximab)
Second-line IL-6 Inhibitor	
Kevzara (sarilumab) SC	**Kevzara (sarilumab) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **AND** • Has had an inadequate response or intolerance to two of the following agents: ○ Actemra (tocilizumab) SC **OR** Tyenne (tocilizumab-aazg) SC ○ Enbrel (etanercept) ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded)

Agent	Medical Necessity, Rheumatoid Arthritis
	○ Rinvoq (upadacitinib) ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release)
Second-line Anti-CD-20	
• **Rituxan (rituximab) IV** • **Ruxience (rituximab-pvvr) IV** • **Truxima (rituximab-abbs) IV**	**See policy number 5.01.556 Rituximab: Non-oncologic and Miscellaneous Uses**
Second-line IL-1 Inhibitors	
Kineret (anakinra) SC	**Kineret (anakinra) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **AND** • Has had an inadequate response or intolerance to two of the following agents: ○ Actemra (tocilizumab) SC **OR** Tyenne (tocilizumab-aazg) SC ○ Enbrel (etanercept) ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) ○ Rinvoq (upadacitinib) ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release)
Second-line T-Cell Costimulation Modulators	
Orencia (abatacept) IV/SC	**Orencia (abatacept) IV is subject to review for site of service administration.**

Agent	Medical Necessity, Rheumatoid Arthritis
	Orencia (abatacept) IV/SC may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when: • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **AND** • Has had an inadequate response or intolerance to two of the following agents: o Actemra (tocilizumab) SC **OR** Tyenne (tocilizumab-aazg) SC o Enbrel (etanercept) o Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) o Rinvoq (upadacitinib) o Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release)
Second-line Janus Kinase Inhibitors	
Olumiant (baricitinib) oral	**Olumiant (baricitinib) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **AND** • Has had an inadequate response or intolerance to two of the following agents: o Actemra (tocilizumab) SC **OR** Tyenne (tocilizumab-aazg) SC o Enbrel (etanercept)

Agent	Medical Necessity, Rheumatoid Arthritis
	○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) ○ Rinvoq (upadacitinib) ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release) **Note:** The use of baricitinib in the setting of alopecia is considered cosmetic and is not covered by this policy.

Step therapy tiers are listed below; please refer to the Policy section for details.

Polymyalgia Rheumatica (PMR)
First-line Agents
IL-6 Inhibitors
Kevzara (SC)

Agent	Medical Necessity, Polymyalgia Rheumatica
First-line IL-6 Inhibitors	
Kevzara	**Kevzara (sarilumab) may be considered medically necessary for the treatment of adult individuals with polymyalgia rheumatica (PMR) when:** • The individual has had an inadequate response to one systemic corticosteroid **AND** • Medication is being prescribed by or in consultation with a rheumatologist

Step therapy tiers are listed below; please refer to the Policy section for details.

Psoriatic Arthritis
First-line Agents

<table>
<tr><th colspan="6">Psoriatic Arthritis</th></tr>
<tr><th>TNF-α Inhibitors</th><th>IL-17 Inhibitor</th><th>IL-12/23 Inhibitor</th><th>IL-23 Inhibitor</th><th>Janus Kinase Inhibitor</th><th>PDE-4 Inhibitor</th></tr>
<tr><td>Inflectra (IV)
Infliximab (Janssen – unbranded) (IV)
Remicade (IV)
Simponi Aria (IV)</td><td rowspan="3">Taltz (SC)</td><td rowspan="3">Stelara (SC)</td><td>Tremfya (SC)</td><td rowspan="3">Rinvoq/Rinvoq LQ (oral)
Xeljanz/Xeljanz XR (oral)</td><td rowspan="3">Otezla (oral)</td></tr>
<tr><td>Cyltezo (SC)
Humira (AbbVie) [NDCs starting with 00074] (SC)
Simlandi (adalimumab-ryvk) (SC)
Adalimumab-adaz (Hyrimoz unbranded) (SC)
Adalimumab-adbm (Cyltezo unbranded) (SC)
Adalimumab-ryvk (Simlandi unbranded) (SC)</td><td>Skyrizi (SC)</td></tr>
<tr><td>Enbrel (SC)</td></tr>
<tr><th colspan="6">Second-line Agents</th></tr>
<tr><th colspan="2">TNF-α Inhibitors</th><th colspan="2">IL-17 Inhibitor</th><th colspan="2">T-Cell Costimulation Modulator</th></tr>
<tr><td colspan="2">Avsola (IV)
Renflexis (IV)</td><td colspan="2" rowspan="7">Cosentyx (IV/SC)</td><td colspan="2" rowspan="7">Orencia (IV/SC)</td></tr>
<tr><td colspan="2">Cimzia (SC)</td></tr>
<tr><td colspan="2">Simponi(SC)</td></tr>
<tr><td colspan="2">Abrilada (SC)</td></tr>
<tr><td colspan="2">Adalimumab-aacf (Idacio unbranded) (SC)</td></tr>
<tr><td colspan="2">Adalimumab-aaty (Yuflyma unbranded) (SC)</td></tr>
<tr><td colspan="2">Adalimumab-fkjp (Hulio unbranded) (SC)</td></tr>
</table>

Psoriatic Arthritis		
Amjevita (SC)		
Hadlima (SC)		
Hulio (SC)		
Humira (Cordavis) [NDCs starting with 83457] (SC)		
Hyrimoz (SC)		
Idacio (SC)		
Yuflyma (SC)		
Yusimry (SC)		

Agent	Medical Necessity, Psoriatic Arthritis
First-line TNF-α Antagonists	
• **Cyltezo (adalimumab-adbm) SC** • **Humira (adalimumab) (AbbVie) [NDCs starting with 00074] SC** • **Simlandi (adalimumab-ryvk) SC** • **Adalimumab-adaz (Hyrimoz unbranded) SC** • **Adalimumab-adbm (Cyltezo unbranded) SC** • **Adalimumab-ryvk (Simlandi unbranded) SC** • **Enbrel (etanercept) SC** • **Simponi Aria (golimumab) IV**	**Simponi Aria (golimumab) IV is subject to review for site of service administration.** **Cyltezo (adalimumab-adbm), Simlandi (adalimumab-ryvk), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Enbrel (etanercept) or Simponi Aria (golimumab) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist **Humira (adalimumab) (AbbVie) [NDCs starting with 00074] may be considered medically necessary for the treatment of active psoriatic arthritis when:** • The individual has had an inadequate response or intolerance to one of the following agents:[1] ○ Enbrel (etanercept)

Agent	Medical Necessity, Psoriatic Arthritis
	○ Cyltezo (adalimumab-adbm) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) ○ Otezla (apremilast) ○ Skyrizi (risankizumab-rzaa) SC ○ Stelara (ustekinumab) SC ○ Taltz (ixekizumab) ○ Tremfya (guselkumab) **AND** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist [1]Note: Only applies to individuals not previously treated with requested therapy
• **Inflectra (infliximab-dyyb) IV** • **Infliximab (Janssen – unbranded) IV** • **Remicade (infliximab) IV**	**Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) are subject to review for site of service administration.** **Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist
First-line IL-17 Inhibitor	
Taltz (ixekizumab) SC	**Taltz (ixekizumab) SC may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist
First-line IL-12/23 Inhibitor	
Stelara (ustekinumab) SC	**Stelara (ustekinumab) SC may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist
First-line IL-23 Inhibitors	

Agent	Medical Necessity, Psoriatic Arthritis
Tremfya (guselkumab) SC	**Tremfya (guselkumab) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist
Skyrizi (risankizumab-rzaa) SC	**Skyrizi (risankizumab-rzaa) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist
First-line Janus Kinase Inhibitors	
• **Rinvoq (upadacitinib) oral** • **Rinvoq LQ (upadacitinib) oral** • **Xeljanz (tofacitinib) oral** • **Xeljanz XR (tofacitinib extended-release) oral**	**Rinvoq (upadacitinib), Rinvoq LQ (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended-release) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • The individual has had an inadequate response or intolerance to one or more TNF blockers **AND** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist
First-line PDE4 Inhibitor	
Otezla (apremilast) oral	**Otezla (apremilast) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist
Second-line TNF-α Antagonists	
• **Abrilada (adalimumab-afzb) SC** • **Adalimumab-aacf (Idacio unbranded) SC** • **Adalimumab-aaty (Yuflyma unbranded) SC** • **Adalimumab-fkjp (Hulio unbranded) SC** • **Amjevita (adalimumab-atto) SC** • **Hadlima (adalimumab-bwwd) SC**	**Abrilada (adalimumab-afzb), adalimumab-aacf (Idacio unbranded), adalimumab-aaty (Yuflyma unbranded), adalimumab-fkjp (Hulio unbranded), Amjevita (adalimumab-atto), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), Humira (adalimumab) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz), Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist **AND**

Agent	Medical Necessity, Psoriatic Arthritis
• **Hulio (adalimumab-fkjp) SC** • **Humira (adalimumab) (Cordavis) [NDCs starting with 83457] SC** • **Hyrimoz (adalimumab-adaz) SC** • **Idacio (adalimumab-aacf) SC** • **Yuflyma (adalimumab-aaty) SC** • **Yusimry (adalimumab-aqvh) SC**	• The individual has had an inadequate response or intolerance to ALL the following agents: ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded) ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074] ○ Adalimumab-adaz (Hyrimoz unbranded) ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
• **Cimzia (certolizumab pegol) SC** • **Simponi (golimumab) SC**	**Cimzia (certolizumab pegol) and Simponi (golimumab) SC may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist **AND** • The individual has had an inadequate response or intolerance to TWO of the following agents: ○ Enbrel (etanercept) ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) ○ Otezla (apremilast) ○ Rinvoq (upadacitinib) or Rinvoq LQ (upadacitinib) ○ Skyrizi (risankizumab-rzaa) SC ○ Stelara (ustekinumab) SC ○ Taltz (ixekizumab) ○ Tremfya (guselkumab) ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release)
• **Avsola (infliximab-axxq) IV**	**Avsola (infliximab-axxq) and Renflexis (infliximab-abda) are subject to review for site of service administration.**

Agent	Medical Necessity, Psoriatic Arthritis
• **Renflexis (infliximab-abda) IV**	**Avsola (infliximab-axxq) and Renflexis (infliximab-abda) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist **AND** • The individual has had a documented trial and treatment failure with Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), or Remicade (infliximab)
Second-line IL-17 Inhibitors	
Cosentyx (secukinumab) IV/SC	**Cosentyx (secukinumab) IV is subject to review for site of service administration.** **Cosentyx (secukinumab) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • The individual has had an inadequate response or intolerance to two of the following agents: ○ Enbrel (etanercept) – TNF-α Inhibitor ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) – TNF-α Inhibitor ○ Otezla (apremilast) – PDE-4 Inhibitor ○ Rinvoq (upadacitinib) **OR** Rinvoq LQ (upadacitinib) – Janus Kinase Inhibitor ○ Skyrizi (risankizumab-rzaa) – IL-23 Inhibitor ○ Stelara (ustekinumab) – IL-12/23 Inhibitor ○ Taltz (ixekizumab) – IL-17 Inhibitor ○ Tremfya (guselkumab) – IL-23 Inhibitor ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release) – Janus Kinase Inhibitor **AND** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist

Agent	Medical Necessity, Psoriatic Arthritis
Second-line T-Cell Costimulation Modulators	
Orencia (abatacept) IV/SC	**Orencia (abatacept) IV is subject to review for site of service administration.** **Orencia (abatacept) IV/SC may be considered medically necessary for the treatment of adults with active psoriatic arthritis when:** • The individual is aged 18 years or older **AND** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist **AND** • Has had an inadequate response or intolerance to TWO of the following agents: ○ Enbrel (etanercept) ○ Cyltezo (adalimumab-adbm) **OR** Humira (adalimumab) (AbbVie) [NDCs starting with 00074] **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) ○ Otezla (apremilast) ○ Rinvoq (upadacitinib) **OR** Rinvoq LQ (upadacitinib) ○ Skyrizi (risankizumab-rzaa) ○ Stelara (ustekinumab) SC ○ Taltz (ixekizumab) ○ Tremfya (guselkumab) ○ Xeljanz (tofacitinib) **OR** Xeljanz XR (tofacitinib extended-release) **Orencia (abatacept) SC may be considered medically necessary for the treatment of pediatric individuals with active psoriatic arthritis when:** • The individual is aged 2 years or older **AND** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist

Agent	Medical Necessity, Psoriatic Arthritis

	AND
	• Has had an inadequate response or intolerance to ONE of the following agents:
	  ○ Enbrel (etanercept)
	  ○ Rinvoq (upadacitinib) **OR** Rinvoq LQ (upadacitinib)
	  ○ Stelara (ustekinumab) SC

Step therapy tiers are listed below; please refer to the Policy section for details.

Non-Radiographic Axial Spondyloarthritis		
First-line Agents		
TNF-α Inhibitors	**IL-17 Inhibitor**	**Janus Kinase Inhibitor**
Cimzia (SC)	Taltz (SC)	Rinvoq (oral)
Second-line Agents		
IL-17 Inhibitors		
Cosentyx (IV/SC)		

Agent	Medical Necessity, Non-Radiographic Axial Spondyloarthritis
First-line TNF-α Inhibitors	

Cimzia (certolizumab pegol) SC	**Cimzia (certolizumab pegol) may be considered medically necessary for the treatment of non-radiographic axial spondyloarthritis in adults when:**
	• The individual has objective signs of inflammation, defined as at least one of the following:
	  ○ C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory
	OR
	  ○ Sacroiliitis reported on magnetic resonance imaging (MRI)
	AND
	• Cimzia (certolizumab pegol) is prescribed by or in consultation with a rheumatologist

First-line IL-17 Inhibitor	

Agent	Medical Necessity, Non-Radiographic Axial Spondyloarthritis

Taltz (ixekizumab) SC	**Taltz (ixekizumab) may be considered medically necessary for the treatment of non-radiographic axial spondyloarthritis in adults when:**
	• The individual has objective signs of inflammation, defined as at least one of the following:
	  ○ C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory
	OR
	  ○ Sacroiliitis reported on magnetic resonance imaging (MRI)
	AND
	• Taltz (ixekizumab) is prescribed by or in consultation with a rheumatologist

First-line Janus Kinase Inhibitor	

Rinvoq (upadacitinib) oral	**Rinvoq (upadacitinib) may be considered medically necessary for the treatment of non-radiographic axial spondyloarthritis in adults when:**
	• The individual has objective signs of inflammation, defined as at least one of the following:
	  ○ C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory
	OR
	  ○ Sacroiliitis reported on magnetic resonance imaging (MRI)
	AND
	• Has had an inadequate response or intolerance to Cimzia (certolizumab pegol)
	AND
	• Rinvoq (upadacitinib) is prescribed by or in consultation with a rheumatologist

Second-line IL-17 Inhibitor	
Cosentyx (secukinumab) IV/SC	**Cosentyx (secukinumab) IV is subject to review for site of service administration.** **Cosentyx (secukinumab) may be considered medically necessary for the treatment of non-radiographic axial spondyloarthritis in adults when:**

Agent	Medical Necessity, Non-Radiographic Axial Spondyloarthritis

	• The individual has objective signs of inflammation, defined as at least one of the following:
	  ○ C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory
	OR
	  ○ Sacroiliitis reported on magnetic resonance imaging (MRI)
	AND
	• Has had an inadequate response or intolerance to two of the following agents:
	  ○ Cimzia (certolizumab pegol)
	  ○ Rinvoq (upadacitinib)
	  ○ Taltz (ixekizumab)
	AND
	• Cosentyx (secukinumab) is prescribed by or in consultation with a rheumatologist

Drug	Investigational
As listed	**All other uses of the above-named agents when used in combination with each other, in quantities that exceed the FDA labeled dosing for condition, or for conditions not outlined in this policy, policy 5.01.563, policy 5.01.564, or policy 5.01.629 are considered investigational.**

Drug	Not Medically Necessary
As listed	**All other uses of the drugs for approved conditions listed in this policy are considered not medically necessary.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in policy may be approved up to 12 months.**
Re-authorization criteria	**Future re-authorization of all drugs listed in policy may be approved up to 3 years as long as the drug-specific coverage criteria are met, and chart notes demonstrate that the**

Length of Approval	
Approval	**Criteria**
	individual continues to show a positive clinical response to therapy.

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	
C9166	Injection, secukinumab, intravenous (Cosentyx), 1 mg (new code effective 4/1/2024) (code terminated effective 7/1/2024)
J0129	Injection, abatacept (Orencia), 10 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J0135	Injection, adalimumab (Humira), 20 mg
J0717	Injection, certolizumab pegol (Cimzia), 1 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J1438	Injection, etanercept (Enbrel), 25mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J1602	Injection, golimumab (Simponi Aria), 1 mg, for intravenous use
J1628	Injection, guselkumab (Tremfya), 1 mg
J1745	Injection, infliximab, excludes biosimilar (Remicade or Janssen unbranded), 10mg
J3247	Injection, secukinumab, intravenous, (Cosentyx) 1 mg (new code effective 7/1/2024)
J3262	Injection, tocilizumab (Actemra), 1 mg
J3357	Injection, usekinumab (Stelera), 1mg.

Code	Description
J3590	Unclassified biologics (use only to report Amjevita , Kevzara, Kineret, Simponi, Skyrizi, Taltz, Cyltezo, Hyrimoz HCF, Adalimumab-adaz HCF (Sandoz – unbranded), Abrilada, Hadlima, Hulio, Hyrimoz LCF, Yuflyma and Yusimry and Simlandi)
Q5103	Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg
Q5115	Injection, rituximab-abbs, biosimilar, (Truxima), 10 mg
Q5121	Injection, infliximab-axxq, biosimilar, (Avsola), 10 mg
Q5131	Injection, adalimumab-aacf (Idacio), biosimilar, 20 mg
Q5132	Injection, adalimumab-afzb (Abrilada), biosimilar, 10 mg (new code effective 1/1/2024)
Q5133	Injection, tocilizumab-bavi (tofidence), biosimilar (Tofidence), 1 mg (new code effective 4/1/2024)
Q5135	Injection, tocilizumab-aazg (tyenne), biosimilar, 1 mg (new code effective 10/1/2024)

Related Information

Consideration of Age

Age limits specified in this policy are determined according to FDA-approved indications, where applicable.

For site of service for medical necessity the age described in this policy is 13 years of age or older. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home. The age criterion for site of service for medical necessity is based on the following: Pediatric individuals are not small adults. Pediatric individuals differ physiologically, developmentally, cognitively, and emotionally from adult individuals, and vary by age groups from infancy to teen. Children often require smaller doses than adults, lower infusion rates, appropriately sized equipment, the right venipuncture site determined by therapy and age, and behavioral management during administration of care. Specialty infusion training is therefore necessary for pediatric IV insertions and therapy. Due to pediatrics unique physiology and psychology, site of service review is limited to individuals above the age of 13.

Rheumatoid Arthritis

Rheumatoid Arthritis (RA) is a chronic, progressive, inflammatory, autoimmune disease affecting about 1% of the US adult population and occurs approximately three times more frequently in women than in men (ACR Subcommittee on Rheumatoid Arthritis Guidelines, 2002). Almost 80% of RA cases occur in individuals between 35 and 50 years of age (Kavanaugh and Lipsky, 1996); usually a time of peak social productivity. The underlying cause of RA is unknown, but the disease is characterized by persistent inflammation of the synovium, cartilage loss, and bone erosion in peripheral joints, usually in a symmetric fashion. This inflammation is believed to be mediated by both B- and T-cells and a variety of cytokines (messenger proteins), including tumor necrosis factor-alpha (TNF-α). Research has shown that joint damage occurs within the first two years of symptoms and diagnosis and progresses rapidly if not treated. Although RA primarily affects the joints, it is a systemic disease and does cause systemic and extra-articular clinical features (e.g., fever, fatigue, anorexia, weight loss, and anemia), which contribute to the significant work disability and impaired quality of life which occur. Individuals with RA also have earlier mortality than the general population averaging 7-10 years, primarily due to an increased risk of cardiovascular disease, infection, and lymphoma associated with more severe inflammation.

The American College of Rheumatology (ACR) has established clinical guidelines for the treatment of RA. While both non-pharmacologic (e.g., individual education, exercise, and physical and occupational therapy) and pharmacologic therapies are recommended, the mainstay of RA treatment is pharmacologic therapy. Pharmacologic management often consists of nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs (DMARDs) (including biologic response modifiers/cytokine antagonists), and/or corticosteroids. Because of the evidence showing that joint damage can occur early in the disease process, physicians are now encouraged to treat individuals more aggressively earlier by initiating a DMARD (or combinations of DMARDs) within three months of diagnosis.

Emerging evidence also suggests that the DMARD subclass of tumor necrosis factor-alpha (TNF-α) antagonists retard radiographic progression of the disease better than methotrexate (MTX), particularly in individuals with rapidly progressive disease. The predictive risk factor found to be most associated with this subset of individuals was a CRP ≥4.1 mg/dl. Other predictors are currently being investigated. This should lead to improved ability for the clinician to determine the best DMARD for an individual; however, the choice will continue to be influenced by

numerous factors, including but not limited to relative efficacy, convenience of administration, adverse effects, monitoring requirements, comorbidities, and cost. Orencia (abatacept) and Rituxan (rituximab) have also gained labeling regarding ability to inhibit progressive structural damage.

Psoriatic Arthritis

Psoriatic Arthritis (PsA) is characterized as a spondyloarthropathy associated with psoriasis. The true incidence is unknown and is variably reported to occur in 6-42% (25% is considered a reasonable estimate) of individuals with psoriasis, an immunologic skin disease which occurs in 2-3% of the general population. There is similarity in the histopathogenesis of PsA and RA, including the role of cytokines such as tumor necrosis factor alpha (TNF- α), although there are important differences as well. Several subsets of PsA have also been described. PsA is characterized by stiffness - both peripheral and spine inflammation and pain - joint deformities related to joint destruction, dactylitis, enthesitis (inflammation at insertion sites of tendons, ligaments, and joint capsule fibers), and psoriasis skin plaques. The course of PsA is variable, but the majority of individuals develop a chronic progressive form of the disease resulting in joint destruction, unless treated effectively. Although less well characterized than in RA, similar levels of disability, decreased quality of life, increased co-morbidities, and premature mortality are now being noted in long term registry studies.

Pharmacologic therapy combined with a physical rehabilitation program is the most effective available treatment for psoriatic arthritis (PsA). As with RA, early initiation of pharmacologic therapy is needed to avoid joint damage and disability.

NSAIDs have customarily been used in milder disease along with corticosteroids or traditional DMARDs. Moderate to severe disease requires the use of traditional DMARDs such as MTX, sulfasalazine, or the anti-TNF agents. Azathioprine and cyclosporine are rarely used. Retinoids, phototherapy, and topical and systemic corticosteroids have also been used to treat the skin manifestations of PsA. In January 2002, etanercept, a TNF-α inhibitor became the first therapy to be approved for the indication. Adalimumab has also recently received FDA-approval for this indication. Additionally, infliximab has been demonstrated effective for this condition in at least one randomized, double-blind, controlled clinical trial. FDA has since approved the newer TNF-α inhibitors certolizumab pegol and golimumab for this indication. More recently, the IL12/IL23 inhibitor ustekinumab and the phosphodiesterase four inhibitor apremilast are now approved.

Other Spondyloarthropathies

The spondyloarthropathies (SpAs) are a heterogeneous set of disorders characterized by axial skeletal involvement and frequent association with the HLA-B27 antigen. Ankylosing spondylitis (AS) is probably the most familiar spondyloarthropathy, which is characterized predominantly by progressive vertebral enthesitis and facet joint inflammation of the spine and sacroiliac joints, leading to eventual spine fusion and decreased range of motion, as well as peripheral joint synovitis, although much less than is seen in RA. Variations in incidence among different racial groups support the hypothesis of a genetic role in AS, as is also postulated in other arthropathies. In the United States, AS is believed to affect approximately 1-3 persons/1000, or about 350,000 to 1 million individuals.

While peripheral arthritis is commonly seen in association with psoriasis, approximately 20-40% of individuals with PsA may have some degree of sacroiliitis with paravertebral ossification. The skin manifestations associated with the arthropathy are not necessarily widespread and may be localized.

About 20% of individuals with inflammatory bowel disease may have evidence of sacroiliitis and some 20% of these individuals may progress to spondylitis. The course of the spondylitis does not necessarily correlate with bowel inflammatory activity.

Treatment of mild spondyloarthropathy may be benefited by symptomatic therapy with NSAIDs, corticosteroids, or sulfasalazine. These agents have shown to have little clinical benefit in individuals with moderate to severe or progressive disease. The paucity of treatment options contrasts with the treatment of RA where there are several different categories of DMARDs (disease-modifying anti-rheumatic drugs) that are used alone or in combination to try and alter the natural history of the disease. Like PsA, etanercept became the first therapy approved by the FDA for the treatment of AS, followed by infliximab and adalimumab.

Juvenile Idiopathic Arthritis

Juvenile Idiopathic Arthritis (JIA) is the most common type of arthritis in children under the age of 17. It causes persistent joint pain, swelling, and stiffness. Some children may experience symptoms for only a few months, while others have symptoms for the rest of their lives. In some cases this disease can cause complications, such as growth problems and eye inflammation. Treatment usually focuses on controlling pain, improving function, and preventing joint damage.

JIA occurs when the body's immune systems attacks its own cells and tissues. It is not clear why this happens, however, both heredity and environment seem to play a role. Many different

blood tests are used to diagnose JIA. Examples of some are: erythrocyte sedimentation rate (ESR), anti-nuclear antibody, rheumatoid factor, cyclic citrullinated peptide (CCP).

Treatment modalities depend on the extent of the disease, and individual child's needs. Some children benefit from one medication; others may need combination of a few different medications. Each drug comes with its own side-effect potential which needs to be taken into consideration based on the child's overall health condition and needs. First-line therapy includes the nonsteroidal anti-inflammatory drugs (NSAIDs)-examples of which are: ibuprofen, naproxen, and others. NSAIDs help to reduce pain and swelling of the joints. Disease-Modifying Antirheumatic Drugs (DMARDs) is another option for drug therapy and include methotrexate, sulfasalazine, and others may be used when NSAIDs alone fail. Their purpose is to slow the progression of JIA. Tumor Necrosis Factor (TNF) Blockers, such as etanercept and adalimumab can help reduce pain, morning stiffness, and swollen joints. Immune suppressants, such as: abatacept, rituximab, anakinra, and tocilizumab are useful because JIA is caused by an overactive immune system, and agents that suppress the immune system can help. Corticosteroids, such as prednisone may also be used to control the symptoms until a DMARD agent takes effect or to prevent complications. Agents discussed in this policy include, etanercept, adalimumab, abatacept, anakinra, and tocilizumab.

Polymyalgia Rheumatica (PMR)

Polymyalgia rheumatica (PMR) is an inflammatory rheumatic condition characterized by symmetrical aching and morning stiffness in the shoulder, hip girdle, and neck. Individuals affected by PMR often experience a gel phenomenon where pain and stiffness worsens with inactivity. PMR affects adults aged over 50 years. Individuals with PMR typically exhibit elevated level of inflammatory markers (e.g., IL-6) and reduction in numbers of circulating B cells. The reduction in B cells is inversely associated with elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). A PMR diagnosis is based on history and physical examination, laboratory testing that evaluates acute phase reactants such as ESR and CRP, and in some cases, magnetic resonance imaging (MRI)/ultrasound. In cases where PMR is suspected, the individuals are given low-dose glucocorticoids (e.g., prednisone 15 to 25 mg/day or its equivalent) to see if individuals have rapid resolution of symptoms. If the individuals do have rapid resolution of the symptoms, then the individual is most likely to have PMR.

The overall goal of the treatment is the relief of the symptoms. Initial treatment includes low dose glucocorticoids. The initial dose of glucocorticoids depends on the individual's severity of symptoms. Comorbidities and individual's weight. There is lack of data regarding the optimal

starting dose of glucocorticoids. If the symptoms do not improve in a week, then the dose escalation of the glucocorticoid is warranted.

Toxicities of TNF-α Antagonists

All TNF-α antagonists have treatment-limiting toxicities. Some of the toxicities associated with these agents include Concomitant use of TNF-α inhibitors and MTX consistently scored better with respect to ACR scores, disease activity in 28 joints (DAS28) scores, radiographical progression and health assessment questionnaire (HAQ) scores compared to TNF-α inhibitor monotherapy. The ACR70 scores ranged from 15-20% for all agents, with etanercept showing the highest treatment effect over the control group at three years in the TEMPO trial. While infliximab showed high efficacy at both 3mg/kg and 10mg/kg dosing every eight weeks, the ACR50, ACR70 scores, HAQ scores were slightly higher with 10mg/kg dosing. The DAS28 scores and HAQ scores varied from study to study, but over-all showed improvement over controls across the TNF-α inhibitor class at 12 weeks and greater. Radiographical changes are subject to interpretation by the individual investigator, even with standardized scoring, so comparing across the TNF-α inhibitor trials is not practical. However, of the studies that did assess radiographical progression of the disease, the overall rate of radiographical progression was slowed significantly with adalimumab, certolizumab, etanercept and infliximab compared to MTX therapy alone. In the three-year TEMPO trial, the scores for the etanercept + MTX arm showed reversal of radiographical progression, but this is debatable and requires further investigation. There is no radiographical progression data for golimumab, as they did not assess this in their clinical trials.

There have been no prospective trials evaluating safety among the TNF-α inhibitors. The risk of malignancies and serious infections has been studied to some depth retrospectively with the three older agents (adalimumab, etanercept and infliximab). The FDA did a meta-analysis of the available data in 2006 and found that the malignancy rates of individuals on TNF-α inhibitors are no higher than what is to be expected in this individual population. Another study done in 2007 found a higher incidence of cutaneous cancers among the TNF-α inhibitor treated individuals, irrespective of the agent. The newer agents are limited in their data breadth to demonstrate safety with respect to malignancies, but so far, they compare similarly to the older agents. Long-term safety evaluations are necessary to validate this finding.

With regards to serious infections and tuberculosis, there are higher rates of serious infections while on the TNF-α inhibitors, compared to MTX alone. However, the retrospective studies do not come to an agreement on the actual risk. Infliximab showed higher rates of any infection compared to etanercept and adalimumab, and also showed higher rates of serious infections

with the 10mg/kg dosing regimen versus the 3mg/kg dosing regimen. The newer agents (certolizumab and golimumab) showed increased risk of serious infections, but this data is not comparable with the older agents. This class of agents also has been associated with hepatitis B reactivation, CHF exacerbations, and new onset or exacerbation of demyelinating disorders.

The evidence suggests that etanercept and adalimumab are more cost-effective than infliximab in both early aggressive and long-standing RA. The evidence also demonstrates that combination therapy with methotrexate is more cost-effective than TNF-α inhibitor monotherapy. The majority of the published incremental cost-utility ratios fall within the willingness to pay threshold of $100,000 per quality-adjusted life year (QALY) gained, and many are less than $50,000 per QALY. The models were most sensitive to changes in drug cost. The newer agents, certolizumab and golimumab, could not be evaluated for cost-effectiveness due to lack of data.

Newer Antirheumatic Agents

Actemra (tocilizumab), a humanized monoclonal antibody targeted to antagonize interleukin-6 (IL-6) receptor both soluble and membrane bound, resulting in a decline of cytokine and acute phase reactant production, was approved by FDA in 2009. The inflammatory response induces the production of IL-6 from numerous synovial and endothelial cells, leading to IL-6 to congregate within the joints and mediating various other immunologic responses. Tocilizumab is indicated for moderate to severe active RA with inadequate response to one or more Disease Modifying Anti-Rheumatic Drugs (DMARDs).

The evidence of efficacy of tocilizumab in rheumatoid arthritis consists primarily of four randomized controlled trials (RADIATE, OPTION, AMBITION, and TOWARD). The primary endpoint for all studies was the proportion of individuals to reach an ACR20 response at week 24, which was achieved in all tocilizumab groups when compared to placebo. In the RADIATE trial, the 8 mg/kg, 4 mg/kg, and placebo results were 50.0%, 30.4%, and 10.1%, $p<0.001$. In the OPTION trial, the 8 mg/kg, 4 mg/kg, and placebo results were 59%, 48%, and 26%, $p<0.0001$. In the AMBITION trial, the results for the 8 mg/kg group compared to the MTX group were 69.9% and 52.5%, $p<0.001$. In the TOWARD trial, the results for the 8 mg/kg group compared to the DMARD placebo group was 61% and 25%, $p<0.0001$.

All studies showed positive secondary endpoints in the ACR50, ACR70, and remission rates defined as DAS28 score <2.6. The ACR50 scores in the RADIATE trial were 28.8% ($p<0.001$), 16.8% ($p<0.001$), and 3.8% in the tocilizumab 8 mg/kg, 4 mg/kg, and placebo group, respectively. In the OPTION trial, the ACR50 response was 44% and 31% in the 8 mg/kg and 4

mg/kg group compared to 11% (p<0.0001) in the placebo group. In the AMBITION trial, the ACR50 response for the tocilizumab group compared to the MTX group was 44.1% and 33.5% (p=0.002). In the TOWARD trial, the ACR50 response in the 8 mg/kg and placebo group was 38% and 9% (p<0.0001). No comparative effectiveness studies of this product have been reported to date.

The overall rate of serious infections with tocilizumab in the all-exposure population was 4.7 events per 100 individual-years and the overall rate of fatal serious infections was 0.13 per 100 individual-years. Because tocilizumab is the first in this therapeutic class, further long-term studies are still needed to evaluate the safety profile, and these infections are a concern.

Radiographic progression data for abatacept is now available for up to five years in biologic-naïve RA individuals with an inadequate response to methotrexate (AIM study) and up to 2 years in methotrexate-naïve moderate to severe early RA (AGREE study). In a long-term extension of the 1-year, Phase III, randomized, double-blind, placebo-controlled AIM study, 291 of the initial 378 individuals (77%), 290 (77%), 293 (78%), 287 (76%), and 235 (62%) individuals had paired radiographs at baseline and at years 1, 2, 3, 4, and 5, respectively. Mean change from baseline in Genant-modified Total Sharp Score (range 0-290) was 0.80 at year 1, 0.41 at year 2, 0.37 at year 3, 0.34 at Year 4, and 0.26 at Year 5, indicating long-term inhibition of radiographic progression in biologic-naïve RA individuals. In an open-label long-term extension of the 1-year, Phase III, randomized, double-blind, active (methotrexate)-controlled AGREE study, 207 biologic- and DMARD-naïve individuals with moderate to severe early RA treated with the combination of abatacept and methotrexate had a mean change from baseline in Genant-modified Total Sharp Score (range 0-290) of 0.66 at year 1 vs. 1.06 (p=0.04) for the control (methotrexate alone) arm and 0.18 for abatacept + methotrexate at year 2; indicating a maintenance disease-modifying effect on bone damage over time in this population also.

Six-years of cumulative safety data integrated from eight key clinical trials in the abatacept clinical development program were also recently reported. Cumulative experience included 11,658 individual-years in 4,149 individuals, of which 1,030 individuals had ≥5 years of exposure to abatacept. Mean duration of exposure was 34.2 years (range: 1.9-94.0 months). Rates were stratified by short-term (ST), long-term (LT), and cumulative exposure. The short-term period included 3,173 individuals (2,331 individual-years) and the long-term period included 3,256 individuals (9,278 individual-years).

The incidence rates of overall adverse events per 100 individual–years (95% confidence interval [CI]) were 386.70 (372.31–401.51) in the ST period, 228.23 (220.03–236.66) in the LT period, and 284.42 (275.50–293.55) in the cumulative period. Incidence rates of deaths and serious adverse events were low and did not increase with increased duration of abatacept exposure. The overall incidence of serious adverse events per 100 individual-years (95% CI) was 18.15 (16.41-20.02) in

the ST period, 14.52 (13.66-15.43) in the LT period, and 14.82 (14.04-15.63) cumulatively. Mortality rates per 100 individual-years were 0.51 (0.27-0.90), 0.61 (0.47-0.80), and 0.60 (0.47-0.76) in the ST, LT, and cumulative periods, respectively. No increases in the annual incidence of events of special interest including rates of infections, malignancies, autoimmune events, serious cardiac events and acute infusional events were observed. Based on these data, the LT safety profile of abatacept appears consistent with its short-term safety profile.

Tofacitinib, a first-in-class oral Janus kinase inhibitor approved in 2012 for treatment of moderate to severe RA. Efficacy of tofacitinib 5 mg and 10 mg was established in five Phase III clinical trials and three Phase II dose ranging studies. All are prospective, randomized, placebo controlled, double-blind studies that conclude statistically and clinically significant improvement. Approximately twice as many individuals reached ACR 20 (20% clinical improvement) in the tofacitinib groups as placebo after three months of treatment. This ratio widened even more for ACR 50 and ACR 70 endpoints. Improvements in HAQ-DI and DAS28-4[ESR] scores were also statistically and clinically significant. Individuals showed improvement as soon as two weeks. Results are consistent among the studies. In some studies, prior DMARD use and/or nonresponse were not clearly stated. Trials including an adalimumab arm suggest fairly comparable efficacy to this first line agent but were not powered for the direct comparison.

Significant safety concerns exist for tofacitinib. The rate of serious infections, opportunistic infection, and death from serious infection was higher in the tofacitinib groups than adalimumab or placebo, even after adjusting for individual-years of treatment. Pooled data in the FDA review also identified an increased risk of lymphoproliferative disorders. Some of this may be attributable to the underlying risk of lymphoma in RA, but long-term safety is not known. Tofacitinib consistently elevates LDL and HDL cholesterol levels. Data were given as means, so individual variation in cholesterol level elevation is not available. No increase in cardiovascular events was seen in the studies; however, as RA individuals are already at increased risk for cardiovascular disease this is a concern. The FDA approved tofacitinib with a black box warning for infection, lymphoma, and malignancies, and testing for tuberculosis before and during treatment. Overall, the long-term safety of tofacitinib is not known. As it has a novel mechanism of action, there is no long-term safety data from similar products.

Sarilumab, interleukein-6 (IL-6) receptor antagonist, is indicated for the treatment of the adult individuals with moderately to severely active rheumatoid arthritis who have had trial and failure to one or more disease-modifying antirheumatic drugs (DMARDS). Sarilumab is also indicated for adult individuals with polymyalgia rheumatica (PMR) who have had inadequate response to corticosteroids or who cannot tolerate corticosteroid taper. The efficacy and safety of Kevzara in individuals with moderate to severe rheumatoid arthritis was accessed in two randomized, double-blind, placebo-controlled multicenter studies.

Study 1 included 1197 individuals with moderate to severe rheumatoid arthritis who had inadequate response to methotrexate (MTX). Individuals received Kevzara 200 mg or Kevzara 150 mg or placebo every two weeks along with MTX. The primary efficacy endpoint was the proportion of the individuals who achieved an ACR20 response at week twenty-four. Other endpoints included change in HAQ-FI from baseline to week 16 and change in Vander Heijden-modified total sharp score (mTSS) from baseline to week 52. The individuals in the treatment groups had low level of disease activity, measured by a Disease Activity Score 28 C-Reactive Protein (DAS28-CRP). At the end of week 24, 10.1% in the placebo group, 27.8% in the Kevzara 150 mg group and 34.1% in the Kevzara 200 mg group had DAS28-CRP <2.6.

Study 2 included 546 individuals with moderate to severe rheumatoid arthritis who had an inadequate response or intolerance to one or more TNFα antagonists. Individuals received Kevzara 200 mg, Kevzara 150 mg or placebo every two weeks along with conventional DMARDs. The primary efficacy endpoint was the proportion of the individuals who achieved an ACR20 response in week twenty-four. Other endpoints included change in HAQ-DI from baseline to week 12. The individuals in the treatment groups had low level of disease activity, measured by a Disease Activity Score 28 C-Reactive Protein (DAS28-CRP). At the end of week 24, 7.2% in the placebo group, 24.9% in the Kevzara 150 mg group and 28.8% in the Kevzara 200 mg group had DAS28-CRP <2.6.

The efficacy and safety of Kevzara in adult individuals with PMR was studied in a 52-weeks, randomized, double-blind, placebo-controlled trial. The individuals were randomized to receive Kevzara 200 mg every two weeks with a pre-defined 14-week taper of prednisone (n = 60) or placebo every two weeks with a pre-defined 52-week taper of prednisone (n = 58). The primary efficacy endpoint was proportion of individuals with sustained remission at week fifty-two. An additional efficacy endpoint was total cumulative corticosteroid dose over 52 weeks. The individuals in treatment group had statistically significant higher number of individuals with sustained remission with 28.3% in Kevzara arm and 10.3% in the placebo arm. In the Kevzara arm, the mean total cumulative corticosteroid dose was 1039.5 mg, while in the placebo arm, the mean total cumulative corticosteroid dose was 839.4 mg.

2018 Update

Added criteria for newly approved Janus Kinase inhibitor, Olumiant (baricitinib). Literature search did not identify any other required changes. The American College of Rheumatology guidelines are currently being updated, but the next version is not expected until late 2019.

2019 Update

Added criteria for Skyrizi (risankizumab-rzaa) which was approved by the FDA in April 2019 for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. Added to Cimzia (certolizumab pegol) criteria for the treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation. Literature search did not identify any other required changes.

2020 Update

Updated Actemra (tocilizumab) coverage criteria for rheumatoid arthritis with requirement that the patient had an inadequate response or intolerance to both methotrexate and Humira (adalimumab) prior to Actemra. The changes in Actemra coverage criteria are effective on January 1, 2021.

2021 Update

Added Xeljanz Oral Solution (tofacitinib) as a first-line product for treatment of polyarticular JIA and updated References.

2022 Update

Added coverage criteria for Skyrizi (risankizumab-rzaa) for the treatment of psoriatic arthritis. Added coverage criteria for Adbry (tralokinumab-ldrm), Cibinqo (abrocitinib), and Rinvoq (upadacitinib) for the treatment of moderate-to-severe atopic dermatitis. References were reviewed and updated.

2023 Update

Reviewed prescribing information for all drugs. Added note to baricitinib criteria that the use of baricitinib in the setting of alopecia is considered cosmetic and is not covered by this policy. Added coverage criteria for Kevzara criteria for the treatment of adult individuals with polymyalgia rheumatica (PMR). Added coverage for the biosimilars Hyrimoz LCF (adalimumab-adaz) SC, Abrilada (adalimumab-afzb) SC, Hulio ((adalimumab-fkjp) SC, Yusimry (adalimumab-

aqvh) SC, Hadlima (adalimumab-bwwd) SC and Yuflyma (adalimumab-aaty) SC for the treatment of AS, RA, JIA, and PsA as non-preferred products and with the identical coverage criteria as Amjevita (adalimumab-atto) [NDCs starting with 72511]. Added coverage for Cyltezo LCF (adalimumab-adbm), Hyrimoz HCF (adalimumab-adaz) and Adalimumab-adaz HCF (Sandoz – unbranded) SC for the treatment of AS, RA, JIA, and PsA as preferred products and with the identical coverage criteria as Amjevita (adalimumab-atto) [NDCs starting with 55513]. Removed "individual is being started on Amjevita (adalimumab-atto) [NDCs starting with 72511], Humira (adalimumab), or Enbrel (etanercept) concurrently with leflunomide, methotrexate, or sulfasalazine" from non-preferred agents' indication of treatment of polyarticular juvenile idiopathic arthritis. Updated preferred Humira biosimilars (Cyltezo LCF, Hyrimoz HCF, Adalimumab-adaz HCF (Sandoz-unbranded)) along with Humira and Amjevita (NDC starting with 55513) in the list of agents to be tried and failed prior to using nonpreferred agents, such as cosentyx (AS), Actempra (JIA), Orencia (JIA), Simponi Aria (JIA), Actemra (RA), Kevzara (RA), Kineret (RA), Orencia (RA), Olumiant (RA), Cosentyx (Psoriatic Arthritis), Orencia (Psoriatic Arthritis). Moved Simponi Aria from 2nd line to 1st line for all indications with the effective date of 01/01/2024. Moved Avsola to 1st line for all the indications with the effective date of 01/01/2024. Added Avsola to a list of preferred infliximab products to be tried and failed prior to trying non-preferred infliximab products with the effective date of 01/01/2024. Moved Inflectra to 2nd line (non-preferred) agent with the effective date of 01/01/2024. Removed Inflectra from the list of preferred products to be tried and failed prior to trying non-preferred infliximab products with the effective date of 01/01/2024. Added Humira biosimilars Idacio (adalimumab-aacf) and Adalimumab-fkjp (Biocon-unbranded) as non-preferred products with similar criteria as Amjevita (adalimumab-atto) [NDCs starting with 72511]. Updated Cosentyx coverage criteria for psoriatic arthritis, ankylosing spondylitis, and non-radiographic axial spondyloarthritis. For ankylosing spondylitis, added Rinvoq as a qualifier. For psoriatic arthritis, changed the requirement of trying three products to two products and removed the requirement of trying agents from two or more different drug classes. For non-radiographic axial spondylarthritis, added Rinvoq as a qualifier and added requirement of trying two of the three agents. Added coverage criteria for Tofidence (tocilizumab-bavi) for the treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis (PJIA), and systemic juvenile idiopathic arthritis (SJIA). Updated Amjevita [NDCs starting with 55513] to a non-preferred product effective January 1, 2024. Added Hyrimoz (Cordavis) [NDCs starting with 83457] and adalimumab-aacf (Idacio unbranded) as a non-preferred product effective January 1, 2024. Added adalimumab-adbm (Cyltezo unbranded) as a preferred product effective January 1, 2024. Updated Hyrimoz LCF (Sandoz) from a non-preferred to a preferred product effective January 1, 2024. Added IV Cosentyx (secukinumab) as a non-preferred product.

2024 Update

Reviewed prescribing information for all drugs. Removed Stelara (ustekinumab) subcutaneous (SC) injection site of service requirement. Added Humira (adalimumab) (Cordavis) [NDCs starting with 83457] as a non-preferred product. Updated Orencia (abatacept) to include coverage criteria for individuals 2 years and older with active psoriatic arthritis. Added adalimumab-aaty (Yuflyma unbranded) as a non-preferred product. Added Simlandi (adalimumab-ryvk) and adalimumab-ryvk (Simlandi unbranded) as preferred products. Updated non-preferred adalimumab coverage criteria to require trial and treatment failure with all preferred adalimumab products. Updated Rinvoq (upadacitinib) to include coverage criteria for the treatment of certain individuals with polyarticular juvenile idiopathic arthritis (PJIA). Added Rinvoq LQ (upadacitinib) coverage criteria for the treatment of certain individuals with PJIA and psoriatic arthritis. Added Tyenne (tocilizumab-aazg) IV/SC coverage criteria for the treatment of certain individuals with rheumatoid arthritis, polyarticular juvenile idiopathic arthritis (PJIA), and systemic juvenile idiopathic arthritis (SJIA). Added site of service review for Cosentyx (secukinumab) IV and Tofidence (tocilizumab-bavi) IV. Updated Kevzara (sarilumab) to include coverage criteria for the treatment of certain individuals with PJIA. Changed Inflectra (infliximab-dyyb) to a first-line agent. The following changes are effective January 3, 2025. Changed Avsola (infliximab-axxq) to a second-line agent. Updated coverage criteria for Avsola and Renflexis to require the individual to have an adequate trial and failure with Inflectra, Infliximab (Janssen – unbranded), or Remicade. Updated Hyrimoz (Sandoz) (adalimumab-adaz) [NDCs starting with 61314] from a preferred product to a non-preferred product. Updated Humira (AbbVie) (adalimumab) [NDCs starting with 00074] to require that the individual has had an inadequate response or intolerance to a preferred product for new starts.

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52. Stelara (ustekinumab). Prescribing Information. Janssen Biotech, Inc. Horsham, PA. Revised August 2022.
53. Orencia (abatacept). Prescribing Information. Bristol-Myers Squibb. Princeton, NJ. Revised October 2023.
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History

Date	Comments
03/10/14	New policy. This policy is added to the Prescription Drug section addressed prescription drug medications used to treat autoimmune disorders. The policy replaces previously active policies which have now been deleted: 5.01.526; 5.01.531; 5.01.600; 5.01.601; and 5.01.602.
03/27/14	Coding update: ICD-9 procedure code 99.29 and diagnosis codes 714.0 and 714.2 removed. These are not utilized for adjudication of the policy; informational only.
04/21/14	Update Related Policies. Add 5.01.521.
07/14/14	Interim Review. Additional agent added to the policy: Psoriasis: PDE4 Inhibitors; apremilast (Otezla) may be considered medically necessary for the treatment of adult patients with psoriatic arthritis when ALL of the criteria are met. References 211 – 221 added.
08/11/14	Interim Review. Vedolizumab (Entyvio) added for the treatment of Crohn's and ulcerative colitis; supportive information added to the Rationale section. References 222-224 added. Correction made to therapeutic drug class table. CPT codes and

Date	Comments
	HCPCS code J7050 removed from policy; these do not suspend and are not reviewed at this time.
09/12/14	Coding correction. HCPCS code J0717 added to the policy. This code replaced J0718 as of 1/1/14 and appeared on policies 5.01.601 and 5.01.602; it should have been carried over to this policy at the time it was originally effective.
11/10/14	Interim Review. Policy updated with a new Otezla indication for plaque psoriasis. Reference 22 added; 24 and 25 updated.
01/13/15	Annual Review. Drug table within the Policy section updated to include indications for treatment of Pyoderma Gangrenosum: first line, Humira and Enbrel; and, second line, Remicade.
03/10/15	Interim Update. Policy updated with Anti-CD52, alemtuzumab (Lemtrada) as a first-line treatment for relapsing MS; and, IL-17 inhibitors, secukinumab (Cosentyx) as a second-line treatment for plaque psoriasis. HPCPS code J1602 added to policy.
04/15/15	Editing correction: Policy statement on secukinumab (Cosentyx) as medically necessary as a second-line agent for the FDA-approved indication to treat adult patients with moderate to severe plaque psoriasis, clarified: approval is allowed once etanercept and adalimumab have been tried and failed; no additional criteria are required.
07/14/15	Interim Review. Indications for rituximab removed; readers referred to policies which address these indications.
12/08/15	Interim Update. Moderate to severe hidradenitis suppurativa added to the list of medically necessary indications of Humira.
01/04/16	Minor edit. Typo corrected; investigational policy statement within IL-17 inhibitors corrected to read secukinumab (ustekinumab was listed in error).
01/19/16	Coding update. New HCPCS codes J0202 and J3380, effective 1/1/16, add to the policy.
02/09/16	Annual Review. Medically necessary indications for Promacta updated; ITP removed; chronic immune ITP added with additional criteria for eligibility; and severe aplastic anemia added.
02/23/16	Coding update. Added HCPCS J1595, J1826, J1830, Q3027 and Q3028.
05/01/16	Interim Review, approved April 12, 2016: inclusion of two new indications for Cosentyx (psoriatic arthritis and ankylosing spondylitis); addition of a new agent, ixekizumab (Taltz); addition of tofacitinib extended-release (Xeljanz XR). Revision of the alphabetical (generic and brand) table.
07/01/16	Interim Review, approved June 14, 2016. Policy scope narrowed; this policy now focuses on treatment of arthropathies, and all other diseases are addressed in policies specific to condition - see related policies 5.01.563, 5.01.564, 5.01.565 and 5.01.566. Removed HCPCS codes J0135, J1595, J1826, J1830, J0202, J0490, J1602, J2323, J2796, J3380, J8499, Q3027, and Q3028. Title changed from "Pharmacotherapy of Autoimmune Diseases" to "Pharmacotherapy of Arthropathies". Site of service drug

Date	Comments
	administration review criteria added to the policy; this applies to specific drugs and is now part of the review process.
10/01/16	Interim Review, approved September 13, 2016. Minor dosing update for Xeljanz.
11/01/16	Interim Review, approved October 11, 2016. Clarified age criteria language indicating that site of service review is applicable to only those age 13 and older; drug criteria review applies to all ages.
02/01/17	Annual Review, approved January 10, 2017. Added new agent (prior to approval) baricitinib to the RA section, alongside Xeljanz.
04/01/17	Interim Review, approved March 14, 2017. Criteria for all of the agents described in this policy have changed (i.e., criteria are now less restrictive, step therapy re-arranged). Also included a statement on the status of IV agents being processed exclusively through the medical benefit. Removed baricitinib from the list of prior authorized drugs, pending FDA-approval.
04/10/17	Interim Review, approved April 10, 2017. Policy section updated with infliximab (Remicade) IV moving to a first-line agent, considered medically necessary as when criteria are met.
05/05/17	Minor update; added hyperlinks and step therapy tier charts.
06/01/17	Interim Review, approved May 16, 2017. Added a statement regarding tofacitinib's use in the setting of alopecia as being cosmetic. Added new agent, sarilumab to the IL-6 section as a second-line option.
06/13/17	Coding updated, added HCPCS code J1602 back to coding table as it was inadvertently removed.
07/01/17	Interim Review, approved June 13, 2017. Added coverage criteria for Renflexis (infliximab-abda).
08/18/17	Minor update, clarified History section for the July 1, 2016, revision.
09/01/17	Interim Review, approved August 15, 2017. Added Infliximab-abda to coverage criteria and coding section.
09/22/17	Minor update. Clarified policy statements regarding plaque psoriasis.
10/01/17	Interim Review, approved September 21, 2017. Clarified Taltz & Siliq criteria. Added criteria for Tremfya and Plivensia.
11/01/17	Interim Review, approved October 3, 2017. Clarified site of service exception criterion related to access: There is no outpatient infusion center within 50 miles of the patient's home and there is no contracted home infusion agency that will travel to their home, or a hospital is the only place that offers infusions of this drug.
02/14/18	Interim Review, approved February 13, 2018, effective February 14, 2018. Xeljanz/Xeljanz XR criteria updated for rheumatoid arthritis indication, Taltz and Siliq criteria updated for plaque psoriasis indication, Xeljanz/Xeljanz XR indication for

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	psoriatic arthritis as a first line agent, Taltz added as a second line agent for psoriatic arthritis. Updated hospital-based outpatient coverage from 30 days to 90 days.
04/01/18	Interim Review, approved March 20, 2018. Orencia was included as second-line agent for psoriatic arthritis. Plivensia was removed from policy as the drug never gained FDA approval. Dosage and quantity limit prescribing table was removed. Added HCPCS codes Q5103 and Q5104, noted that HCPCS code Q5102 terminated 4/1/18.
05/01/18	Interim Review, approved April 18, 2018. Ilumya criteria for psoriasis indication has been added.
06/01/18	Interim Review, approved May 17, 2018. Criteria updated for Tremfya's plaque psoriasis indication and Xeljanz/Xeljanz XR for psoriatic arthritis indication.
06/20/18	Added 11.01.523 to Related Policies.
08/01/18	Annual Review, approved July 13, 2018. Added criteria for newly approved Janus Kinase inhibitor, Olumiant (baricitinib). Literature search did not identify any other required changes.
09/21/18	Interim Review, approved September 11, 2018. Added criteria for Cimzia as second line treatment of plaque psoriasis.
11/01/18	Minor update, the Site of Service criteria was updated for clarity.
01/01/19	Coding update, added new HCPCS codes J3245, J9311, J9312, and Q5109 (new codes effective 1/1/19).
02/01/19	Interim Review, approved January 8, 2019. Added tocilizumab to second-line treatment for juvenile idiopathic arthritis; added tofacitinib/tofacitinib ER to first-line treatment for psoriatic arthritis; updated Actemra criteria.
02/20/19	Coding update, added HCPCS code J1602.
03/01/19	Coding update added HCPCS codes J0135, J1628, and J3358. Removed HCPCS codes J3490, J9311, Q5102, and Q5109. Added link to future version of policy that becomes effective June 9, 2019.
04/01/19	Coding update, removed HCPCS code J0215.
05/01/19	Interim Review, approved April 2, 2019. Added Simponi Aria as second line therapy for psoriatic arthritis and ankylosing spondylitis.
06/21/19	Revised the effective date of the updated policy from July 1, 2019, to July 31, 2019.
07/01/19	Annual Review, approved June 11, 2019. Added criteria for Skyrizi. Updated criteria for Siliq, Taltz, Cimzia and Ilumya when used for plaque psoriasis. Added non-radiographic axial spondyloarthritis criteria to Cimzia.
07/18/19	Removed link and note regarding updated policy.
11/01/19	Interim Review, approved October 8, 2019. Added criteria for Taltz when used for ankylosing spondylitis. Added criteria for Rinvoq for rheumatoid arthritis. Updated

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	criteria for Cimzia, Kevzara, Kineret, Olumiant, Orencia, Simponi, Xeljanz and Xeljanz XR when used for rheumatoid arthritis.
01/01/20	Interim Review, approved December 17, 2019, effective for dates of service on or after April 3, 2020, following provider notification. Added Ruxience (rituximab-pvvr) as second-line Anti-CD-20 agent. Removed HCPCS code J9310 as it terminated 1/1/19.
02/01/20	Interim Review, approved January 23, 2020. Placed investigational table with not medically necessary table at last page of criteria. Added Avsola to same status as Inflectra/Renflexis.
07/01/20	Interim Review, approved June 18, 2020. Added Avsola as drug subject to site of service review. Changes to Avsola for site of service review are effective for dates of service on or after October 2, 2020, following 90-day provider notification. Updated coverage criteria for Taltz for plaque psoriasis to add coverage for patients 6 years of age or older. For psoriatic arthritis Otezla was moved from second-line to first-line treatment. Updated criteria for Cimzia, Simponi, Simponi Aria, Taltz, and Orencia for the treatment of psoriatic arthritis to include Otezla as one of the qualifying first-line treatments. Updated the Investigational table to include quantities that exceed the FDA labeled dosing for condition. Added HCPCS code Q5121 for Avsola. Removed HCPCS code J9312.
08/01/20	Interim Review, approved July 23, 2020. Removed from Otezla for psoriatic arthritis the requirement to use one conventional DMARD.
10/01/20	Annual Review, approved September 8, 2020, effective January 1, 2021. Updated Actemra coverage criteria for RA by requiring Humira prior to Actemra. Updated Actemra coverage criteria is for dates of service on or after January 1, 2021.
12/01/20	Interim Review, approved November 10, 2020. Added Tremfya (guselkumab) as a second-line agent for the treatment of psoriatic arthritis. Added Xeljanz (tofacitinib) as a second-line agent for the treatment of polyarticular juvenile idiopathic arthritis.
01/01/21	Interim Review, approved December 8, 2020. For ankylosing spondylitis moved Taltz to first-line and Cosentyx to second-line. Updated criteria for second-line agents Cimzia, Simponi, and Simponi Aria to list Taltz as first-line therapy. For polyarticular juvenile idiopathic arthritis moved Xeljanz to first-line and added coverage criteria for Simponi Aria as second-line agent. Updated criteria for second-line agent Orencia to list Xeljanz as first-line therapy. Moved Actemra to first-line and updated criteria to include sulfasalazine and leflunomide as initial treatment options. For plaque psoriasis moved Enbrel and Taltz to first-line and Cosentyx to second-line. Updated criteria for second-line agents Siliq, Cimzia, and Ilumya to list Enbrel and Taltz as first-line therapy. For psoriatic arthritis moved Taltz to first-line and Cosentyx to second-line. Added coverage criteria for Tremfya as a first-line agent. Updated criteria for second-line agents Cimzia, Simponi, and Orencia to list Taltz and Tremfya as first-line therapies. For non-radiographic axial spondyloarthritis added coverage criteria for Taltz as first-line therapy and coverage criteria for Cosentyx as second-line therapy.

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04/01/21	Interim Review, approved March 9, 2021. Updated coverage criteria for Cosentyx for the treatment of plaque psoriasis to require four different products from ≥ 3 different drug classes and for the treatment of psoriatic arthritis to require three different products from ≥ 2 different drug classes. Updated policy to clarify that site of service applies to Simponi Aria which is the IV dosage form.
05/01/21	Annual Review, approved April 22, 2021. Added Xeljanz Oral Solution (tofacitinib) as a first-line product for treatment of polyarticular JIA.
08/01/21	Interim Review, approved July 22, 2021. Removed reference that Actemra (tocilizumab) SC and Orencia (abatacept) SC are subject to review for site of service administration. Site of service only applies to Actemra IV and Orencia IV route of administration.
11/01/21	Interim Review, approved October 21, 2021. Added site of service review for Stelara (ustekinumab) SC for dates of service on or after February 4, 2022.
01/01/22	Interim Review, approved December 14, 2021. For ankylosing spondylitis added prescriber specialty to Humira, Enbrel, Remicade, Taltz, Cimzia, Simponi, Simponi Aria, Inflectra, Renflexis, and Avsola. For PJIA expanded initial coverage to include leflunomide, methotrexate, or sulfasalazine for Humira and Enbrel. For PJIA updated Xeljanz and Xeljanz Oral Solution to require an inadequate response to one or more TNF blockers. For RA added prescriber specialty to Humira, Enbrel, Remicade, Cimzia, Simponi, Simponi Aria, Inflectra, Renflexis, Avsola, Kevzara, Kineret, Orencia, and Olumiant. For RA updated Rinvoq, Xeljanz, and Xeljanz XR to require an inadequate response to one or more TNF blockers. For RA expanded initial coverage to include methotrexate, leflunomide, sulfasalazine, or hydroxychloroquine for Cimzia, Simponi, Simponi Aria, Kevzara, Kineret, Orencia, and Olumiant. For plaque psoriasis added patient age based on FDA-approval to Enbrel, Humira, Remicade, Stelara, Skyrizi, Tremfya, Otezla, Siliq, Cosentyx, Cimzia, Inflectra, Renflexis, Avsola, and Ilumya. For plaque psoriasis added prescriber specialty to Enbrel, Humira, Remicade, Stelara, Otezla, Inflectra, Renflexis, and Avsola. For psoriatic arthritis added prescriber specialty to Humira, Enbrel, Remicade, Stelara, Cimzia, Simponi, Simponi Aria, Inflectra, Renflexis, Avsola, and Orencia. For psoriatic arthritis removed conventional DMARD requirement from Humira, Enbrel, Remicade, Otezla, Cimzia, Simponi, Simponi Aria, Inflectra, Renflexis, Avsola, and Orencia. For psoriatic arthritis updated Xeljanz and Xeljanz XR to require an inadequate response to one or more TNF blockers. Changed the re-authorization duration from 1-year to 3 years.
03/01/22	Interim Review, approved February 8, 2022. Removed reference to first-line treatment and second-line treatment from within the coverage criteria for all drugs. Added coverage criteria for Xeljanz and Xeljanz XR for the treatment of ankylosing spondylitis. Updated coverage criteria for Cimzia, Simponi, Simponi Aria, and Cosentyx for the treatment of ankylosing spondylitis to include Xeljanz and Xeljanz XR in the list of prerequisite drugs. Updated Xeljanz and Xeljanz Oral Solution for the treatment of PJIA to require an inadequate response or intolerance to Enbrel or Humira. Updated Orencia and Simponi Aria for the treatment of PJIA to include Xeljanz Oral Solution in the list of prerequisite drugs. Updated Rinvoq, Xeljanz, and Xeljanz XR criteria for the treatment of rheumatoid arthritis to require an inadequate response or intolerance to

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	Enbrel or Humira. Added coverage criteria for Rinvoq for the treatment of psoriatic arthritis. Updated Xeljanz and Xeljanz XR coverage criteria for the treatment of psoriatic arthritis to require an inadequate response or intolerance to Enbrel or Humira. Updated coverage criteria for Cimzia, Simponi, Simponi Aria, Cosentyx, and Orencia for the treatment of psoriatic arthritis to include Rinvoq in the list of prerequisite drugs.
04/01/22	Annual Review, approved March 8, 2022. Added coverage criteria for Skyrizi (risankizumab-rzaa) for the treatment of psoriatic arthritis. Updated coverage criteria for Cimzia, Simponi, Simponi Aria, Orencia, and Cosentyx for the treatment of psoriatic arthritis to include Skyrizi in the list of prerequisite drugs. Added coverage criteria for Adbry (tralokinumab-ldrm), Cibinqo (abrocitinib), and Rinvoq (upadacitinib) for the treatment of moderate-to-severe atopic dermatitis. Added Adbry to HCPC code J3590.
06/01/22	Interim Review, approved May 10, 2022. Added Infliximab (Janssen – unbranded) to policy with identical site-of-service requirements and coverage criteria as brand Remicade (infliximab) for the treatment of ankylosing spondylitis, RA, plaque psoriasis, and psoriatic arthritis. Moved Inflectra (infliximab-dyyb) to a first-line TNF-α antagonists for the treatment of ankylosing spondylitis, RA, plaque psoriasis, and psoriatic arthritis. Updated coverage criteria for Renflexis (infliximab-abda) and Avsola (infliximab-axxq) for the treatment of ankylosing spondylitis, RA, plaque psoriasis, and psoriatic arthritis to require the patient has had an inadequate response or intolerance to Infliximab (Janssen – unbranded), Inflectra (infliximab-dyyb), or Remicade (infliximab). Updated Xeljanz and Xeljanz XR for the treatment of ankylosing spondylitis, PJIA, RA, and psoriatic arthritis to require a trial and treatment failure with one or more TNF blockers. Updated Rinvoq for the treatment of RA and psoriatic arthritis to require a trial and treatment failure with one or more TNF blockers. Added coverage for Rinvoq for the treatment of ankylosing spondylitis. Added coverage for Cosentyx (secukinumab) for the treatment of active enthesitis-related arthritis. Moved Adbry (tralokinumab-ldrm), Cibinqo (abrocitinib), and Rinvoq (upadacitinib) for the treatment of moderate-to-severe atopic dermatitis, from Policy 5.01.550 to Policy 5.01.628 Pharmacologic Treatment of Atopic Dermatitis with no changes to coverage criteria. Removed Adbry from HCPC code J3590.
11/01/22	Interim Review, approved October 11, 2022. For the treatment of plaque psoriasis moved Enbrel, Humira, Infliximab (Janssen – unbranded), Inflectra, Remicade, Taltz, Stelara SC, Skyrizi, Tremfya, Otezla, Siliq, Cosentyx, Cimzia, Renflexis, Avsola, and Ilumya from Policy 5.01.550 to Policy 5.01.629 Pharmacologic Treatment of Psoriasis. Removed Siliq from HCPC code J3590. Removed HCPC codes J3245 & J3358. Changed the wording from "patient" to "individual" throughout the policy for standardization.
01/01/23	Interim Review, approved December 13, 2022. Added coverage for Rinvoq (upadacitinib) for the treatment of non-radiographic axial spondyloarthritis.
02/01/23	Interim Review, approved January 10, 2023. Added coverage for the biosimilar Amjevita (adalimumab-atto) for the treatment of AS, RA, JIA, and PsA with the identical coverage criteria as Humira (adalimumab). Added Amjevita as a prerequisite

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	medication, on par with Humira, to all the medications in policy that include Humira as a prerequisite medication. Added Amjevita to HCPC code J3590.
04/01/23	Annual Review, approved March 14, 2023. Added clarification of coverage for the biosimilar Amjevita (adalimumab-atto) with NDCs starting with 55513 versus NDCs starting with 72511. Changed the wording from "patient" to "individual" throughout the policy for standardization.
06/01/23	Interim Review, approved May 9, 2023. Added note to baricitinib criteria that the use of baricitinib in the setting of alopecia is considered cosmetic and is not covered by this policy. Added coverage criteria for Kevzara criteria for the treatment of adult individuals with polymyalgia rheumatica (PMR).
08/01/23	Interim Review, approved July 11, 2023. Added coverage for the biosimilars Hyrimoz LCF (adalimumab-adaz) SC, Abrilada (adalimumab-afzb) SC, Hulio ((adalimumab-fkjp) SC, Yusimry (adalimumab-aqvh) SC, Hadlima (adalimumab-bwwd) SC and Yuflyma (adalimumab-aaty) SC for the treatment of AS, RA, JIA, and PsA as non-preferred products and with the identical coverage criteria as Amjevita (adalimumab-atto) [NDCs starting with 72511]. Added coverage for Cyltezo LCF (adalimumab-adbm), Hyrimoz HCF (adalimumab-adaz) and Adalimumab-adaz HCF (Sandoz – unbranded) SC for the treatment of AS, RA, JIA, and PsA as preferred products and with the identical coverage criteria as Amjevita (adalimumab-atto) [NDCs starting with 55513]. Removed "individual is being started on Amjevita (adalimumab-atto) [NDCs starting with 72511], Humira (adalimumab), or Enbrel (etanercept) concurrently with leflunomide, methotrexate, or sulfasalazine" from non-preferred agents' indication of treatment of polyarticular juvenile idiopathic arthritis. Added Cyltezo, Hyrimoz HCF, Adalimumab-adaz HCF (Sandoz – unbranded), Abrilada, Hadlima, Hulio, Hyrimoz LCF, Yuflyma and Yusimry to code J3590
08/01/23	Interim Review, approved July 24, 2023. Updated preferred Humira biosimilars (Cyltezo LCF, Hyrimoz HCF, Adalimumab-adaz HCF (Sandoz-unbranded)) along with Humira and Amjevita (NDC starting with 55513) in the list of agents to be tried and failed prior to using nonpreferred agents, such as cosentyx (AS), Actempra (JIA), Orencia (JIA), Simponi Aria (JIA), Actemra (RA), Kevzara (RA), Kineret (RA), Orencia (RA), Olumiant (RA), Cosentyx (Psoriatic Arthritis), Orencia (Psoriatic Arthritis).
09/01/23	Interim Review, approved August 8, 2023. The following policy changes are effective September 1, 2023: added Humira biosimilars Idacio (adalimumab-aacf) and Adalimumab-fkjp (Biocon-unbranded) as non-preferred products with similar criteria as Amjevita (adalimumab-atto) [NDCs starting with 72511]; updated Cosentyx coverage criteria for psoriatic arthritis, ankylosing spondylitis, and non-radiographic axial Spondyloarthritis; for ankylosing spondylitis, added Rinvoq as a qualifier; for psoriatic arthritis, changed the requirement of trying three products to two products and removed the requirement of trying agents from two or more different drug classes; for non-radiographic axial spondylarthritis, added Rinvoq as a qualifier and added requirement of trying two of the three agents. The following policy changes are effective January 1, 2024 following 90-day provider notification due to changes in the preferred medical benefit drugs: moved Simponi Aria from 2nd line to 1st line for all

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	indications; moved Avsola to 1st line for all the indications; added Avsola to a list of preferred infliximab products to be tried and failed prior to trying non-preferred infliximab products; moved Inflectra to 2nd line (non-preferred) agent; removed Inflectra from the list of preferred products to be tried and failed prior to trying non-preferred infliximab products.
01/01/24	Interim Review, approved December 12, 2023. Added coverage criteria for Tofidence (tocilizumab-bavi) for the treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis (PJIA), and systemic juvenile idiopathic arthritis (SJIA). Updated Amjevita [NDCs starting with 55513] from a preferred to a non-preferred product. Added Hyrimoz (Cordavis) [NDCs starting with 83457] and adalimumab-aacf (Idacio unbranded) as a non-preferred product. Added adalimumab-adbm (Cyltezo unbranded) as a preferred product. Updated Hyrimoz LCF (Sandoz) from a non-preferred to a preferred product. Added IV Cosentyx (secukinumab) as a non-preferred product. Tofidence added to HCPC code J3590. Added new HCPCS code Q5132.
03/01/24	Annual Review, approved February 13, 2024. Removed Stelara (ustekinumab) subcutaneous (SC) injection site of service requirement.
04/01/24	Coding update. Added new HCPCS codes C9166 and Q5133.
05/01/24	Interim Review, approved April 9, 2024. Added Humira (adalimumab) (Cordavis) [NDCs starting with 83457] as a non-preferred product. Updated Orencia (abatacept) to include coverage criteria for individuals 2 years and older with active psoriatic arthritis.
07/01/24	Interim Review, approved June 11, 2024. Added adalimumab-aaty (Yuflyma unbranded) as a non-preferred product. Added Simlandi (adalimumab-ryvk) and adalimumab-ryvk (Simlandi unbranded) as preferred products. Updated non-preferred adalimumab coverage criteria to require trial and treatment failure with all preferred adalimumab products. Added Simlandi to HCPCS code J3590. Added HCPCS code Q5131 for Idacio and Q5115 for Truxima. Added HCPCS code J3247 and terminated HCPCS code C9166 effective 7/1/2024.
08/01/24	Interim Review, approved July 9, 2024. Updated Rinvoq (upadacitinib) to include coverage criteria for the treatment of certain individuals with polyarticular juvenile idiopathic arthritis (PJIA). Added Rinvoq LQ (upadacitinib) coverage criteria for the treatment of certain individuals with PJIA and psoriatic arthritis.
09/01/24	Interim Review, approved August 13, 2024. Added Tyenne (tocilizumab-aazg) IV/SC coverage criteria for the treatment of certain individuals with rheumatoid arthritis, polyarticular juvenile idiopathic arthritis (PJIA), and systemic juvenile idiopathic arthritis (SJIA). Updated Kevzara (sarilumab) to include coverage criteria for the treatment of certain individuals with PJIA. The following policy change is effective December 5, 2024, following 90-day provider notification. Added site of service review for Cosentyx (secukinumab) IV and Tofidence (tocilizumab-bavi) IV. Added drug Tyenne to HCPCS code J3590.
10/01/24	Interim Review, approved September 10, 2024. The following policy changes are effective January 3, 2025, following a 90-day provider notification. Changed Inflectra

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	(infliximab-dyyb) to a first-line agent. Changed Avsola (infliximab-axxq) to a second-line agent. Updated coverage criteria for Avsola and Renflexis to require the individual to have an adequate trial and failure with Inflectra, Infliximab (Janssen – unbranded), or Remicade. Updated Hyrimoz (Sandoz) (adalimumab-adaz) [NDCs starting with 61314] from a preferred product to a non-preferred product. Updated Humira (AbbVie) (adalimumab) [NDCs starting with 00074] to require that the individual has had an inadequate response or intolerance to a preferred product for new starts. Injection, tocilizumab-aazg (tyenne), biosimilar, 1 mg (new code effective 10/1/2024)

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.