Pharmacotherapy of Arthropathies

Effective Date: Nov. 1, 2019
Last Revised: Oct. 8, 2019
Replaces: N/A

RELATED MEDICAL POLICIES:
5.01.563 Pharmacotherapy of Inflammatory Bowel Disorder
5.01.566 Pharmacotherapy of Thrombocytopenia
5.01.607 Continuity of Coverage for Maintenance Medications
11.01.523 Site of Service: Infusion Drugs and Biologic Agents

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, psoriatic arthritis, and plaque psoriasis.

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.
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)
- Inflectra® (infliximab-dyyb)
- Orencia® (abatacept)
- Remicade® (infliximab)
- Renflexis® (infliximab-abda)
- Rituxan® (rituximab)
- Simponi® and Simponi® Aria (golimumab)

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

- Ankylosing Spondylitis
- Psoriasis: Plaque Psoriasis
- Arthropathies: Polyarticular Juvenile Idiopathic Arthritis
- Psoriasis: Psoriatic Arthritis
- Arthropathies: Systemic Juvenile Idiopathic Arthritis
- Non-Radiographic Axial Spondyloarthritis
- Arthropathies: Rheumatoid Arthritis
- Site of Service for Infusion
<table>
<thead>
<tr>
<th>Site of Service Administration</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| **Medically necessary sites of service** | 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. |
  • Physician’s office  
  • Infusion center  
  • Home infusion  
| **Hospital-based outpatient setting** | 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 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.  
This site is considered medically necessary only when the patient has a clinical condition which puts him or her at increased risk of complications for infusions, including any ONE of the following:  
  • Known cardiac condition (eg, symptomatic cardiac arrhythmia) or pulmonary condition (eg, significant respiratory disease, serious obstructive airway disease, %FVC ≤ 40%) that may increase the risk of an adverse reaction |
Site of Service Administration | Medical Necessity
--- | ---
- | 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 FDA labeled dosing.

**Agent** | **Investigational**
--- | ---
As listed below | All other uses of the below-named agents when used in combination with each other or for conditions not outlined in this policy are considered investigational.
Step therapy tiers are listed below; please refer to the Policy section for details.

### First-line Agents
- **TNF-α Inhibitors (first-line)**
  - Remicade® (IV)
  - Enbrel® (SC)
  - Humira® (SC)
- **IL-17 Inhibitor (first-line)**
  - Cosentyx® (SC)

### Second-line Agents
- **TNF-α Inhibitors (second-line)**
  - Inflectra® (IV) (must try and fail Remicade® (IV))
  - Taltz® (SC)
- **IL-17 Inhibitor (second-line)**
  - Cimzia® (SC)
  - Simponi® (SC)

### Agent | Medical Necessity, Ankylosing Spondylitis
--- | ---
**First-line TNF-α Antagonists**
- **Humira® (adalimumab) SC**
  - First-line
- **Enbrel® (etanercept) SC**
  - First-line
  - Humira® (adalimumab) or Enbrel® (etanercept) may be considered medically necessary as a first-line agent in the treatment of ankylosing spondylitis when:
    - Patient has a documented diagnosis of moderate to severe ankylosing spondylitis
- **Remicade® (infliximab) IV**
  - First-line
  - Remicade® (infliximab) is subject to review for site of service administration.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Ankylosing Spondylitis</th>
</tr>
</thead>
</table>
| **Remicade® (infliximab)** | may be considered medically necessary as a first-line agent in the treatment of ankylosing spondylitis when:  
  - Patient has a documented diagnosis of moderate to severe ankylosing spondylitis |

### First-line IL-17 Inhibitors

| Cosentyx® (secukinumab) SC | Cosentyx® (secukinumab) may be considered medically necessary as a first-line agent in the treatment of ankylosing spondylitis when:  
  - Patient has a documented diagnosis of moderate to severe ankylosing spondylitis |

### Second-line TNF-α Antagonists

<table>
<thead>
<tr>
<th>Cimzia® (certolizumab pegol) SC</th>
<th>Simponi® (golimumab) SC and Simponi Aria (golimumab) IV are subject to review for site of service administration.</th>
</tr>
</thead>
</table>
| Simponi® (golimumab) SC or Simponi Aria (golimumab) IV | Simponi® (golimumab) SC and Simponi Aria® (golimumab) IV may be considered medically necessary as a second-line agent in the treatment of ankylosing spondylitis when:  
  - Patient has a documented diagnosis of moderate to severe ankylosing spondylitis  
  - Patient has had an inadequate response or intolerance to two of the following drugs:  
    - Enbrel® (etanercept)  
    - Humira® (adalimumab)  
    - Cosentyx® (secukinumab) |

### Inflectra® (infliximab-dyyb) IV and Renflexis™ (infliximab-abda) IV

<table>
<thead>
<tr>
<th>Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) are subject to review for site of service administration.</th>
</tr>
</thead>
</table>
| Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) may be considered medically necessary as second-line agents in the treatment of ankylosing spondylitis when:  
  - Patient has a documented diagnosis of moderate to severe ankylosing spondylitis  
  - Patient has had an inadequate response or intolerance to two of the following drugs:  
    - Enbrel® (etanercept)  
    - Humira® (adalimumab)  
    - Cosentyx® (secukinumab)  
    - Inflectra® (infliximab-dyyb)  
    - Renflexis™ (infliximab-abda) |
### Agent

<table>
<thead>
<tr>
<th>Medical Necessity, Ankylosing Spondylitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patient has had a documented trial and treatment failure with Remicade® (infliximab)</td>
</tr>
</tbody>
</table>

### Second-line IL-17 Inhibitors

**Taltz® (ixekizumab) SC**

- **Second-line**

  Taltz® (ixekizumab) may be considered medically necessary as a second-line agent in the treatment of ankylosing spondylitis when:

  - Patient has a documented diagnosis of moderate to severe ankylosing spondylitis

  **AND**

  - Patient has had an inadequate response or intolerance to two of the following drugs:
    - Enbrel® (etanercept)
    - Humira® (adalimumab)
    - Cosentyx® (secukinumab)
Step therapy tiers are listed below; please refer to the Policy section for details.

### First-line Agents
- **TNF-α Inhibitors (first-line)**
  - Humira® (SC)
  - Enbrel® (SC)

### Second-line Agents
- **T-Cell Costimulation Modulator (second-line)**
  - Orencia® (IV/SC)
- **IL-6 Inhibitor (second-line)**
  - Actemra® (IV/SC)

### Agent Medical Necessity, Arthropathies: Polyarticular Juvenile Idiopathic Arthritis

**First-line TNF-α Antagonists**
- Humira® (adalimumab) SC
  - First-line
- Enbrel® (etanercept) SC
  - First-line

*Humira® (adalimumab) or Enbrel® (etanercept) may be considered medically necessary as the first-line agent in the treatment of polyarticular juvenile idiopathic arthritis when:*
  - Patient has not responded to or does not tolerate methotrexate
  - Humira® (adalimumab) or Enbrel® (etanercept) is being added to the regimen after the patient has had an inadequate partial response to methotrexate monotherapy
  - Patient is being started on Humira® (adalimumab) or Enbrel® (etanercept) concurrently with methotrexate
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Arthropathies: Polyarticular Juvenile Idiopathic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second-line IL-6 Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Actemra® (tocilizumab) IV/SC</td>
<td>Actemra® (tocilizumab) IV/SC is subject to review for site of service administration.</td>
</tr>
<tr>
<td>• Second-line</td>
<td>Actemra® (tocilizumab) IV/SC may be considered medically necessary as a second-line agent in the treatment of polyarticular juvenile idiopathic arthritis when:</td>
</tr>
<tr>
<td></td>
<td>• Patient has had an inadequate response or intolerance to methotrexate and Humira® (adalimumab)</td>
</tr>
<tr>
<td><strong>Second-line T-Cell Costimulation Modulators</strong></td>
<td></td>
</tr>
<tr>
<td>Orencia® (abatacept) IV/SC</td>
<td>Orencia® (abatacept) IV/SC is subject to review for site of service administration.</td>
</tr>
<tr>
<td>• Second-line</td>
<td>Orencia® (abatacept) IV/SC may be considered medically necessary as a second-line agent in the treatment of polyarticular juvenile idiopathic arthritis when:</td>
</tr>
<tr>
<td></td>
<td>• Patient has had an inadequate response or intolerance to methotrexate, and two of the following drugs:</td>
</tr>
<tr>
<td></td>
<td>o Enbrel® (etanercept)</td>
</tr>
<tr>
<td></td>
<td>o Humira® (adalimumab)</td>
</tr>
<tr>
<td></td>
<td>o Actemra® (tocilizumab)</td>
</tr>
</tbody>
</table>
Step therapy tiers are listed below; please refer to the Policy section for details.

### Agent

<table>
<thead>
<tr>
<th>Medical Necessity, Arthropathies: Systemic Juvenile Idiopathic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line IL-6 Inhibitors</strong></td>
</tr>
<tr>
<td><strong>Actemra® (tocilizumab)</strong> VIS/SC</td>
</tr>
<tr>
<td>• First-line</td>
</tr>
<tr>
<td><strong>Actemra® (tocilizumab)</strong> IV/SC is subject to review for site of service administration.</td>
</tr>
<tr>
<td><strong>Actemra® (tocilizumab)</strong> IV/SC may be considered medically necessary as a first-line agent in the treatment of systemic juvenile idiopathic arthritis when:</td>
</tr>
<tr>
<td>• Patient has had an inadequate response or intolerance to a nonsteroidal anti-inflammatory drug (NSAID)</td>
</tr>
</tbody>
</table>
Step therapy tiers are listed below; please refer to the Policy section for details.

### Rheumatoid Arthritis

#### First-line Agents
- TNF-α Inhibitors (first-line)
  - Remicade® (IV)
  - Humira® (SC)
  - Enbrel® (SC)
- IL-6 Inhibitor (first-line)
  - Actemra® (IV/SC)
- Janus Kinase Inhibitor (first-line)
  - Xeljanz® / Xeljanz® XR (oral)
- TNF-α Inhibitors (second-line)
  - Rinoq™ (oral)

#### Second-line Agents
- IL-6 Inhibitor (second-line)
  - Inflectra® (IV)
  - Cimzia® (SC)
  - Simponi® (SC/IV)
- IL-1 Inhibitor (second-line)
  - Actemra® (IV)
  - Kevzara® (SC)
  - Orenica® (IV/SC)
  - Ollumiant® (oral)
- T-Cell Costimulation Modulator (second-line)
  - Renflexis®

### Agent

#### First-line TNF-α Antagonists
- Humira® (adalimumab) SC
  - First-line
- Enbrel® (etanercept) SC
  - First-line

#### Medical Necessity, Arthropathies: Rheumatoid Arthritis

Humira® (adalimumab) or Enbrel® (etanercept) may be considered medically necessary as the first-line agent in the treatment of moderate to severe rheumatoid arthritis when:

- Patient has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine

OR

- Humira® (adalimumab) or Enbrel® (etanercept) is being added to the regimen after the patient has had an inadequate partial response to methotrexate monotherapy

OR

- Patient is being started on Humira® (adalimumab) or Enbrel® (etanercept) concurrently with methotrexate
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Arthropathies: Rheumatoid Arthritis</th>
</tr>
</thead>
</table>
| Remicade® (infliximab) IV  
  • First-line | Remicade® (infliximab) is subject to review for site of service administration.  
Remicade® (infliximab) may be considered medically necessary as a first-line agent in the treatment of moderate to severe rheumatoid arthritis when:  
  • Patient has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine  
  OR  
  • Remicade® (infliximab) is being added to the regimen after the patient has had an inadequate partial response to methotrexate monotherapy  
  OR  
  • Patient is being started on Remicade® (infliximab) concurrently with methotrexate |

| First-line IL-6 Inhibitor | Actemra® (tocilizumab) IV/SC is subject to review for site of service administration.  
Actemra (tocilizumab) IV/SC may be considered medically necessary as a first-line agent in the treatment of moderate to severe rheumatoid arthritis when:  
  • Patient had an inadequate response or intolerance to methotrexate |

| First-line Janus Kinase Inhibitors | Rinvoq™ (upadacitinib), Xeljanz® (tofacitinib), and Xeljanz® XR (tofacitinib extended-release) may be considered medically necessary as a first-line agent in the treatment of moderate to severe rheumatoid arthritis when:  
  • Patient is 18 years of age or older  
  AND  
  • Patient 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  
Xeljanz® (tofacitinib) oral  
  • First-line  
Xeljanz® XR (tofacitinib extended-release) oral  
  • First-line |
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Arthropathies: Rheumatoid Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Note: The use of tofacitinib in the setting of alopecia is considered cosmetic and is not covered by this policy.</td>
</tr>
</tbody>
</table>

### Second-line TNF-α Antagonists

<table>
<thead>
<tr>
<th>Cimzia® (certolizumab pegol) SC</th>
<th>Simponi® (golimumab) SC and Simponi Aria® (golimumab) IV are subject to review for site of service administration.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cimzia® (certolizumab pegol), Simponi® (golimumab) SC and Simponi Aria® (golimumab) IV may be considered medically necessary as a second-line agent in the treatment of moderate to severe rheumatoid arthritis when:</td>
</tr>
<tr>
<td>• Second-line</td>
<td>• Patient has had an inadequate response or intolerance to methotrexate, and two of the following agents:</td>
</tr>
</tbody>
</table>
| Simponi® (golimumab) SC or Simponi Aria® (golimumab) IV | o Enbrel® (etanercept)  
| • Second-line                            | o Humira® (adalimumab)  
|                                           | o Actemra® (tocilizumab)  
|                                           | o Rinvoq™ (upadacitinib)  
|                                           | o Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release) |

<table>
<thead>
<tr>
<th>Inflectra® (infliximab-dyyb) IV and Renflexis™ (infliximab-abda) IV</th>
<th>Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) are subject to review for site of service administration.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Second-line</td>
<td>Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) may be considered medically necessary as a second-line agent in the treatment of moderate to severe rheumatoid arthritis when:</td>
</tr>
<tr>
<td></td>
<td>• Patient has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine OR</td>
</tr>
<tr>
<td></td>
<td>• Inflectra® (infliximab-dyyb) or Renflexis™ (infliximab-abda) is being added to the regimen after the patient has had an inadequate partial response to methotrexate monotherapy OR</td>
</tr>
<tr>
<td></td>
<td>• Patient is being started on Inflectra® (infliximab-dyyb) or Renflexis™ (infliximab-abda) concurrently with methotrexate. AND</td>
</tr>
<tr>
<td>Agent</td>
<td>Medical Necessity, Arthropathies: Rheumatoid Arthritis</td>
</tr>
<tr>
<td>-------</td>
<td>--------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>• Patient has had a documented trial and treatment failure with Remicade® (infliximab)</td>
</tr>
<tr>
<td><strong>Second-line IL-6 Inhibitor</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Kevzara® (sarilumab) SC | Kevzara® (sarilumab) may be considered medically necessary as a second-line agent in the treatment of moderate to severe rheumatoid arthritis when:  
• Patient has had an inadequate response or intolerance to methotrexate, and two of the following agents:  
  o Enbrel® (etanercept)  
  o Humira® (adalimumab)  
  o Actemra® (tocilizumab)  
  o Rinvoq™ (upadacitinib)  
  o Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release) |
| • Second-line | |
| **Second-line Anti-CD-20** | See policy number 5.01.556 Rituximab: Non-oncologic and Miscellaneous Uses |
| Rituxan® (rituximab) IV |   |
| • Second-line | |
| **Second-line IL-1 Inhibitors** | |
| Kineret® (anakinra) SC | Kineret® (anakinra) may be considered medically necessary as a second-line agent in the treatment of moderate to severe rheumatoid arthritis when:  
• Patient has had an inadequate response or intolerance to methotrexate, and two of the following agents:  
  o Enbrel® (etanercept),  
  o Humira® (adalimumab)  
  o Actemra® (tocilizumab)  
  o Rinvoq™ (upadacitinib)  
  o Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release) |
| • Second-line | |
| **Second-line T-Cell Costimulation Modulators** | |
| Orencia® (abatacept) IV/SC | Orencia® (abatacept) IV/SC is subject to review for site of service administration.  
Orencia® (abatacept) IV/SC may be considered medically necessary as a second-line agent in the treatment of moderate to severe rheumatoid arthritis when: |
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Arthropathies: Rheumatoid Arthritis</th>
</tr>
</thead>
</table>
| • Patient has had an inadequate response or intolerance to methotrexate, and two of the following agents:  
  o Enbrel® (etanercept)  
  o Humira® (adalimumab)  
  o Actemra® (tocilizumab)  
  o Rinvoq™ (upadacitinib)  
  o Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release) |

<table>
<thead>
<tr>
<th>Second-line Janus Kinase Inhibitors</th>
<th></th>
</tr>
</thead>
</table>
| Olumiant® (baricitinib) oral | Olumiant® (baricitinib) may be considered medically necessary as a second-line agent in the treatment of moderate to severe rheumatoid arthritis when:  
  • Patient has had an inadequate response or intolerance to methotrexate, and two of the following agents:  
    o Enbrel® (etanercept)  
    o Humira® (adalimumab)  
    o Actemra® (tocilizumab)  
    o Rinvoq™ (upadacitinib)  
    o Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release) |
Step therapy tiers are listed below; please refer to the Policy section for details.

### Plaque Psoriasis

#### First-line Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Psoriasis: Plaque Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Humira® (adalimumab) SC</strong></td>
<td></td>
</tr>
<tr>
<td>• First-line</td>
<td><strong>Humira® (adalimumab) may be considered medically necessary as the first-line agent in the treatment of plaque psoriasis when:</strong></td>
</tr>
<tr>
<td></td>
<td>• Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)</td>
</tr>
<tr>
<td></td>
<td>o <strong>Exception:</strong> This may be granted when ANY of the following are true:</td>
</tr>
<tr>
<td></td>
<td>▪ There is extensive recalcitrant facial involvement OR</td>
</tr>
<tr>
<td></td>
<td>▪ There is pustular involvement of the hands and feet OR</td>
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<tr>
<td></td>
<td>▪ There is genital involvement which interferes with normal sexual function</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IL-23 Inhibitors (first-line)</th>
<th>TNF-α Inhibitors (first-line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skyrizi™ (SC)</td>
<td>Remicade® (IV)</td>
</tr>
<tr>
<td>Tremfya™ (SC)</td>
<td>Humira® (SC)</td>
</tr>
<tr>
<td>IL-17 Inhibitor (first-line)</td>
<td>IL-12/23 Inhibitor (first-line)</td>
</tr>
<tr>
<td>IL-17 Inhibitors (second-line)</td>
<td>PDE-4 Inhibitor (first-line)</td>
</tr>
</tbody>
</table>

<p>| Second-line Agents |</p>
<table>
<thead>
<tr>
<th>IL-17 Inhibitors (second-line)</th>
<th>TNF-α Inhibitors (second-line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taltz® (SC)</td>
<td>Inflectra® (IV) Renflexis™ (IV) (must try and fail Remicade® (IV))</td>
</tr>
<tr>
<td>Ilumya™ (SC)</td>
<td>Siliq™ (SC)</td>
</tr>
<tr>
<td>Enbrel® (SC)</td>
<td>Cimzia® (SC)</td>
</tr>
<tr>
<td>Stelara® (SC)</td>
<td>Skyrizi™ (SC)</td>
</tr>
<tr>
<td>Cosentyx® (SC)</td>
<td>Tremfya™ (SC)</td>
</tr>
</tbody>
</table>
### Agent

#### Medical Necessity, Psoriasis: Plaque Psoriasis

- Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated.

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<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Psoriasis: Plaque Psoriasis</th>
</tr>
</thead>
</table>
| **Remicade® (infliximab) IV**  
- First-line | **Remicade® (infliximab) is subject to review for site of service administration.**  
Remicade (infliximab) may be considered medically necessary as a first-line agent in the treatment of moderate to severe plaque psoriasis when:  
- Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)  
  - **Exception:** This may be granted when ANY of the following are true:  
    - There is extensive recalcitrant facial involvement  
    - There is pustular involvement of the hands and feet  
    - There is genital involvement which interferes with normal sexual function  
  AND  
- Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated.  

**NOTE:**  
Infliximab may be considered medically necessary as emergent treatment for severe pustular, exfoliative or inflammatory psoriasis without prior use or failure/intolerance of a first-line drug, in contrast to stable plaque psoriasis. |

| First-line IL-17 Inhibitors | Cosentyx® (secukinumab) may be considered medically necessary as a first-line drug in the treatment of moderate to severe plaque psoriasis when:  
- Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA) |  
| Cosentyx® (secukinumab)  
SC |  
- First-line |  

---
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Psoriasis: Plaque Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>o <strong>Exception:</strong> This may be granted when ANY of the following are true:</td>
</tr>
</tbody>
</table>
|       | ▪ There is extensive recalcitrant facial involvement  
|       | OR  
|       | ▪ There is pustular involvement of the hands and feet  
|       | OR  
|       | ▪ There is genital involvement which interferes with normal sexual function  
|       | AND  
|       | • Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated |

**First-line IL-12/23 Inhibitors**

**Stelara® (ustekinumab) SC**
- First-line

Stelara® (ustekinumab) SC may be considered medically necessary as a first-line agent in the treatment of moderate to severe plaque psoriasis when:

- Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)
  - **Exception:** This may be granted when ANY of the following are true:
    ▪ There is extensive recalcitrant facial involvement
    OR
    ▪ There is pustular involvement of the hands and feet
    OR
    ▪ There is genital involvement which interferes with normal sexual function

  AND
  - Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated

**First-line IL-23 Inhibitors**

**Skyrizi™ (risankizumab-rzaa) SC**
- First-line

Skyrizi™ (risankizumab-rzaa) may be considered medically necessary as a first-line agent in the treatment of moderate to severe plaque psoriasis in adults when:
### Agent | Medical Necessity, Psoriasis: Plaque Psoriasis
---|---
- Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)
  - **Exception**: This may be granted when ANY of the following are true:
    - There is extensive recalcitrant facial involvement
    - OR
    - There is pustular involvement of the hands and feet
    - OR
    - There is genital involvement which interferes with normal sexual function

AND
- Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated

AND
- Medication is being prescribed by or in consultation with a dermatologist

---
**Tremfya® (guselkumab) SC**
- **First-line**

**Tremfya® (guselkumab) may be considered medically necessary as a first-line agent in the treatment of moderate to severe plaque psoriasis in adults when:**

- Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)
  - **Exception**: This may be granted when ANY of the following are true:
    - There is extensive recalcitrant facial involvement
    - OR
    - There is pustular involvement of the hands and feet
    - OR
    - There is genital involvement which interferes with normal sexual function

AND
- Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated

AND
### Medical Necessity, Psoriasis: Plaque Psoriasis

<table>
<thead>
<tr>
<th>Agent</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line PDE4 Inhibitor</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Otezla® (apremilast) oral</strong></td>
<td></td>
</tr>
<tr>
<td>• <strong>First-line</strong></td>
<td><strong>Otezla® (apremilast) may be considered medically necessary as a first-line agent in the treatment of moderate to severe plaque psoriasis when:</strong></td>
</tr>
<tr>
<td></td>
<td>• Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)</td>
</tr>
<tr>
<td></td>
<td>o <strong>Exception:</strong> This may be granted when ANY of the following are true:</td>
</tr>
<tr>
<td></td>
<td>▪ There is extensive recalcitrant facial involvement</td>
</tr>
<tr>
<td></td>
<td>▪ There is pustular involvement of the hands and feet</td>
</tr>
<tr>
<td></td>
<td>▪ There is genital involvement which interferes with normal sexual function</td>
</tr>
<tr>
<td></td>
<td><strong>AND</strong></td>
</tr>
<tr>
<td></td>
<td>• Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated</td>
</tr>
</tbody>
</table>

| **Second-line IL-17 Inhibitors** |  |
| **Siliq™ (brodalumab) SC** |  |
| • **Second-line** | **Siliq™ (brodalumab) may be considered medically necessary as a second-line agent in the treatment of moderate to severe plaque psoriasis in adults when:**  |
| | • Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)  |
| | o **Exception:** This may be granted when ANY of the following are true:  |
| | ▪ There is extensive recalcitrant facial involvement  |
| | ▪ There is pustular involvement of the hands and feet  |
| | ▪ There is genital involvement which interferes with normal sexual function  |
| | **AND**  |
Agent | Medical Necessity, Psoriasis: Plaque Psoriasis
--- | ---
| • Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated
AND
• Patient has had an inadequate response or is intolerant to two of the following agents:
  o Humira® (adalimumab)
  o Otezla® (apremilast)
  o Cosentyx® (secukinumab)
  o Stelara® (ustekinumab)
  o Tremfya® (guselkumab)
  o Skyrizi™ (risankizumab-rzza)
AND
• Medication is being prescribed by or in consultation with a dermatologist

Taltz® (ixekizumab) SC • Second-line

Taltz® (ixekizumab) may be considered medically necessary as a second-line agent in the treatment of moderate to severe plaque psoriasis in adults when:
• Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)
  o Exception: This may be granted when ANY of the following are true:
    ▪ There is extensive recalcitrant facial involvement
    OR
    ▪ There is pustular involvement of the hands and feet
    OR
    ▪ There is genital involvement which interferes with normal sexual function
AND
• Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated
AND
• Patient has had an inadequate response or is intolerant to three of the following agents:
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Psoriasis: Plaque Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Humira® (adalimumab)</td>
<td></td>
</tr>
<tr>
<td>• Otezla® (apremilast)</td>
<td></td>
</tr>
<tr>
<td>• Cosentyx® (secukinumab)</td>
<td></td>
</tr>
<tr>
<td>• Stelara® (ustekinumab)</td>
<td></td>
</tr>
<tr>
<td>• Tremfya® (guselkumab)</td>
<td></td>
</tr>
<tr>
<td>• Skyrizi™ (risankizumab-rzaa)</td>
<td></td>
</tr>
<tr>
<td><strong>AND</strong></td>
<td></td>
</tr>
<tr>
<td>• Medication is being prescribed by or in consultation with a dermatologist</td>
<td></td>
</tr>
</tbody>
</table>

### Second-line TNF-α Antagonists

<table>
<thead>
<tr>
<th>Enbrel® (etanercept) SC</th>
<th>Enbrel (etanercept) may be considered medically necessary as the second-line agent in the treatment of plaque psoriasis when:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Second-line</td>
<td>• Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Exception:</strong> This may be granted when ANY of the following are true:</td>
</tr>
<tr>
<td></td>
<td>▪ There is extensive recalcitrant facial involvement</td>
</tr>
<tr>
<td></td>
<td>▪ <strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>▪ There is pustular involvement of the hands and feet</td>
</tr>
<tr>
<td></td>
<td>▪ <strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>▪ There is genital involvement which interferes with normal sexual function</td>
</tr>
<tr>
<td><strong>AND</strong></td>
<td>• Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated</td>
</tr>
<tr>
<td><strong>AND</strong></td>
<td>• For patients ≥ 18 years of age there has been an adequate trial and treatment failure with Humira® (adalimumab)</td>
</tr>
</tbody>
</table>

### Second-line TNF-α Antagonists

<table>
<thead>
<tr>
<th>Cimzia® (certolizumab pegol) SC</th>
<th>Cimzia® (certolizumab pegol) may be considered medically necessary as the second-line agent in the treatment of plaque psoriasis when:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Second-line</td>
<td></td>
</tr>
</tbody>
</table>
### Agent Medical Necessity, Psoriasis: Plaque Psoriasis

- Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)
  - **Exception:** This may be granted when **ANY** of the following are true:
    - There is extensive recalcitrant facial involvement
    - OR
    - There is pustular involvement of the hands and feet
    - OR
    - There is genital involvement which interferes with normal sexual function

**AND**

- Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated

**AND**

- Patient has had an inadequate response or is intolerant to two of the following agents:
  - Humira® (adalimumab)
  - Otezla® (apremilast)
  - Cosentyx® (secukinumab)
  - Stelara® (ustekinumab)
  - Tremfya® (guselkumab)
  - Skyrizi™ (risankizumab-rzaa)

**Inflectra® (infliximab-dyyb) IV and Renflexis™ (infliximab-abda) IV**
- **Second-line**

**Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) are subject to review for site of service administration.**

**Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) may be considered medically necessary as a second-line agent in the treatment of moderate to severe plaque psoriasis when:**

- Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)
  - **Exception:** This may be granted when **ANY** of the following are true:
    - There is extensive recalcitrant facial involvement
    - OR
    - There is pustular involvement of the hands and feet
### Agent

<table>
<thead>
<tr>
<th>Medical Necessity, Psoriasis: Plaque Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OR</strong></td>
</tr>
<tr>
<td>• There is genital involvement which interferes with normal sexual function</td>
</tr>
<tr>
<td><strong>AND</strong></td>
</tr>
<tr>
<td>• Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated</td>
</tr>
<tr>
<td><strong>AND</strong></td>
</tr>
<tr>
<td>• Patient has had a documented trial and treatment failure with Remicade® (infliximab)</td>
</tr>
</tbody>
</table>

**NOTE:**
Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) may be considered medically necessary as emergent treatment for severe pustular, exfoliative or inflammatory psoriasis without prior use or failure/intolerance of a first-line agent, in contrast to stable plaque psoriasis.

### Second-line IL-23 inhibitors

<table>
<thead>
<tr>
<th>Ilumya™ (tildrakizumab-asmn) SC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Second-line</td>
</tr>
</tbody>
</table>

Ilumya™ (tildrakizumab-asmn) may be considered medically necessary as a second-line agent in the treatment of moderate to severe plaque psoriasis when:

• Patient has a diagnosis of chronic plaque psoriasis involving ≥10% of his or her body surface area (BSA)
  0 **Exception**: This may be granted when ANY of the following are true:
  • There is extensive recalcitrant facial involvement
  **OR**
  • There is pustular involvement of the hands and feet
  **OR**
  • There is genital involvement which interferes with normal sexual function

**AND**

• Patient has a history of an adequate trial and treatment failure with ≥1 approved systemic therapy (eg, methotrexate,
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Psoriasis: Plaque Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cyclosporine, acitretin or psoralen plus ultraviolet A light (PUVA) unless contraindicated or not tolerated</td>
</tr>
<tr>
<td><strong>AND</strong></td>
<td></td>
</tr>
<tr>
<td>• Patient has had an inadequate response or is intolerant to two of the following agents:</td>
<td></td>
</tr>
<tr>
<td>o Humira® (adalimumab)</td>
<td></td>
</tr>
<tr>
<td>o Otezla® (apremilast)</td>
<td></td>
</tr>
<tr>
<td>o Cosentyx® (secukinumab)</td>
<td></td>
</tr>
<tr>
<td>o Stelara® (ustekinumab)</td>
<td></td>
</tr>
<tr>
<td>o Tremfya® (guselkumab)</td>
<td></td>
</tr>
<tr>
<td>o Skyrizi™ (risankizumab-rzaa)</td>
<td></td>
</tr>
</tbody>
</table>
Step therapy tiers are listed below; please refer to the Policy section for details.

Psoriatic Arthritis

**First-line Agents**

- TNF-α Inhibitors (first-line)
  - Remicade® (IV)
  - Humira® (SC)
  - Enbrel® (SC)
- IL-17 Inhibitor (first-line)
  - Cosentyx® (SC)
- IL-12/23 Inhibitor (first-line)
  - Stelara® (SC)
- Janus Kinase Inhibitor (first-line)
  - Xeljanz® / Xeljanz® XR (oral)

**Second-line Agents**

- TNF-α Inhibitors (second-line)
  - Inflectra® (IV)
  - Otezla® (oral)
  - Taltz® (SC)
  - Orencia® (IV/SC)
- PDE-4 Inhibitor (second-line)
  - Cimizia® (SC)
  - Simponi® (SC)
- IL-17 Inhibitor (second-line)
  - Remicade® (infliximab) (must try and fail Remicade® (IV))
  - T-Cell Costimulation Modulator (second-line)

**Agent Medical Necessity, Psoriasis: Psoriatic Arthritis**

**First-line TNF-α Antagonists**

- **Humira® (adalimumab) SC**
  - First-line
- **Enbrel® (etanercept) SC**
  - First-line

Humira® (adalimumab) or Enbrel® (etanercept) may be considered medically necessary as the first-line agent in the treatment of active psoriatic arthritis when:

- Patient has not responded to or does not tolerate methotrexate
  **OR**
  - Humira® (adalimumab) or Enbrel® (etanercept) is being added to the regimen after the patient has had an inadequate partial response to methotrexate monotherapy
  **OR**
  - Patient is being started on Humira® (adalimumab) or Enbrel® (etanercept) concurrently with methotrexate

**Remicade® (infliximab)**

- **First-line**

Remicade® (infliximab) is subject to review for site of service administration.

**Remicade® (infliximab)** is subject to review for site of service administration.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Psoriasis: Psoriatic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Remicade® (infliximab)</strong> may be considered medically necessary as a first-line agent in the treatment of active psoriatic arthritis when:</td>
<td></td>
</tr>
<tr>
<td>• Patient has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine <strong>OR</strong></td>
<td></td>
</tr>
<tr>
<td>• Remicade® (infliximab) is being added to the regimen after the patient has had an inadequate partial response to methotrexate monotherapy <strong>OR</strong></td>
<td></td>
</tr>
<tr>
<td>• Patient is being started on Remicade® (infliximab) concurrently with methotrexate</td>
<td></td>
</tr>
<tr>
<td><strong>First-line IL-17 Inhibitor</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Cosentyx® (secukinumab) SC</strong></td>
<td></td>
</tr>
<tr>
<td>• First-line</td>
<td></td>
</tr>
<tr>
<td><strong>Cosentyx® (secukinumab) SC</strong> may be considered medically necessary as a first-line agent in the treatment of active psoriatic arthritis.</td>
<td></td>
</tr>
<tr>
<td><strong>First-line IL-12/23 Inhibitor</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Stelara® (ustekinumab) SC</strong></td>
<td></td>
</tr>
<tr>
<td>• First-line</td>
<td></td>
</tr>
<tr>
<td><strong>Stelara® (ustekinumab) SC</strong> may be considered medically necessary as a first-line agent in the treatment of active psoriatic arthritis.</td>
<td></td>
</tr>
<tr>
<td><strong>First-line Janus Kinase Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Xeljanz® (tofacitinib) oral</strong></td>
<td></td>
</tr>
<tr>
<td>• First-line</td>
<td></td>
</tr>
<tr>
<td><strong>Xeljanz® XR (tofacitinib extended-release) oral</strong></td>
<td></td>
</tr>
<tr>
<td>• First-line</td>
<td></td>
</tr>
<tr>
<td><strong>Xeljanz® (tofacitinib) and Xeljanz® XR (tofacitinib extended-release) may be considered medically necessary as a first-line agent in the treatment of moderate to active psoriatic arthritis when used in combination with methotrexate or another conventional synthetic DMARD (eg, sulfasalazine or leflunomide):</strong></td>
<td></td>
</tr>
<tr>
<td>• Patient has had trial of at least 3 months of one conventional DMARD (eg, methotrexate, leflunomide, sulfasalazine) unless contraindicated/not tolerated <strong>AND</strong></td>
<td></td>
</tr>
<tr>
<td>• Medication is being prescribed by or in consultation with a rheumatologist or dermatologist</td>
<td></td>
</tr>
<tr>
<td>Agent</td>
<td>Medical Necessity, Psoriasis: Psoriatic Arthritis</td>
</tr>
<tr>
<td>-------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td><strong>Note:</strong> The use of tofacitinib in the setting of alopecia is considered cosmetic and is not covered by this policy.</td>
<td></td>
</tr>
</tbody>
</table>

### Second-line TNF-α Antagonists

<table>
<thead>
<tr>
<th>Cimzia® (certolizumab pegol) SC</th>
<th>Simponi® (golimumab) SC and Simponi Aria® (golimumab) IV are subject to review for site of service administration.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Second-line</td>
<td>Cimzia® (certolizumab pegol), Simponi® (golimumab) SC and Simponi Aria® (golimumab) IV may be considered medically necessary as a second-line agent in the treatment of active psoriatic arthritis when:</td>
</tr>
<tr>
<td>Simoni® (golimumab) SC or Simponi Aria® (golimumab) IV</td>
<td>• Patient has had an inadequate response or intolerance to methotrexate, and two of the following agents:</td>
</tr>
<tr>
<td>• Second-line</td>
<td>o Enbrel® (etanercept)</td>
</tr>
<tr>
<td></td>
<td>o Humira® (adalimumab)</td>
</tr>
<tr>
<td></td>
<td>o Cosentyx® (secukinumab)</td>
</tr>
<tr>
<td>Inflectra® (infliximab-dyyb) IV and Renflexis™ (infliximab-abda) IV</td>
<td>o Stelara® (ustekinumab)</td>
</tr>
<tr>
<td>• Second-line</td>
<td>o Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release)</td>
</tr>
<tr>
<td>Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) are subject to review for site of service administration.</td>
<td></td>
</tr>
<tr>
<td>Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda) may be considered medically necessary as a second-line agent in the treatment of active psoriatic arthritis when:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Patient has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine OR</td>
</tr>
<tr>
<td></td>
<td>• Inflectra® (infliximab-dyyb) or Renflexis™ (infliximab-abda) is being added to the regimen after the patient has had an inadequate partial response to methotrexate monotherapy OR</td>
</tr>
<tr>
<td></td>
<td>• Patient is being started on Inflectra® (infliximab-dyyb) or Renflexis™ (infliximab-abda) concurrently with methotrexate AND</td>
</tr>
<tr>
<td></td>
<td>• Patient has had a documented trial and treatment failure with Remicade® (infliximab)</td>
</tr>
</tbody>
</table>
### Second-line PDE4 Inhibitor

**Otezla® (apremilast) Oral**  
- **Second-line**

Otezla® (apremilast) may be considered medically necessary as a second-line agent in the treatment of active psoriatic arthritis when:

- Patient has had an inadequate response or intolerance to one of the following agents:
  - Enbrel® (etanercept)
  - Humira® (adalimumab)
  - Cosentyx® (secukinumab)
  - Stelara® (ustekinumab)
  - Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release)

### Second-line IL-17 Inhibitors

**Taltz® (ixekizumab) SC**  
- **Second-line**

Taltz® (ixekizumab) may be considered medically necessary as a second-line agent in the treatment of active psoriatic arthritis when:

- Patient has had an inadequate response or intolerance to two of the following agents:
  - Enbrel® (etanercept)
  - Humira® (adalimumab)
  - Cosentyx® (secukinumab)
  - Stelara® (ustekinumab)
  - Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release)

AND

- Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist

### Second-line T-Cell Costimulation Modulators

**Orencia® (abatacept) IV/SC**  
- **Second-line**

Orencia® (abatacept) IV/SC is subject to review for site of service administration.

Orencia® (abatacept) IV/SC may be considered medically necessary as a second-line agent in the treatment of active psoriatic arthritis when:

- Patient has had an inadequate response or intolerance to methotrexate, and two of the following agents:
### Medical Necessity, Psoriasis: Psoriatic Arthritis

- Enbrel® (etanercept)
- Humira® (adalimumab)
- Cosentyx® (secukinumab)
- Stelara® (ustekinumab)
- Xeljanz® (tofacitinib) OR Xeljanz® XR (tofacitinib extended-release)

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

#### Non-Radiographic Axial Spondyloarthritis

<table>
<thead>
<tr>
<th>First-line Agent</th>
<th>TNF-α Inhibitors (first-line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimzia® (SC)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Agent</th>
<th>Medical Necessity, Non-Radiographic Axial Spondyloarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line TNF-α Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Cimzia® (certolizumab pegol) SC</td>
<td><strong>Cimzia® (certolizumab pegol) may be considered medically necessary as a first-line agent in the treatment of non-radiographic axial spondyloarthritis in adults when:</strong></td>
</tr>
<tr>
<td>• First-line</td>
<td>• Patient has objective signs of inflammation, defined as at least one of the following:</td>
</tr>
</tbody>
</table>
### Agent Medical Necessity, Non-Radiographic Axial Spondyloarthritis

- 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

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td><strong>HCPCS</strong></td>
<td></td>
</tr>
<tr>
<td>J0129</td>
<td>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)</td>
</tr>
<tr>
<td>J0135</td>
<td>Injection, adalimumab (Humira®), 20 mg</td>
</tr>
<tr>
<td>J0717</td>
<td>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)</td>
</tr>
<tr>
<td>J1438</td>
<td>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)</td>
</tr>
<tr>
<td>J1602</td>
<td>Injection, golimumab (Simponi Aria®), 1 mg, for intravenous use</td>
</tr>
<tr>
<td>J1628</td>
<td>Injection, guselkumab (Tremfya®), 1 mg</td>
</tr>
<tr>
<td>J1745</td>
<td>Injection, infliximab (Remicade®), 10mg</td>
</tr>
<tr>
<td>J3245</td>
<td>Injection, tildrakizumab (Ilumya™), 1 mg (new code effective 1/1/19)</td>
</tr>
<tr>
<td>J3262</td>
<td>Injection, tocilizumab (Actemra®), 1 mg</td>
</tr>
<tr>
<td>J3357</td>
<td>Injection, ustekinumab (Stelara®), 1mg.</td>
</tr>
<tr>
<td>J3358</td>
<td>Ustekinumab (Stelara®), for intravenous injection, 1 mg</td>
</tr>
<tr>
<td>J3590</td>
<td>Unclassified biologics (Use only to report Actemra® ACTPen™, Cosentyx®, Kevzara®, Kineret®, Siliq™, Simponi®, Skyrizi™, and Taltz®)</td>
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<td>J9310</td>
<td>Injection, rituximab (Rituxan®, generic rituximab), 100 mcg (code terminated 1/1/19)</td>
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<td>Code</td>
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<td>J9312</td>
<td>Injection, rituximab (Rituxan®), 10 mg (new code effective 1/1/19)</td>
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<tr>
<td>Q5103</td>
<td>Injection, infliximab-dyyb, biosimilar, (Inflectra®), 10 mg</td>
</tr>
<tr>
<td>Q5104</td>
<td>Injection, infliximab-abda, biosimilar, (Renflexis™), 10 mg</td>
</tr>
</tbody>
</table>

**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 patients are not small adults. Pediatric patients differ physiologically, developmentally, cognitively, and emotionally from adult patients, 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 patients above the age of 13.

**Evidence Review**

**Rheumatoid Arthritis (RA)**

RA is a chronic, progressive, inflammatory, autoimmune disease affecting about 1% of the US adult population and occurs approximately 3 times more frequently in women than in men (ACR Subcommittee on Rheumatoid Arthritis Guidelines, 2002). Almost 80% of RA cases occur in patients 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 2 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 (eg, fever, fatigue, anorexia, weight loss, and anemia), which contribute to the significant work disability and impaired quality of life which occur. Patients 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 rheumatoid arthritis (RA). While both non-pharmacologic (eg, patient 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 patients more aggressively earlier by initiating a DMARD (or combinations of DMARDs) within 3 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 patients with rapidly progressive disease. The predictive risk factor found to be most associated with this subset of patients 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 patient; 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 (PsA)

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 patients 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 patients 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 4 inhibitor apremilast are now approved.

Other Spondyloarthropathies (SpAs)

The spondyloarthropathies 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 spondyloarthropy, 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 patients 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 patients with inflammatory bowel disease may have evidence of sacroiliitis and some 20% of these patients 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 patients 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.

**Psoriasis**

Psoriasis is a chronic, multifactorial, noncontagious skin disorder that affects about 2.1% of the U.S. population and 1-3% of persons worldwide. About 4.5 million, or 1 in 65, Americans have psoriasis. Onset is typically between the ages of 15 and 35 and prevalence is slightly greater in women. It is also more common in some ethnic groups (Caucasians) than others (African American or Asians). A genetic component has also been identified. There are several forms of psoriasis, but plaque psoriasis (or psoriasis vulgaris) is the most common form of the disease, affecting about 80% of psoriatic patients.

About 20-30% of people with psoriasis have cases that are considered moderate to severe (covering more than 3% of their body). Although not typically life-threatening, psoriasis can have a large impact on quality of life. Seventy-five percent of people with moderate to severe psoriasis report their disease has a moderate to large impact on their everyday lives. Patients with palmar-plantar disease may have less than 3% involvement, but often have debilitating and recalcitrant disease. Further, approximately 7% of psoriatic patients have concurrent arthritis (which may be particularly relevant to one’s choice of therapy).

Psoriasis is a chronic immune-mediated inflammatory disease characterized by T-cell activation and accumulation in the epidermis and dermis, leading to abnormal differentiation and hyperproliferation of keratinocytes. Recent advances in the understanding of the cellular
mechanisms underlying psoriasis have given rise to a generation of highly targeted biotechnologies for this indication.

As the severity of psoriasis ranges from mild to severe, with or without concurrent arthritis, available treatments lie along a spectrum from minimally invasive with a low risk of systemic side effects, to systemic therapy with a risk of potentially severe side effects. Non-invasive, topical treatments may also have significant side effects; for example, topical corticosteroids applied to large areas of skin may result in significant levels of systemic absorption. Many treatments have a cumulative toxicity potential, but the benefit of prolonged remissions makes the use of the more potent treatments relatively attractive.

Topical therapy, usually corticosteroids, is recommended as first-line treatment in psoriasis because these products are easy to administer, inexpensive, and safe. However, application to large areas of involvement can be time-consuming, expensive, and messy. Most patients with moderate to severe disease will not achieve clearance or long-term remission. Tachyphylaxis may also develop with long-term use of topical corticosteroids. In patients whose moderate to severe psoriasis fails topical therapy, the therapeutic options that remain are systemic agents, phototherapy and biologics.

Approved systemic agents (methotrexate, cyclosporine, and acitretin) are highly effective in the treatment of psoriasis; however, these therapies have limitations due to serious toxicities that require monitoring. Methotrexate can cause hepatotoxicity. Methotrexate is also associated with bone marrow toxicity, severe pulmonary toxicity, and serious drug-drug interactions (eg, trimethoprim-sulfamethoxazole). Cyclosporine is nephrotoxic, and can cause interstitial fibrosis and renal tubular atrophy in patients treated for more than 2 years. Hypertension, laboratory abnormalities (electrolytes, liver function tests, lipids), and numerous drug-drug interactions are also among the problems associated with cyclosporine. Because methotrexate and cyclosporine are potent immunosuppressive drugs, patients are at increased risk of infections and malignancies, including skin cancers and lymphoproliferative disorders. Like all retinoids, acitretin is highly teratogenic, posing a long-lasting risk (up to 3 years) in women of childbearing potential. Elevation in liver function tests, hyperlipidemia, and mucocutaneous reactions are additional adverse events associated with acitretin. Systemic corticosteroids are generally avoided as they may be associated with severe exacerbations, both during and after treatment.

Phototherapy (eg, UVB, narrowband UVB, PUVA) is used for patients who fail topicals or those with disease too extensive for topical therapy. Phototherapy can be effective for many patients, but may be inconvenient and time-consuming, if frequent office or clinic visits are required and the availability of specialized phototherapy clinics may be limited. Patients with a durable medical equipment (DME) benefit may purchase a home unit for easier access. Cumulative
exposure to PUVA is associated with an increased risk of squamous cell carcinoma and malignant melanoma.

Various other strategies using traditional therapies have also been used to maintain remission and decrease the risk of cumulative end-organ toxicities. Rotational therapy involves the use of a therapy for some time and then switching to another form of therapy. Combination therapy uses low-dosages of different treatments concurrently to minimize toxicity and enhance efficacy. Traditionally, these strategies usually involve topicals, phototherapy, and systemics in various combinations.

Biologic agents have been shown effective for many patients in randomized, double-blind, placebo-controlled clinical trials, but few head-to-head clinical trials comparing these agents with traditional therapies exist. NBUVB continues to appear a very effective therapy in terms of achievement of ≥75% response, global assessment (“clear or almost clear”), and length of remission. While the long-term risks of PUVA, methotrexate, and cyclosporine use in psoriatic patients have become more clearly identified, these data are not available for the biologics in this population. The new biologic agents are clearly more widely available and convenient than the mainstay of psoriasis therapy, NBUVB, which may require anywhere from 30-100 outpatient visits to specialized facilities per year, unless a home system is purchased. On the other hand, biologics are all administered by injection, making them less convenient than systemic oral therapy.

Remicade® (infliximab) is approved for the treatment of adults with chronic severe plaque psoriasis who are candidates for systemic therapies and clinical trial results for Humira® (adalimumab), Remicade®, and Enbrel® (etanercept) have been published. Of these, three Humira studies added enough new information to warrant off-label use consideration. In the first multicenter, randomized, double-blind, placebo-controlled study, 147 patients received Humira 80 mg at week 0, then 40 mg every other week beginning week 1, Humira 80 mg at week 0 and 1, then 40 mg every week beginning at week 1, or placebo for 12 weeks, after which placebo patients were crossed over to Humira 40 mg every other week in a 48-week open label extension trial. At week 12, 53% of patients taking Humira every other week, 80% of patients taking Humira weekly, and 4% of patients taking placebo achieved 75% improvement in Psoriasis Area and Severity Index score (P<0.001). Responses were sustained for 60 weeks. Humira was safe and well tolerated in this population.

In the Phase III REVEAL study (Randomized Controlled Evaluation of adalimumab Every Other Week Dosing in Moderate to Severe Psoriasis TriAL), 1,212 patients with moderate to severe chronic plaque psoriasis were randomized to treatment with Humira 80 mg at week 0, then 40 mg every other week beginning at week 1 or placebo. The trial was comprised of 3 periods, a 16-week, double-blind period for assessment of initial response; a 17-week open-label sustained
response period, in which responders to either treatment (those achieving a PASI-75) received Humira 40 mg every other week; and a final 19-week, double-blind loss of response period, in which patients receiving Humira throughout the previous 2 study periods were re-randomized to either Humira every other week or placebo. In the initial response phase, more Humira-treated patients achieved a PASI-75 compared to those receiving placebo beginning at week 4 and at every visit throughout the 16-week evaluation period. At week 16, 71% of Humira- and 6.5% of placebo-treated patients achieved a PASI-75 (P<0.001). In Humira responders, mean PASI scores were maintained throughout the subsequent maintenance of response period (weeks 16-33) of the study. In the last period of the study examining loss of response, 28.4% of patients re-randomized to placebo lost response by week 52 compared to 4.9% of patients maintaining Humira (P<0.001). Humira was generally well tolerated and no unexpected adverse events were observed over the 52 weeks of the trial.

In a second Phase III trial, CHAMPION (Comparative Study of HUMIRA vs. Methotrexate vs. Placebo In PsOriasis Patients), 271 patients were randomized to treatment with Humira 80 mg at week 0, then 40 mg every other week beginning at week 1 (n=108), methotrexate 7.5 mg x 2 weeks, 10 mg x 2 weeks, then 15 mg orally (n=110), or placebo (n=53) for a total of 16 weeks. At week 16, more Humira-treated patients achieved a PASI-75 response (80%) than patients receiving either methotrexate (36%, P<0.001) or placebo (19%, P<0.001). Similar results were observed for PASI-90 response and PGA “clear” or “minimal” response. Humira was generally well-tolerated, with a safety profile similar to that known for an arthritis population.

In September 2009, the FDA approved the use of ustekinumab to treat plaque psoriasis. Ustekinumab is a human IgG1κ monoclonal antibody that binds to the shared p40 subunit of interleukins 12 and 23, blocking signaling of their cognate receptors. It is known that IL-12 and IL-23 plays important roles in the pathogenesis of psoriasis. IL-12 causes differentiation of CD4+ T cells to interferon-gamma (IFN-gamma)-producing T helper 1 (Th1) cells, while IL-23 induces differentiation to IL-17-producing pathogenic Th17 cells. In in vitro models, ustekinumab was shown to disrupt IL-12 and IL-23 mediated signaling and cytokine cascades by disrupting the interaction of these cytokines with a shared cell-surface receptor chain, IL-12 β1.

The evidence of efficacy consists mainly of two pivotal trials (PHOENIX I and PHOENIX II) submitted for FDA approval. Both studies showed robust clinical result against placebo. The primary endpoint for both studies was the proportion of patients achieving a PASI 75 in the 12 week placebo-controlled trial. Both the 45mg and 90 mg groups achieved statistically significantly higher PASI 75 rate compared to placebo (67.1%, 66.4%, 3.1%, respectively; each p<0.0001 vs. placebo). Both studies also showed favorable secondary endpoint results for PGA score and DLQI vs. placebo. Ustekinumab was found more efficacious compared to etanercept during a Phase III, multi-center, active controlled trial with 930 patients (ACCEPT trial). For the
primary efficacy endpoint of PASI 75 at week 12, a greater proportion of patients treated with ustekinumab 45mg and 90mg achieved a PASI 75 compared to those receiving etanercept 50mg.

More recently, phosphodiesterase 4 inhibitor apremilast has been now approved for moderate to severe plaque psoriasis. Two multicenter, randomized, double-blind, placebo-controlled trials (PSOR-1 and PSOR-2) enrolled a total of 1257 subjects with moderate to severe plaque psoriasis. In both studies, subjects were randomized 2:1 to apremilast 30 mg BID or placebo for 16 weeks. Primary endpoints were the proportion of subjects who achieved PASI-75 at Week 16 and the proportion of subjects who achieved a sPGA score of clear (0) or almost clear (1) at Week 16. Approximately 30% of all subjects had received prior phototherapy and 54% had received prior conventional systemic and/or biologic therapy for the treatment of psoriasis with 37% receiving prior conventional systemic therapy and 30% receiving prior biologic therapy. A total of 18% of subjects had a history of psoriatic arthritis. Approximately 33% of patients receiving apremilast in PSOR-1 achieved a PASI-75 (vs. 5% on placebo), and 29% of apremilast patients in PSOR-2 (vs. 6% on placebo). In all groups, approximately two-thirds of patients achieving PASI-75 also had sPGA scores of clear (0) or almost clear (1).

Tremfya (guselkumab): Evidence of efficacy comes from three phase 3 clinical trials: VOYAGE-1, VOYAGE-2, and NAVIGATE in which guselkumab yielded significantly increased symptomatic improvement for patients with moderate to severe PsO symptoms vs adalimumab and among patients who had an inadequate response to ustekinumab. In VOYAGE-1, symptom resolution occurred in significantly more guselkumab patients vs adalimumab as assessed by achieving IGA 0/1 (85.1% vs 65.9%), PASI 90 (73.3% vs 49.7%), and PASI 75 (91.2% vs 73.1%) (P<0.001 for each). In VOYAGE-2, guselkumab yielded higher rates of symptom resolution vs adalimumab as measured by the proportion of patients achieving IGA 0/1 (84.1% vs 67.7%), PASI 90 (70.0% vs 46.8%), and PASI 75 (86.3% vs 68.5%) (P<0.001 for each). In NAVIGATE, guselkumab yielded higher rates of symptom resolution vs ustekinumab at weeks 28 and 52 as measured by the proportion of patients achieving IGA 0/1 (31.1% and 36.3% vs 14.3% and 17.3%), and PASI 90 (48.1% and 51.1% vs 22.6% and 24.1%) (P≤0.001 for each).1-4

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 get 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.

**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 3 years in the TEMPO trial. While infliximab showed high efficacy at both 3mg/kg and 10mg/kg dosing every 8 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 3 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 patients on TNF-α inhibitors are no higher than what is to be expected in this patient population. Another study done in 2007 found a higher incidence of cutaneous cancers among the TNF-α inhibitor treated patients, 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 from four randomized controlled trials (RADIATE, OPTION, AMBITION, and TOWARD). The primary endpoint for all studies was the proportion of patients 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 patient-years and the overall rate of fatal serious infections was 0.13 per 100 patient-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 5 years in biologic-naïve RA patients 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 patients (77%), 290 (77%), 293 (78%), 287 (76%), and 235 (62%) patients 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 patients. 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 patients 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 8 key clinical trials in the abatacept clinical development program were also recently reported. Cumulative experience included 11,658 patient-years in 4,149 patients, of which 1,030 patients 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 patients (2,331 patient-years) and the long-term period included 3,256 patients (9,278 patient-years).

The incidence rates of overall adverse events per 100 patient-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 patient-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 patient-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 patients reached ACR 20 (20% clinical improvement) in the tofacitinib groups as placebo after 3 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. Patients showed improvement as soon as 2 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 patient-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 patients 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.

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.

References


24. Premera Pharmacy and Therapeutics Committee reviewed and recommended for approval on March 27, 2007.


45. Dougados M, van der Heijde V, Chen YC, et al. Baricitinib, an Oral Janus Kinase (JAK )1/JAK2 Inhibitor, in Patients with Active Rheumatoid Arthritis (RA) and an Inadequate Response to cs DMARD Therapy: Results of the Phase 3 RA-BUILD Study. Abstract.


47. Taylor P, Keystone E, van der Heijde D, et al. Baricitinib Versus Placebo or Adalimumab in Patients with Active Rheumatoid Arthritis (RA) and an Inadequate Response to Background Methotrexate Therapy: Results of a Phase 3 Study (RA-BEAM). Abstract.


### History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/10/14</td>
<td>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.</td>
</tr>
<tr>
<td>03/27/14</td>
<td>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.</td>
</tr>
<tr>
<td>04/21/14</td>
<td>Update Related Policies. Add 5.01.521.</td>
</tr>
<tr>
<td>07/14/14</td>
<td>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.</td>
</tr>
<tr>
<td>08/11/14</td>
<td>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</td>
</tr>
<tr>
<td>Date</td>
<td>Comments</td>
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</tr>
<tr>
<td>09/12/14</td>
<td>HCPCS J7050 removed from policy; these do not suspend and are not reviewed at this time.</td>
</tr>
<tr>
<td></td>
<td>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.</td>
</tr>
<tr>
<td>01/13/15</td>
<td>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®.</td>
</tr>
<tr>
<td>03/10/15</td>
<td>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.</td>
</tr>
<tr>
<td>04/15/15</td>
<td>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.</td>
</tr>
<tr>
<td>07/14/15</td>
<td>Interim Review. Indications for rituximab removed; readers referred to policies which address these indications.</td>
</tr>
<tr>
<td>12/08/15</td>
<td>Interim Update. Moderate to severe hidradenitis suppurativa added to the list of medically necessary indications of Humira.</td>
</tr>
<tr>
<td>01/04/16</td>
<td>Minor edit. Typo corrected; investigational policy statement within IL-17 inhibitors corrected to read secukinumab (ustekinumab was listed in error).</td>
</tr>
<tr>
<td>01/19/16</td>
<td>Coding update. New HCPCS codes J0202 and J3380, effective 1/1/16, add to the policy.</td>
</tr>
<tr>
<td>02/09/16</td>
<td>Annual Review. Medically necessary indications for Promacta updated; ITP removed; chronic immune ITP added with additional criteria for eligibility; and severe aplastic anemia added.</td>
</tr>
<tr>
<td>02/23/16</td>
<td>Coding update. Add J1595, J1826, J1830, Q3027 and Q3028.</td>
</tr>
<tr>
<td>05/01/16</td>
<td>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.</td>
</tr>
</tbody>
</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
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<tbody>
<tr>
<td>10/01/16</td>
<td>Interim Review, approved September 13, 2016. Minor dosing update for Xeljanz.</td>
</tr>
<tr>
<td>11/01/16</td>
<td>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.</td>
</tr>
<tr>
<td>02/01/17</td>
<td>Annual Review, approved January 10, 2017. Added new agent (prior to approval) baricitinib to the RA section, alongside Xeljanz.</td>
</tr>
<tr>
<td>04/01/17</td>
<td>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.</td>
</tr>
<tr>
<td>04/10/17</td>
<td>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.</td>
</tr>
<tr>
<td>05/05/17</td>
<td>Minor update; added hyperlinks and step therapy tier charts.</td>
</tr>
<tr>
<td>06/01/17</td>
<td>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.</td>
</tr>
<tr>
<td>06/13/17</td>
<td>Coding updated, added HCPCS code J1602 back to coding table as it was inadvertently removed.</td>
</tr>
<tr>
<td>08/18/17</td>
<td>Minor update, clarified History section for the July 1, 2016, revision.</td>
</tr>
<tr>
<td>09/01/17</td>
<td>Interim Review, approved August 15, 2017. Added Infliximab-abda to coverage criteria and coding section.</td>
</tr>
<tr>
<td>09/22/17</td>
<td>Minor update. Clarified policy statements regarding plaque psoriasis.</td>
</tr>
<tr>
<td>11/01/17</td>
<td>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.</td>
</tr>
<tr>
<td>02/14/18</td>
<td>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</td>
</tr>
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<tr>
<td>04/01/18</td>
<td>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 Q5102 terminated 4/1/18.</td>
</tr>
<tr>
<td>05/01/18</td>
<td>Interim Review, approved April 18, 2018. Ilumya criteria for psoriasis indication has been added.</td>
</tr>
<tr>
<td>06/20/18</td>
<td>Added 11.01.523 to Related Policies.</td>
</tr>
<tr>
<td>08/01/18</td>
<td>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.</td>
</tr>
<tr>
<td>11/01/18</td>
<td>Minor update, the Site of Service criteria was updated for clarity.</td>
</tr>
<tr>
<td>01/01/19</td>
<td>Coding update, added new HCPCS codes J3245, J9311, J9312, and Q5109 (new codes effective 1/1/19).</td>
</tr>
<tr>
<td>02/01/19</td>
<td>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.</td>
</tr>
<tr>
<td>02/20/19</td>
<td>Coding update, added HCPCS code J1602.</td>
</tr>
<tr>
<td>03/01/19</td>
<td>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.</td>
</tr>
<tr>
<td>04/01/19</td>
<td>Coding update, removed HCPCS code J0215.</td>
</tr>
<tr>
<td>05/01/19</td>
<td>Interim Review, approved April 2, 2019. Added Simponi Aria as second line therapy for psoriatic arthritis and ankylosing spondylitis.</td>
</tr>
<tr>
<td>06/21/19</td>
<td>Revised the effective date of the updated policy from July 1, 2019, to July 31, 2019.</td>
</tr>
<tr>
<td>07/18/19</td>
<td>Removed link and note regarding updated policy.</td>
</tr>
<tr>
<td>11/01/19</td>
<td>Interim Review, approved October 8, 2019. Added criteria for Taltz when used for ankylosing spondylitis. Added criteria for Rinvoq for rheumatoid arthritis. Updated</td>
</tr>
</tbody>
</table>
Example Table Data

<table>
<thead>
<tr>
<th>Date</th>
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<tbody>
<tr>
<td></td>
<td>criteria for Cimzia, Kevzara, Kineret, Olumiant, Orenica, Simponi, Xeljanz and Xeljanz XR when used for rheumatoid arthritis.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2019 Premera All Rights Reserved.

**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.
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  • Qualified sign language interpreters
  • Written information in other formats (large print, audio, accessible electronic formats, other formats)
• Provides free language services to people whose primary language is not English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance:
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PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can also file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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