Drug and Biologic Coverage Policy

Effective Date .............................................. 3/1/2020
Next Review Date........................................... 3/1/2021
Coverage Policy Number ................................. 1805

Immunomodulators – Oral and Subcutaneous (Employer Group Benefit Plans)

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Related Coverage Resources

Abatacept Intravenous
Golimumab Intravenous
Immunomodulators (Individual and Family Plans)
Infliximab
Multiple Sclerosis Therapy
Natalizumab for Crohn’s Disease
Phototherapy, Photochemotherapy, and Excimer Laser Therapy for Dermatologic Conditions
Rituximab for Non-Oncology Indications
Oncology Medications
Tocilizumab Intravenous
Vedolizumab

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

This coverage policy addresses the use of oral and subcutaneous immunomodulators for Employer Group Benefit Plans. Coverage for Individual and Family Benefit Plans is addressed in a separate coverage policy. Please refer to the related coverage policy link above.

Coverage for intravenous immunomodulators for Employer Group Benefit Plans are addressed in separate coverage policies. Please refer to the related coverage policy links above.

This coverage policy addresses the use of immunomodulators for non-oncology indications. The use of immunomodulators for oncology indications is addressed in a separate coverage policy. Please refer to the related coverage policy link above (Oncology Medications).
Oral and Subcutaneous Immunomodulators for Employer Group Benefit Plans include the following:

- Actemra® subcutaneous injection (tocilizumab)
- Cimzia® (certolizumab pegol)
- Cosentyx® (secukinumab)
- Enbrel® (etanercept)
- Humira® (adalimumab)
- Ilumya™ (tildrakizumab-asmn)
- Kevizara™ (sarilumab)
- Kineref® (anakinra)
- Olumiant® (baricitinib)
- Orencia® subcutaneous injection (abatacept)
- Otezla® (apremilast)
- Rinoq (upadacitinib)
- Siliq™ (broladumab)
- Simponi® (golimumab)
- Skyrizi™ (risankizumab-rzaa)
- Stelara® (ustekinumab)
- Taltz® (ixekizumab)
- Tremfya™ (guselkumab)
- Xeljanz®/Xeljanz XR® (tofacitinib)

Coverage for Immunomodulators varies across plans. Refer to the customer’s benefit plan document for coverage details.

Immunomodulators are covered as medically necessary when the specified criteria are met:

### Ankylosing Spondylitis

<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred Product</th>
<th>Criteria for Use: Ankylosing Spondylitis Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
| Cosentyx (secukinumab) | Cimzia (certolizumab pegol) | Ankylosing spondylitis and documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ONE non-steroidal anti-inflammatory drug (NSAIDs) AND the following criteria for non-preferred products (by drug/class):  
  Cimzia, Simponi (Standard/Performance and Legacy Prescription Drug List plans), Taltz  
  • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for TWO preferred products  
  Simponi (Value/Advantage Prescription Drug List plans)  
  • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ALL preferred products and ONE non-preferred product (Cimzia) |
| Enbrel (etanercept) | Simponi 50 mg (golimumab) | |
| Humira (adalimumab) | Taltz (ixekizumab) | |

### Behcet's Disease

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Behcet's Disease Employer Group Benefit Plans</th>
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</thead>
</table>
| Otezla (apremilast) | Behcet’s Disease AND ALL of the following criteria:  
  • Treatment of oral ulcers |
<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Behcet's Disease Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
|         | • Documented failure, contraindication per FDA label, or intolerance to at least ONE other systemic therapy (for example: colchicine, systemic corticosteroids, azathioprine, thalidomide, interferon alpha)  
|         | • Prescribed by, or in consultation with a rheumatologist or dermatologist |

**Crohn's Disease – Adults and Pediatrics**

<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred Product</th>
<th>Criteria for Use: Crohn’s Disease Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
| Humira (adalimumab) | Cimzia (certolizumab pegol) | Moderate to severe Crohn’s Disease AND the following criteria for the specified products:  
| Stelara (ustekinumab) | | Humira  
| | • Individual is 6 years of age or older.  
| | Stelara  
| | • Individual is 18 years of age or older.  
| | When criteria are met, a single intravenous infusion dose of Stelara up to a maximum dose of 520 mg will be authorized. The maintenance dosage of 90 mg subcutaneous will be authorized for 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.  
| | Cimzia  
| | • Individual is 18 years of age or older.  
| | • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for TWO preferred product |

**Giant Cell Arteritis**

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Giant Cell Arteritis Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actemra Subcutaneous Injection (tocilizumab)</td>
<td>Giant cell arteritis (GCA)</td>
</tr>
</tbody>
</table>

**Graft versus Host Disease**

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Graft versus Host Disease Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enbrel (etanercept)</td>
<td>Graft versus host disease and documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for systemic corticosteroid</td>
</tr>
</tbody>
</table>

**Hidradenitis Suppurativa**

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Hidradenitis Suppurativa Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
| Humira (adalimumab) | All of the following criteria are met:  
| | • Individual is 12 years of age or older  
| | • Moderate to severe hidradenitis suppurativa with recurrent abscesses/inflammatory nodules and scar formation  
| | • Failure of conventional medical management (for example, good hygiene, antibiotic therapy, and surgical incision and draining) |
### Neonatal-Onset Multisystem Inflammatory Disease (NOMID)

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: NOMID Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kineret (anakinra)</td>
<td>Neonatal-Onset Multisystem Inflammatory Disease (NOMID)</td>
</tr>
</tbody>
</table>

### Non-Radiographic Axial Spondyloarthritis (nr-axSpA)

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Non-Radiographic Axial Spondyloarthritis Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
| Cimzia (certolizumab pegol) | The following criteria are met:  
  • The patient has objective signs of inflammation, defined as ONE of the following:  
    o C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory  
    o Sacroiliitis reported on magnetic resonance imaging (MRI) |

### Plaque Psoriasis - Adults

<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred or non-covered Product</th>
<th>Criteria for Use: Plaque Psoriasis – Adult Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
| Cosentyx (secukinumab) | Cimzia (certolizumab pegol) | Chronic plaque psoriasis AND the following criteria are met:  
  • Body Surface Area (BSA) of greater than 5% OR BSA less than 5% and there is involvement with the face, genitals, hands and feet (for example, nail psoriasis, palmoplantar disease), scalp, or intertriginous areas  
  • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for any of the following:  
    o Systemic therapy (for example, methotrexate, cyclosporine, Soriatan)  
    o Phototherapy [narrow or broad band ultraviolet B (UVB), or psoralen plus ultraviolet A (PUVA)]  
    o Topical therapy (for example, coal tar, keratolytics, corticosteroids, anthralin, Dovonex, Tazorac)]  
  • AND the following criteria for the specified products:  
    • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for Humira, Cimzia, Ilumya  
    • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for TWO preferred products (Cosentyx, Humira, Otezla, Skyrizi, Stelara, Tremfya)  
    Siliq (Standard/Performance and Value/Advantage Prescription Drug List plans)  
    • Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for FIVE preferred products  
    Siliq (Legacy Prescription Drug List plans) |
| Humira (adalimumab)  | Ilumya (tildrakizumab-asmn) |  |
| Otezla (apremilast)  | Siliq (brodalumab) |  |
| Skyrizi (risankizumab-rzaa) | Taltz (ixekizumab) |  |
| Stelara (ustekinumab) |  |  |
| Tremfya (guselkumab) |  |  |
| *Step therapy required* Enbrel* (etanercept) |  |  |
### Coverage Policy Number: 1805

#### Preferred Product | Non-Preferred or non-covered Product | Criteria for Use: Plaque Psoriasis – Adult Employer Group Benefit Plans
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<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred or non-covered Product</th>
<th>Criteria for Use: Plaque Psoriasis – Adult Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cosentyx</td>
<td>Humira, Otezla, Skyrizi, Stelara, Tremfya</td>
<td></td>
</tr>
<tr>
<td>Taltz</td>
<td>Humira, Otezla, Skyrizi, Stelara, Tremfya</td>
<td></td>
</tr>
</tbody>
</table>

#### Plaque Psoriasis - Pediatrics and Adolescents

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Plaque Psoriasis - Pediatrics and Adolescents Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
| Enbrel (etanercept) | Chronic plaque psoriasis AND the following criteria are met:  
  - For Enbrel: Individual is 4 years of age to less than 18 years of age  
  - For Stelara: Individual is 12 years of age to less than 18 years of age  
  - Body Surface Area (BSA) of greater than 5% OR BSA less than 5% and there is involvement with the face, genitals, hands and feet (for example, nail psoriasis, palmoplantar disease), scalp, or intertriginous areas  
  - Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for any of the following:  
    - Systemic therapy (for example, methotrexate, cyclosporine, Soriatane)  
    - Phototherapy [narrow or broad band ultraviolet B (UVB), or psoralen plus ultraviolet A (PUVA)]  
    - Topical therapy (for example, coal tar, keratolytics, corticosteroids, anthralin, Dovonex, Tazorac) |
| Stelara (ustekinumab) | |

#### Polyarticular Juvenile Idiopathic Arthritis (PJIA)

<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred or non-covered Product</th>
<th>Criteria for Use: PJIA Employer Group Benefit Plans</th>
</tr>
</thead>
</table>
| Enbrel (etanercept) | Orencia Subcutaneous Injection (abatacept) | Polyarticular Juvenile Idiopathic Arthritis in a child 2 years of age and older AND the following criteria for the specified products:  
  - Actemra Subcutaneous Injection  
    - Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for Humira  
  - Orencia Subcutaneous Injection  
    - Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for TWO preferred products |
| Humira (adalimumab) | |
| *Step therapy required* | Actemra Subcutaneous Injection* (tocilizumab) |

#### Psoriatic Arthritis

<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred or non-covered Product</th>
<th>Criteria for Use: Psoriatic Arthritis Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cosentyx (secukinumab)</td>
<td>Cimzia (certolizumab pegol)</td>
<td>Psoriatic arthritis AND documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ONE disease-modifying anti-rheumatic drug (DMARD) (for example,</td>
</tr>
<tr>
<td>Preferred Product</td>
<td>Non-Preferred or non-covered Product</td>
<td>Criteria for Use: Psoriatic Arthritis Employer Group Benefit Plans</td>
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<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Enbrel (etanercept)</td>
<td>Ocrevus (abatacept)</td>
<td>methotrexate, leflunomide, sulfasalazine) AND the following criteria for the specified products:</td>
</tr>
<tr>
<td>Humira (adalimumab)</td>
<td>Simponi 50 mg (golimumab)</td>
<td>Otezla&lt;br&gt;Both of the following:&lt;br&gt;• Individual is 18 years of age and older&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ONE preferred product (Cosentyx, Enbrel, Humira, Stelara, Xeljanz/Xeljanz XR)</td>
</tr>
<tr>
<td>Stelara (ustekinumab)</td>
<td>Taltz (ixekizumab)</td>
<td>Simplicity, Ocrevus, Simpioni (Standard/Performance and Legacy Prescription Drug List plans), Taltz&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for TWO preferred products (Cosentyx, Enbrel, Humira, Stelara, Xeljanz/Xeljanz XR)</td>
</tr>
<tr>
<td>Xeljanz/Xeljanz XR (tacrolimus)</td>
<td><em>Step therapy required&lt;br&gt;Otezla</em> (apremilast)</td>
<td>Simplicity, Ocrevus, Simpioni (Value/Advantage Prescription Drug List plans)&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for FIVE preferred products</td>
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</tbody>
</table>

### Rheumatoid Arthritis

<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred or non-covered Product</th>
<th>Criteria for Use: Rheumatoid Arthritis Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actemra Subcutaneous Injection (tocilizumab)</td>
<td>Cimzia (certolizumab pegol)</td>
<td>Rheumatoid arthritis and documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ONE disease-modifying anti-rheumatic drug (DMARD) (for example, methotrexate, leflunomide, sulfasalazine) AND the following criteria for non-preferred products (by drug/class):</td>
</tr>
<tr>
<td>Enbrel (etanercept)</td>
<td>Kevzara (sarilumab)</td>
<td>Cimzia, Kevzara, Kineret (Standard/Performance and Legacy Prescription Drug List plans), Olumiant, Ocrevus, Simpioni (Standard/Performance and Legacy Prescription Drug List plans)&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for TWO preferred products</td>
</tr>
<tr>
<td>Humira (adalimumab)</td>
<td>Kineret (anakinra)</td>
<td>Kineret (Value/Advantage Prescription Drug List plans)&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for FIVE products* [From Rheumatoid Arthritis Preferred and Non-Preferred Product list]</td>
</tr>
<tr>
<td>Rinvoq (upadacitinib)</td>
<td>Olumiant (baricitinib)</td>
<td>Simpioni (Value/Advantage Prescription Drug List plans)&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ALL preferred products</td>
</tr>
<tr>
<td>Xeljanz/Xeljanz XR (tacrolimus)</td>
<td>Ocrevus Subcutaneous Injection (abatacept)</td>
<td>Simpioni (Value/Advantage Prescription Drug List plans)&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for FIVE products* [From Rheumatoid Arthritis Preferred and Non-Preferred Product list]</td>
</tr>
<tr>
<td></td>
<td>Simponi 50 mg (golimumab)</td>
<td>Simpioni (Value/Advantage Prescription Drug List plans)&lt;br&gt;• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ALL preferred products</td>
</tr>
</tbody>
</table>
### Systemic Juvenile Idiopathic Arthritis (SJIA)

<table>
<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: SJIA Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actemra Subcutaneous Injection (tocilizumab)</td>
<td>Systemic Juvenile Idiopathic Arthritis (SJIA)</td>
</tr>
<tr>
<td>Kineret (anakinra)</td>
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</table>

### Ulcerative Colitis - Adult

<table>
<thead>
<tr>
<th>Preferred Product</th>
<th>Non-Preferred or non-covered Product</th>
<th>Criteria for Use: Ulcerative Colitis – Adult Employer Group Benefit Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humira (adalimumab)</td>
<td>Simponi 100mg (golimumab)</td>
<td>Ulcerative colitis in an adult AND documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for at least ONE conventional therapy: (for example, aminosalicylate, corticosteroids or immunosuppressants) AND the following criteria for the specified products:</td>
</tr>
<tr>
<td>*Step therapy required</td>
<td></td>
<td>Simponi, Xeljanz/Xeljanz XR</td>
</tr>
<tr>
<td>Stelara* (ustekinumab)</td>
<td></td>
<td>• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for Humira</td>
</tr>
<tr>
<td>Xeljanz*/ Xeljanz XR* (tobacitinib)</td>
<td></td>
<td>Stelara</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for Humira</td>
</tr>
<tr>
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<td>When criteria are met, a single intravenous infusion dose of Stelara up to a maximum dose of 520 mg will be authorized. The maintenance dosage of 90 mg subcutaneous will be authorized for 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.</td>
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### Uveitis

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<thead>
<tr>
<th>Product</th>
<th>Criteria for Use: Uveitis Employer Group Benefit Plans</th>
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</thead>
<tbody>
<tr>
<td>Humira (adalimumab)</td>
<td>Uveitis (including intermediate, posterior and panuveitis) AND both of the following:</td>
</tr>
<tr>
<td></td>
<td>• Individual is 2 years of age or older</td>
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<tr>
<td></td>
<td>• Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for conventional therapy (such as corticosteroids or immunosuppressive drugs [for example, azathioprine, cyclosporine, or methotrexate])</td>
</tr>
</tbody>
</table>

Initial and reauthorization is up to 12 months unless otherwise stated.

Xeljanz/Xeljanz XR (tobacitinib) is considered cosmetic and not medically necessary for the treatment of EITHER of the following in any setting. Services that are cosmetic are not covered under most benefit plans.

- Alopecia areata
- Localized or generalized vitiligo

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and
adjusted based upon severity, alternative available treatments, and previous response to Immunomodulators.

Immunomodulators are considered experimental, investigational or unproven for ANY other use including the following:
- Concomitant use with any other biologic including all non-tumor necrosis factor (non-TNF) biologics, anti-TNF biologics, or oral immunomodulatory agents for example, Otezla or Xeljanz/ Xeljanz XR

Anti-Tumor Necrosis Factor (Anti-TNF) Biologics:
- Behcet’s disease
- Granulomatosis with polyangiitis
- Pyoderma gangrenosum
- Enbrel for Crohn’s Disease

Kineret (anakinra):
- Ankylosing spondylitis
- Chronic infantile neurological, cutaneous and articular syndrome, treatment-refractory
- Gout
- Gouty arthritis
- Inflammatory bowel disease arthritis
- Pericarditis
- Reactive arthritis
- Still’s disease (adult)

Otezla (apremilast):
- Ankylosing spondylitis

Xeljanz/Xeljanz XR (tofacitinib)
- Alopecia areata (including persistent patchy, totalis, universalis)
- Plaque psoriasis
- Localized or generalized vitiligo

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

### FDA Approved Indications

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>FDA Approved Indications</th>
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</thead>
<tbody>
<tr>
<td>Actemra</td>
<td><strong>Rheumatoid Arthritis (RA)</strong>&lt;br&gt;Actemra is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).&lt;br&gt;<strong>Giant Cell Arteritis (GCA)</strong>&lt;br&gt;Actemra is indicated for the treatment of giant cell arteritis (GCA) in adult patients.&lt;br&gt;<strong>Polyarticular Juvenile Idiopathic Arthritis (PJIA)</strong>&lt;br&gt;Actemra is indicated for the treatment of active PJIA in patients 2 years of age and older.&lt;br&gt;<strong>Systemic Juvenile Idiopathic Arthritis (SJIA)</strong>&lt;br&gt;Actemra is indicated for the treatment of active SJIA in patients 2 years of age and older.&lt;br&gt;<strong>Cytokine Release Syndrome (CRS)</strong> – <em>intravenous only</em></td>
</tr>
<tr>
<td>Brand Name</td>
<td>FDA Approved Indications</td>
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<tr>
<td><strong>Actemra</strong></td>
<td>Actemra is indicated for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older.</td>
</tr>
</tbody>
</table>
| **Cimzia** | **Crohn’s Disease (CD)**  
Cimzia is indicated for reducing signs and symptoms of Crohn’s disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.  
**Rheumatoid Arthritis (RA)**  
Cimzia is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA).  
**Psoriatic Arthritis (PsA)**  
Cimzia is indicated for the treatment of adult patients with active psoriatic arthritis.  
**Ankylosing Spondylitis (AS)**  
Cimzia is indicated for the treatment of adults with active ankylosing spondylitis.  
**Non-radiographic Axial Spondyloarthritis**  
Cimzia is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation  
**Plaque Psoriasis (PsO)**  
Cimzia is indicated for the treatment of adults with moderate-to-severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy |
| **Cosentyx** | **Plaque Psoriasis**  
Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.  
**Psoriatic Arthritis**  
Cosentyx is indicated for the treatment of adult patients with active psoriatic arthritis.  
**Ankylosing Spondylitis**  
Cosentyx is indicated for the treatment of adult patients with active ankylosing spondylitis. |
| **Enbrel** | **Rheumatoid Arthritis (RA)**  
Enbrel is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid RA. Enbrel can be initiated in combination with methotrexate (MTX) or used alone.  
**Polyarticular Juvenile Idiopathic Arthritis (PJIA)**  
Enbrel is indicated for reducing signs and symptoms of moderately to severely active PJIA in patients ages 2 and older.  
**Psoriatic Arthritis**  
Enbrel is indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis (PsA). Enbrel can be used with or without MTX.  
**Ankylosing Spondylitis**  
Enbrel is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis (AS).  
**Plaque Psoriasis** |

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<table>
<thead>
<tr>
<th>Brand Name</th>
<th>FDA Approved Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enbrel</td>
<td>Indicated for the treatment of patients 4 years or older with chronic moderate to severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy</td>
</tr>
</tbody>
</table>
| Humira     | Rheumatoid Arthritis (RA)  
Used alone or in combination with methotrexate or other disease-modifying anti-rheumatic drugs (DMARDs), to reduce signs and symptoms, including major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active disease.  
Juvenile Idiopathic Arthritis (JIA)  
Reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older. Humira can be used alone or in combination with methotrexate.  
Psoriatic Arthritis  
Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function  
Ankylosing Spondylitis  
Reducing signs and symptoms in patients with active disease  
Crohn’s Disease (CD)  
Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn’s disease who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.  
Pediatric Crohn’s Disease (CD)  
Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active Crohn’s disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate.  
Plaque Psoriasis  
The treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy and when other systemic therapies are medically less appropriate.  
Ulcerative Colitis (UC)  
Inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). The effectiveness of Humira has not been established in patients who have lost response to or were intolerant to TNF blockers.  
Hidradenitis Suppurativa  
The treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older.  
Uveitis  
The treatment of non-infectious intermediate, posterior, and panuveitis in adults and pediatric patients 2 years of age and older. |
| Kevzara    | Rheumatoid Arthritis (RA)  
Kevzara is indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs). |
| Kineret    | Rheumatoid Arthritis (RA)  

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<table>
<thead>
<tr>
<th>Brand Name</th>
<th>FDA Approved Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kineret</td>
<td>is indicated for the reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active RA, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs). Kineret can be used alone or in combination with DMARDs other than Tumor Necrosis Factor (TNF) blocking agents.</td>
</tr>
<tr>
<td><strong>Cryopyrin-Associated Periodic Syndromes (CAPS)</strong></td>
<td>Kineret is indicated for the treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID).</td>
</tr>
<tr>
<td>Orencia</td>
<td>is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. Orencia may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists.</td>
</tr>
<tr>
<td><strong>Juvenile Idiopathic Arthritis</strong></td>
<td>Orencia is indicated for reducing signs and symptoms in patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis. ORENCIA may be used as monotherapy or concomitantly with methotrexate (MTX).</td>
</tr>
<tr>
<td><strong>Adult Psoriatic Arthritis (PsA)</strong></td>
<td>Orencia is indicated for the treatment of adult patients with active psoriatic arthritis (PsA).</td>
</tr>
<tr>
<td><strong>Important Limitations of Use</strong></td>
<td>Orencia should not be administered concomitantly with TNF antagonists. Orencia is not recommended for use concomitantly with other biologic rheumatoid arthritis (RA) therapy, such as anakinra.</td>
</tr>
<tr>
<td>Otezla</td>
<td>is indicated for the treatment of adult patients with active psoriatic arthritis.</td>
</tr>
<tr>
<td><strong>Psoriasis</strong></td>
<td>Otezla is indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.</td>
</tr>
<tr>
<td><strong>Oral Ulcers Associated with Behcet's Disease</strong></td>
<td>Otezla is indicated for the treatment of adult patients with oral ulcers associated with Behcet's Disease</td>
</tr>
<tr>
<td>Rinvoq</td>
<td>Rinvoq (upadacitinib) is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. Limitation of Use: Use of RINVOQ in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine, is not recommended</td>
</tr>
<tr>
<td>Siliq</td>
<td>Plaque Psoriasis</td>
</tr>
<tr>
<td>Simponi</td>
<td>Rheumatoid Arthritis (RA)</td>
</tr>
<tr>
<td></td>
<td>Simponi, in combination with methotrexate, is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis.</td>
</tr>
<tr>
<td></td>
<td>Psoriatic Arthritis (PsA)</td>
</tr>
<tr>
<td>Brand Name</td>
<td>FDA Approved Indications</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Simponi, alone or in combination with methotrexate, is indicated for the treatment of adult patients with active psoriatic arthritis. <strong>Ankylosing Spondylitis (AS)</strong> Simponi is indicated for the treatment of adult patients with active ankylosing spondylitis. <strong>Ulcerative Colitis</strong> Simponi is indicated in adult patients with moderately to severely active ulcerative colitis who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine for: - inducing and maintaining clinical response - improving endoscopic appearance of the mucosa during induction - inducing clinical remission - achieving and sustaining clinical remission in induction responders</td>
<td></td>
</tr>
<tr>
<td>Skyrizi</td>
<td>Skyrizi is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.</td>
</tr>
<tr>
<td>Stelara</td>
<td>Plaque Psoriasis Stelara is indicated for the treatment of adult patients (12 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Psoriatic Arthritis Stelara is indicated for the treatment of adult patients (18 years or older) with active psoriatic arthritis. Stelara can be used alone or in combination with methotrexate (MTX). Crohn’s Disease Stelara is indicated for the treatment of adult patients with moderately to severely active Crohn’s disease who have: • failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed treatment with a tumor necrosis factor (TNF) blocker or • failed or were intolerant to treatment with one or more TNF blockers. Ulcerative Colitis Stelara is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis.</td>
</tr>
<tr>
<td>Taltz</td>
<td>Plaque Psoriasis Taltz is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Psoriatic Arthritis Taltz is indicated for the treatment of adult patients with active psoriatic arthritis.</td>
</tr>
<tr>
<td>Tremfya</td>
<td>Plaque Psoriasis Tremfya is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.</td>
</tr>
<tr>
<td>Xeljanz/ Xeljanz XR</td>
<td>Rheumatoid Arthritis (RA) Xeljanz/Xeljanz XR (tofacitinib) is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. It may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs). Limitations of Use: Use of Xeljanz/Xeljanz XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.</td>
</tr>
</tbody>
</table>
### Psoriatic Arthritis
Xeljanz/Xeljanz XR (tofacitinib) is indicated for the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other disease-modifying antirheumatic drugs (DMARDs).

Limitations of Use: Use of Xeljanz/Xeljanz XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

### Ulcerative Colitis
Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have an inadequate response or who are intolerant to TNF blockers.

Limitations of Use: Use of Xeljanz/Xeljanz XR in combination with biological therapies for UC or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

### Recommended Dosing

<table>
<thead>
<tr>
<th>FDA Recommended Dosing</th>
<th>Actemra</th>
<th>Actemra may be used as monotherapy or concomitantly with methotrexate or other non-biologic DMARDs as an intravenous infusion or as a subcutaneous injection.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rheumatoid Arthritis</strong></td>
<td><strong>Recommended Intravenous (IV) Dosing Regimen:</strong></td>
<td>The recommended dosage of Actemra for adult patients given as a 60-minute single intravenous drip infusion is 4 mg per kg every 4 weeks followed by an increase to 8 mg per kg every 4 weeks based on clinical response. Reduction of dose from 8 mg per kg to 4 mg per kg is recommended for management of certain dose-related laboratory changes including elevated liver enzymes, neutropenia, and thrombocytopenia. Doses exceeding 800 mg per infusion are not recommended in RA patients.</td>
</tr>
<tr>
<td></td>
<td><strong>Recommended Subcutaneous (SQ) Dosing Regimen:</strong></td>
<td>• Patients less than 100 kg weight: 162mg administered subcutaneously every other week, followed by an increase to weekly dosing based on clinical response • Patients at 100 kg weight or greater: 162mg administered subcutaneously every week</td>
</tr>
<tr>
<td><strong>Giant Cell Arteritis</strong></td>
<td><strong>The recommended dose of Actemra for adult patients with GCA is 162 mg given once every week as a subcutaneous injection in combination with a tapering course of glucocorticoids.</strong></td>
<td>A dose of 162 mg given once every other week as a subcutaneous injection in combination with a tapering course of glucocorticoids may be prescribed based on clinical considerations. Actemra can be used alone following discontinuation of glucocorticoids.</td>
</tr>
</tbody>
</table>
- Interruption of dosing may be needed for management of dose-related laboratory abnormalities including elevated liver enzymes, neutropenia, and thrombocytopenia [see Dosage and Administration (2.8)].
- Intravenous administration is not approved for GCA.

### Polyarticular Juvenile Idiopathic Arthritis (PJIA)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommended Intravenous PJIA Dosage Every 4 Weeks</th>
<th>Recommended Subcutaneous PJIA Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients less than 30 kg weight</td>
<td>10 mg per kg</td>
<td>Patients less than 30 kg weight</td>
</tr>
<tr>
<td>Patients at or above 30 kg weight</td>
<td>8 mg per kg</td>
<td>Patients at or above 30 kg weight</td>
</tr>
</tbody>
</table>

### Systemic Juvenile Idiopathic Arthritis (SJIA)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommended Intravenous SJIA Dosage Every 2 Weeks</th>
<th>Recommended Subcutaneous SJIA Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients less than 30 kg weight</td>
<td>12 mg per kg</td>
<td>Patients less than 30 kg weight</td>
</tr>
<tr>
<td>Patients at or above 30 kg weight</td>
<td>8 mg per kg</td>
<td>Patients at or above 30 kg weight</td>
</tr>
</tbody>
</table>

### Cytokine Release Syndrome (CRS)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommended Intravenous CRS Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients less than 30 kg weight</td>
<td>12 mg per kg</td>
</tr>
<tr>
<td>Patients at or above 30 kg weight</td>
<td>8 mg per kg</td>
</tr>
</tbody>
</table>

- If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses of Actemra may be administered. The interval between consecutive doses should be at least 8 hours.
- Doses exceeding 800 mg per infusion are not recommended in CRS patients.
- Subcutaneous administration is not approved for CRS.

### Cimzia

**Crohn’s Disease**
The recommended initial adult dose of is 400 mg (given as two subcutaneous injections of 200 mg) initially, and at weeks 2 and 4. In patients who obtain a clinical response, the recommended maintenance regimen is 400 mg every four weeks.

**Rheumatoid Arthritis**
The recommended dose of for adult patients with rheumatoid arthritis is 400 mg (given as two subcutaneous injections of 200 mg) initially and at weeks 2 and 4, followed by 200 mg every other week. For maintenance dosing, 400 mg every 4 weeks can be considered.

**Psoriatic Arthritis**
The recommended dose of Cimzia for adult patients with psoriatic arthritis is 400 mg (given as 2 subcutaneous injections of 200 mg each) initially and at week 2 and 4, followed by 200 mg every other week. For maintenance dosing, Cimzia 400 mg every 4 weeks can be considered.

**Ankylosing Spondylitis**
The recommended dose of CIMZIA for adult patients with ankylosing spondylitis is 400 mg (given as 2 subcutaneous injections of 200 mg each) initially and at weeks 2 and 4, followed by 200 mg every 2 weeks or 400 mg every 4 weeks.
<table>
<thead>
<tr>
<th>Brand</th>
<th>Condition</th>
<th>FDA Recommended Dosing</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-radiographic Axial</td>
<td>Plaque Psoriasis</td>
<td>The recommended dose of Cimzia for adult patients with non-radiographic axial spondyloarthritis is 400 mg (given as 2 subcutaneous injections of 200 mg each) initially and at weeks 2 and 4, followed by 200 mg every 2 weeks or 400 mg every 4 weeks. For some patients (with body weight of ≤ 90 kg), Cimzia 400 mg (given as 2 subcutaneous injections of 200 mg each) initially and at Weeks 2 and 4, followed by 200 mg every other week can be considered.</td>
<td></td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plaque Psoriasis</td>
<td></td>
<td>The recommended dose of Cimzia for adults with moderate-to-severe plaque psoriasis is 400 mg (given as 2 subcutaneous injections of 200 mg each) every other week. For some patients, a dose of 150 mg may be acceptable.</td>
<td></td>
</tr>
<tr>
<td>Cosentyx</td>
<td>Plaque Psoriasis</td>
<td>The recommended dose is 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks. Each 300 mg dose is given as 2 subcutaneous injections of 150 mg. For some patients, a dose of 150 mg may be acceptable.</td>
<td></td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td></td>
<td>For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosing and administration recommendations for plaque psoriasis. For other psoriatic arthritis patients, administer Cosentyx with or without a loading dosage by subcutaneous injection. The recommended dosage: With a loading dosage is 150 mg at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. Without a loading dosage is 150 mg every 4 weeks. If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg. Cosentyx may be administered with or without methotrexate.</td>
<td></td>
</tr>
<tr>
<td>Ankylosing Spondylitis</td>
<td>Adults for Rheumatoid</td>
<td>Administer Cosentyx with or without a loading dosage by subcutaneous injection. The recommended dosage: With a loading dosage is 150 mg at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. Without a loading dosage is 150 mg every 4 weeks.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arthritis, Psoriatic</td>
<td>Adult Plaque Psoriasis: The recommended starting dose is 50 mg given subcutaneously twice weekly, for three months followed by a reduction to a maintenance dose of 50mg once weekly.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arthritis, and Ankylosing</td>
<td>Pediatric Plaque Psoriasis: 63 kg (138 pounds) or more: Recommended dose is 50mg weekly Less than 63 kg (138 pounds): Recommended dose is 0.8 mg/kg weekly, with a maximum of 50 mg per week To achieve pediatric doses other than 25 mg or 50 mg, use reconstituted Enbrel lyophilized powder. Doses of Enbrel higher than those described above have not been studied in pediatric patients.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spondylitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enbrel</td>
<td>Plaque Psoriasis</td>
<td>The recommended dose is 50 mg per week given as one subcutaneous injection or 25 mg given twice weekly as a subcutaneous injection. Doses higher than 50 mg per week are not recommended.</td>
<td></td>
</tr>
<tr>
<td>Brand</td>
<td>Condition</td>
<td>FDA Recommended Dosing</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Juvenile Idiopathic Arthritis</strong></td>
<td>63 kg (138 pounds) or more: Recommended dose is 50mg weekly</td>
<td>To achieve pediatric doses other than 25 mg or 50 mg, use reconstituted Enbrel lyophilized powder.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Less than 63 kg (138 pounds): Recommended dose is 0.8 mg/kg weekly, with a maximum of 50 mg per week</td>
<td>Doses of Enbrel higher than those described above have not been studied in pediatric patients.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>In JIA patients, glucocorticoids, NSAIDs, or analgesics may be continued during treatment with Enbrel.</td>
<td></td>
</tr>
<tr>
<td><strong>Humira</strong></td>
<td><strong>Adult Patients with Rheumatoid Arthritis, Psoriatic Arthritis, or Ankylosing Spondylitis</strong></td>
<td>40 mg administered every other week as a subcutaneous injection.</td>
<td></td>
</tr>
</tbody>
</table>
| **Juvenile Idiopathic Arthritis or Pediatric Uveitis** | The recommended dose of Humira for patients 2 years of age and older with polyarticular juvenile idiopathic arthritis (JIA) or pediatric uveitis is based on weight as shown below. MTX, glucocorticoids, NSAIDs, and/or analgesics may be continued during treatment with Humira. | Patients (2 years of age and older)  
|                |                                                                            |  
|                | 10 kg (22 lbs) to <15 kg (33 lbs)                                         | 10 mg every other week                                                                                                                                   |
|                | 15 kg (33 lbs) to < 30 kg (66 lbs)                                        | 20 mg every other week                                                                                                                                   |
|                | ≥ 30 kg (66 lbs)                                                          | 40 mg every other week                                                                                                                                   |
|                |                                                                            | Humira has not been studied in patients with polyarticular JIA or pediatric uveitis less than 2 years of age or in patients with a weight below 10 kg. |
| **Crohn's Disease** | The recommended Humira dose regimen for adult patients with Crohn’s disease is 160 mg initially on Day 1 (given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days), followed by 80 mg two weeks later (Day 15). Two weeks later (Day 29) begin a maintenance dose of 40 mg every other week. Aminosalicylates and/or corticosteroids may be continued during treatment. Azathioprine, 6-mercaptopurine (6-MP) or MTX may be continued during treatment with Humira if necessary. The use of Humira in Crohn’s disease beyond one year has not been evaluated in controlled clinical studies. |  |
| **Pediatric Crohn's Disease** | The recommended Humira dose regimen for pediatric patients 6 years of age and older with Crohn’s disease (CD) is based on body weight as shown below for pediatric patients: |  |
|                | 17 kg (37 lbs) to < 40 kg (88 lbs):                                       | • Induction: 80 mg on Day 1 (administered as two 40 mg injections in one day);                                                                         |
|                | • 40 mg two weeks later (on Day 15)                                       | • Maintenance Dose Starting at Week 4 (Day 29): 20 mg every other week                                                                                 |
|                | ≥ 40 kg (88 lbs)                                                          |  |
### Brand | Condition | FDA Recommended Dosing
--- | --- | ---
| **Plaque Psoriasis or Uveitis** | The recommended dose of Humira for adult patients with plaque psoriasis (Ps) or Uveitis (UV) is an initial dose of 80 mg, followed by 40 mg given every other week starting one week after the initial dose. The use of Humira in moderate to severe chronic Ps beyond one year has not been evaluated in controlled clinical studies. |
| **Hidradenitis Suppurativa** | **Body Weight of Adolescent Patients (12 years of age and older)** | **Recommended Dosage Regimen** |
| | 30 kg (66 lbs) to < 60 kg (132 lbs) | • 80 mg initially on Day 1; and |
| | ≥ 60 kg (132 lbs) | • 40 mg on Day 8 and subsequent doses: 40 mg every other week |

### Ulcerative Colitis
The recommended dose regimen for adult patients with ulcerative colitis is 160 mg initially on day 1 (given as four 40 mg injections per day for two consecutive days), followed by 80 mg two weeks later (day 15). Two weeks later (day 29) continue with a dose of 40 mg every other week. Only continue Humira in patients who have shown evidence of clinical remission by eight weeks of therapy. Aminosalicylates and/or corticosteroids may be continued during treatment. Azathioprine and 6-mercaptopurine (6-MP) may be continued during treatment if necessary.

### Kevzara
**Rheumatoid Arthritis**
Kevzara may be used as monotherapy or in combination with methotrexate (MTX) or other conventional DMARDs. The recommended dosage of Kevzara is 200 mg once every two weeks given as a subcutaneous injection. Reduce dose to 150 mg once every two weeks for management of neutropenia, thrombocytopenia and elevated liver enzymes.

### Kineret
**Rheumatoid Arthritis**
The recommended dose of Kineret for the treatment of patients with RA is 100 mg/day administered daily by subcutaneous injection. Higher doses did not result in a higher response. The dose should be administered at approximately the same time every day.

### Cryopyrin-Associated Periodic Syndromes (CAPS)
The recommended starting dose of Kineret is 1-2 mg/kg for NOMID patients. The dose can be individually adjusted to a maximum of 8 mg/kg daily to control active inflammation. Adjust doses in 0.5 to 1.0 mg/kg increments. Once daily administration is generally recommended, but the dose may be split into twice daily administrations.

### Orencia
**Adult Rheumatoid Arthritis (RA)**
For adult patients with RA, Orencia may be administered as an intravenous infusion or as a subcutaneous injection. Orencia may be
used as monotherapy or concomitantly with DMARDs other than TNF antagonists.

**Intravenous Dosing Regimen**

Orencia lyophilized powder should be reconstituted and administered after dilution as a 30-minute intravenous infusion utilizing the weight range based dosing specified in the package insert. Following the initial intravenous administration, an intravenous infusion should be given at 2 and 4 weeks after the first infusion and every 4 weeks thereafter.

**Dose of Orencia for Intravenous Infusion in Adult RA Patients**

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Dose</th>
<th>Number of Vials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 60 kg</td>
<td>500 mg</td>
<td>2</td>
</tr>
<tr>
<td>60 to 100 kg</td>
<td>750 mg</td>
<td>3</td>
</tr>
<tr>
<td>More than 100 kg</td>
<td>1000 mg</td>
<td>4</td>
</tr>
</tbody>
</table>

Each vial provides 250 mg of abatacept for administration.

**Subcutaneous Dosing Regimen**

Orencia 125 mg in prefilled syringes or in Orenica ClickJect autoinjector should be administered by subcutaneous injection once weekly and may be initiated with or without an intravenous loading dose. For patients initiating therapy with an intravenous loading dose, Orencia should be initiated with a single intravenous infusion (as per body weight categories listed in Table 1), followed by the first 125 mg subcutaneous injection administered within a day of the intravenous infusion.

Patients transitioning from Orencia intravenous therapy to subcutaneous administration should administer the first subcutaneous dose instead of the next scheduled intravenous dose.

**Juvenile Idiopathic Arthritis**

For patients with juvenile idiopathic arthritis (JIA), Orencia may be administered as an intravenous infusion (6 years of age and older) or a subcutaneous injection (2 years of age and older). Intravenous dosing has not been studied in patients younger than 6 years of age.

Orencia may be used as monotherapy or concomitantly with methotrexate.

**Intravenous Dosing Regimen**

Orencia should be administered as a 30-minute intravenous infusion based on body weight. Pediatric patients with:
- body weight less than 75 kg should be administered Orencia at a dose of 10 mg/kg
- body weight of 75 kg or more should be administered Orencia following the adult intravenous dosing regimen (see Table 1), not to exceed a maximum dose of 1000 mg.

Following the initial administration, Orencia should be given at 2 and 4 weeks after the first infusion and every 4 weeks thereafter. Any unused portions in the vials must be immediately discarded.
Subcutaneous Dosing Regimen
Orencia for subcutaneous injection should be initiated without an intravenous loading dose and be administered utilizing the weight range-based dosing as specified in Table 2.

<table>
<thead>
<tr>
<th>Body Weight of Patient</th>
<th>Dose (once weekly)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to less than 25 kg</td>
<td>50 mg</td>
</tr>
<tr>
<td>25 to less than 50 kg</td>
<td>87.5 mg</td>
</tr>
<tr>
<td>50 kg or more</td>
<td>125 mg</td>
</tr>
</tbody>
</table>

Dose of Orencia for Subcutaneous Administration in Patients 2 Years of Age or Older with JIA

The safety and efficacy of Orencia ClickJect autoinjector for subcutaneous injection has not been studied in patients under 18 years of age.

Adult Psoriatic Arthritis
For adult patients with psoriatic arthritis, Orencia may be administered as an intravenous infusion (IV) or a subcutaneous (SC) injection. Orencia can be used with or without non-biologic DMARDs.

Intravenous Dosing Regimen
Orencia IV should be administered as a 30-minute intravenous infusion utilizing the weight range-based dosing specified in Table 1. Following the initial intravenous administration, an intravenous infusion should be given at 2 and 4 weeks after the first infusion and every 4 weeks thereafter.

Subcutaneous Dosing Regimen
Orencia SC 125 mg should be administered by subcutaneous injection once weekly without the need for an intravenous loading dose.

Patients switching from Orencia intravenous therapy to subcutaneous administration should administer the first subcutaneous dose instead of the next scheduled intravenous dose.

Dosage Titration Schedule

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
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<th>Day 6 and thereafter</th>
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Psoriatic Arthritis Psoriasis Behcet’s Disease

Rinvoq Rheumatoid Arthritis
The recommended oral dose of Rinvoq is 15 mg once daily with or without food

Rinvoq may be used as monotherapy or in combination with methotrexate or other nonbiologic DMARDs

Siliq Plaque Psoriasis
The recommended Siliq dose is 210 mg administered by subcutaneous injection at Weeks 0, 1, and 2 followed by 210 mg every 2 weeks.

If an adequate response has not been achieved after 12 to 16 weeks of treatment with SILIQ, consider discontinuing therapy. Continued treatment beyond 16 weeks in patients who have not achieved an adequate response is not likely to result in greater success.
<table>
<thead>
<tr>
<th>Brand</th>
<th>Condition</th>
<th>FDA Recommended Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simponi</td>
<td>Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis</td>
<td>The Simponi dose regimen is 50 mg administered by subcutaneous (SC) injection once a month. For patients with rheumatoid arthritis (RA), Simponi should be given in combination with methotrexate. For patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS), Simponi may be given with or without methotrexate or other non-biologic DMARDs. For patients with RA, PsA, or AS, corticosteroids, non-biologic DMARDs, and/or NSAIDs may be continued during treatment with Simponi.</td>
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<td></td>
<td>Ulcerative Colitis</td>
<td>The recommended Simponi induction dosage regimen is a 200 mg subcutaneous injection at week 0, followed by 100 mg at week 2 and then maintenance therapy with 100 mg every 4 weeks.</td>
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<tr>
<td>Skyrizi</td>
<td>Plaque Psoriasis</td>
<td>The recommended dose is 150 mg (two 75 mg injections) administered by subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter.</td>
</tr>
</tbody>
</table>
| Stelara     | Plaque Psoriasis                                                         | • For patients weighing ≤100 kg (220 lbs), the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.  
• For patients weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks. In subjects weighing >100 kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these subjects. |
|             | Psoriatic Arthritis                                                      | The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks. For patients with co-existent moderate-to-severe plaque psoriasis weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.                                                                 |
|             | Crohn's Disease, Ulcerative Colitis                                      | Intravenous Induction Adult Dosage Regimen  
A single intravenous infusion dose of Stelara using the weight-based dosage regimen specified in Table [see Instructions for dilution of Stelara 130 mg vial for intravenous infusion (2.6)].  
Initial Intravenous Dosage of Stelara  
| Body Weight of Patient at time of dosing | Dose   | Number of 130mg/26ml (5mg/ml) Stelara vials |
| 55kg or less | 260mg   | 2                                      |
| More than 55kg to 85kg | 390mg   | 3                                      |
| More than 85 kg   | 520mg   | 4                                      |
### FDA Recommended Dosing

<table>
<thead>
<tr>
<th>Brand</th>
<th>Condition</th>
<th>Recommended Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taltz</td>
<td>Plaque Psoriasis</td>
<td>The recommended dose is 160 mg (two 80 mg injections) at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks.</td>
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<tr>
<td></td>
<td>Psoriatic Arthritis</td>
<td>The recommended dose is 160 mg by subcutaneous injection (two 80 mg injections) at week 0, followed by 80 mg every 4 weeks. For psoriatic arthritis patients with coexistent moderate-to-severe plaque psoriasis, use the dosing regimen for plaque psoriasis. Taltz may be administered alone or in combination with a conventional disease-modifying antirheumatic drug (cDMARD) (e.g., methotrexate).</td>
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<tr>
<td>Tremfya</td>
<td>Plaque Psoriasis</td>
<td>Tremfya is administered by subcutaneous injection. The recommended dose is 100 mg at Week 0, Week 4, and every 8 weeks thereafter.</td>
</tr>
<tr>
<td>Xeljanz/ Xeljanz XR</td>
<td>Rheumaroid Arthritis</td>
<td>Xeljanz/Xeljanz XR may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs). The recommended dose of Xeljanz is 5 mg twice daily and the recommended dose of Xeljanz XR is 11 mg once daily.</td>
</tr>
<tr>
<td></td>
<td>Psoriatic Arthritis</td>
<td>Xeljanz/Xeljanz XR is used in combination with nonbiologic disease modifying antirheumatic drugs (DMARDs) in psoriatic arthritis. The efficacy of Xeljanz/Xeljanz XR as a monotherapy has not been studied in psoriatic arthritis. The recommended dose of Xeljanz is 5 mg twice daily and the recommended dose of Xeljanz XR is 11 mg once daily.</td>
</tr>
<tr>
<td></td>
<td>Ulcerative Colitis</td>
<td>The recommended dose of Xeljanz is 10mg twice daily for at least 8 weeks; then 5 or 10 mg twice daily. Discontinue after 16 weeks of 10 mg twice daily, if adequate therapeutic benefit is not achieved. Use the lowest effective dose to maintain response. The recommended dose of Xeljanz XR for induction is 22 mg once daily for at least 8 weeks; evaluate patients and transition to maintenance therapy depending on therapeutic response. If needed continue 22 mg once daily for a maximum of 16 weeks. Discontinue 22 mg once daily after 16 weeks if adequate therapeutic response is not achieved. The maintenance dose is 11 mg once daily.</td>
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</table>

### Drug Availability

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Drug Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actemra</td>
<td>For intravenous infusion, Actemra is available as single use vials at a concentration of 20mg/ml. Individually packaged, single-use vials are available in the following sizes: 80mg/ 4ml, 200mg/ 10ml and 400mg/ 20ml. For subcutaneous administration, Actemra is available as a single-use, prefilled syringe which provides 162mg/0.9ml.</td>
</tr>
<tr>
<td>Cimzia</td>
<td>Each single-use vial provides approximately 200 mg of Cimzia or a single-use; 1 mL prefilled glass syringe providing 200 mg (1 mL) of Cimzia.</td>
</tr>
<tr>
<td>Cosentyx</td>
<td>Cosentyx for injection is available as 150 mg/mL solution in a single-use Sensoready pen or as 150 mg/mL solution in a single-use prefilled syringe.</td>
</tr>
<tr>
<td>Brand Name</td>
<td>Drug Availability</td>
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<tr>
<td>Enbrel</td>
<td>Each Enbrel single-use prefilled syringe and Enbrel single-use prefilled SureClick autoinjector contains 50 mg/mL of etanercept in a single-dose syringe. Enbrel multiple-use vial is supplied in a carton containing four dose trays. Each dose tray contains one 25 mg vial of etanercept, one diluent syringe (1 mL Sterile Bacteriostatic Water for Injection, USP, containing 0.9% benzyl alcohol)</td>
</tr>
</tbody>
</table>
| Humira     | • Humira Pen Carton 40 mg/0.8 mL  
• Humira Pen 40 mg/0.8 mL Psoriasis Starter Package  
• Prefilled Syringe Carton 40 mg/0.8 mL  
• Prefilled Syringe Carton 40 mg/0.4 mL  
• Prefilled Syringe Carton 20 mg/0.4 mL  
• Prefilled Syringe Carton 10 mg/0.2 mL  
• Humira Prefilled Syringe 40 mg/0.8 mL Pediatric Crohn's Disease Starter Package (6 count)  
• Humira Prefilled Syringe 40 mg/0.8 mL Pediatric Crohn's Disease Starter Package (3 count)  
• Humira is dispensed in a carton containing 4 alcohol preps and 3 dose trays (Pediatric Starter Package). |
| Kevzara    | Kevzara (sarilumab) injection is supplied in a single-dose pre-filled syringe. Strengths: 150mg/1.14mL, 200mg/1.14mL |
| Kineret    | Each prefilled glass syringe contains 0.67 mL (100 mg) of anakinra. Kineret is dispensed in a 4 x 7 syringe dispensing pack containing 28 syringes. Kineret is also dispensed in a 1 x 7 syringe dispensing pack containing 7 syringes. |
| Oencia     | Intravenous Infusion  
For Injection: 250 mg powder in a single-use vial  
Subcutaneous Injection  
Injection: 50 mg/0.4 mL, 87.5 mg/0.7 mL, and 125 mg/mL in a single-dose prefilled glass syringe.  
Injection: 125 mg/mL in a single-dose prefilled ClickJect autoinjector. |
| Oteza      | Otezla is available as 10 mg, 20 mg, and 30 mg tablets. Otezla is packaged as a 2-week starter pack (containing 4 tablets of 10 mg, 4 tablets of 20 mg, 5 tablets of 30 mg with an additional 14 tablets of 30 mg); a 28-count carton (containing 2 blister cards each containing 14 tablets of 30 mg); and bottles of 60 tablets of 30 mg |
| Rinvoq     | Rinvoq 15 mg extended-release tablets for oral administration are purple, biconvex oblong, with dimensions of 14 x 8 mm, and debossed with 'a15' on one side |
| Siliq      | Injection: 210 mg/1.5 mL solution in a single-dose prefilled syringe. |
| Simponi    | Simponi is available as a single dose in a prefilled glass syringe containing 50 mg per 0.5 mL of solution. |
| Skyrizi    | Injection: 75 mg/0.83 mL solution in each single-dose prefilled syringe. |
| Stelara    | Stelara is available in single-use prefilled syringes or single-use vials containing 45 mg/0.5 mL or 90 mg/1 mL of ustekinumab. |
| Taltz      | Taltz is available as: (1) Autoinjector Injection: 80 mg/mL solution of Taltz in a single-dose prefilled autoinjector, (2) Prefilled Syringe Injection: 80 mg/mL solution of Taltz in a single-dose prefilled syringe |
| Tremfya    | Tremfya Injection is supplied as a single-dose 100 mg/mL prefilled syringe |
| Xeljanz/   | Xeljanz is available as 5 mg tablets. Xeljanz XR is available as 11 mg tablets. |
| Xeljanz XR |                                                   |
**General Background**

**Pharmacology**

Abatacept, a selective costimulation modulator, inhibits T cell (T lymphocyte) activation by binding to CD80 and CD86, thereby blocking interaction with CD28. This interaction provides a costimulatory signal necessary for full activation of T lymphocytes. Activated T lymphocytes are implicated in the pathogenesis of RA and PsA and are found in the synovium of patients with RA and PsA.

Anakinra blocks the biologic activity of IL-1 alpha and beta by competitively inhibiting IL-1 binding to the interleukin-1 type I receptor (IL-1RI), which is expressed in a wide variety of tissues and organs.

Anti-TNF agents bind specifically to TNF-alpha and block its interaction with the cell surface TNF receptors. TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. TNF promotes the synthesis of other proinflammatory cytokines, stimulates endothelial cells to express adhesion molecules that attract leukocytes into affected joints, accelerates the production of metalloproteinases, and inhibits the synthesis of cartilage proteoglycans. Increased concentrations of TNF also are found in psoriatic plaques. TNF blockers modulate responses that are induced or regulated by TNF, including expression of adhesion molecules, serum concentrations of matrix metalloproteinase, and serum concentrations of cytokines. Two distinct receptors for TNF (TNFRs), a 55 kilodalton protein (p55) and a 75 kilodalton protein (p75), exist naturally as monomeric molecules on cell surfaces and in soluble forms. Biological activity of TNF is dependent upon binding to either cell surface of TNFR.

Apremilast is an oral phosphodiesterase 4 (PDE4) inhibitor that decreases pro-inflammatory mediators and increases anti-inflammatory mediators.

Brodalumab is a human monoclonal IgG2 antibody that selectively binds to human IL-17RA and inhibits its interactions with cytokines IL-17A, IL-17F, IL-17C, IL-17AF heterodimer and IL-25. IL-17RA is a protein expressed on the cell surface and is a required component of receptor complexes utilized by multiple IL-17 family cytokines. Blocking IL17RA inhibits IL-17 cytokine-induced responses including the release of pro-inflammatory cytokines and chemokines.

Guselkumab is a human monoclonal IgG1λ antibody that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of proinflammatory cytokines and chemokines implicated in the pathogenesis of psoriasis.

Ixekizumab is a humanized IgG4 monoclonal antibody that selectively binds with the interleukin 17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Ixekizumab inhibits the release of proinflammatory cytokines and chemokines.

Sarilumab binds soluble IL-6 receptors (sIL-6R) and membrane-bound IL-6 receptors (mIL-6R), inhibiting IL-6 mediated signaling. This in turn reduces T-cell activation and other inflammatory effects associated with synovial proliferation and joint destruction in patients with RA.

Secukinumab is a recombinant human monoclonal IgG1/k antibody that binds specifically to IL-17A. It is expressed in a recombinant Chinese Hamster Ovary (CHO) cell line.

Tocilizumab binds specifically to both soluble and membrane-bound IL-6 receptors (sIL-6R and mIL-6R), and has been shown to inhibit IL-6-mediated signaling through these receptors. IL-6 is a pleiotropic pro-inflammatory cytokine produced by a variety of cell types including T- and B-cells, lymphocytes, monocytes and fibroblasts. IL-6 has been shown to be involved in diverse physiological processes such as T-cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis, and stimulation of hematopoietic precursor cell proliferation and differentiation. IL-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis.
Tofacitinib inhibits Janus kinase (JAK) enzymes. These enzymes play roles in cytokine and growth factor signaling in humans thereby affecting hematopoiesis and immune cell function. The JAK enzymes block the phosphorylation and thus activation of transcription and signal transducers. Because of this inhibition, some intracellular activity (e.g., gene expression) does not occur. Tofacitinib displays functional selectivity for JAK1 and 3 more than JAK2. (Yazici, 2011; Zerbini, 2012) However, the relevance of this selectivity to efficacy is unknown.

Upadacitinib is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Upadacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs.

Ustekinumab is an immunoglobulin G1-kappa monoclonal antibody specific to the p40 subunits of IL-12 and IL-23. Ustekinumab binds to IL-12 and IL-23 preventing them from activating IL-12R-beta1 receptors on various immune and inflammatory cells. Specific effects of this binding include preventing natural killer cell and IL-17 activation, reducing interferon-gamma production, and reducing CD4+ T-cell differentiation and activation.

Professional Societies/Organizations

**Ankylosing Spondylitis**

**Assessment in SpondyloArthritis International Society (ASAS)/EULAR**

The Assessment in SpondyloArthritis International Society (ASAS)/EULAR published guidelines for the treatment of Ankylosing Spondylitis. These guidelines recommends for axial spondyloarthritis that NSAIDs be used first-line, and for selected patients that glucocorticoids and sulfasalazine are appropriate. Guidelines further state that biologics be considered in patients with high disease activity despite the use of conventional treatments, with the current practice being a TNF inhibitor. If the TNF inhibitor fails, the guidelines recommend switching to another TNF inhibitor or an IL-17 antagonist could be considered (van der Heijde 2017).

**American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritids**

The 2015 recommendations state that in active Ankylosing Spondylitis, NSAIDS are strongly recommended over no treatment (evidence: low quality). In adults with active Ankylosing Spondylitis despite treatment with an NSAID, treatment with TNF inhibitor is strongly recommended over no treatment with TNF inhibitor (evidence: moderate quality). No particular TNF inhibitor is preferred, except for patients with concomitant inflammatory bowel disease or recurrent iritis (evidence: moderate quality). Panel stated in patients with Ankylosing Spondylitis and inflammatory bowel disease or frequently recurrent iritis that treatment with infliximab or adalimumab should be preferred over etanercept. In active nonradiographic axial spondyloarthritis despite treatment with NSAIDs, the guidelines recommend treatment with TNF inhibitors over no treatment with TNF inhibitors (evidence: moderate quality). Guidelines do not address interleukin therapy. (Ward, 2016)

**Crohn’s Disease**

**American College of Gastroenterology (ACG) Clinical Guideline: Management of Crohn’s Disease in Adults**

Recommendations for immunomodulatory therapies are as follows:

**Moderate to severe disease/moderate to high risk disease**

- Infliximab, adalimumab, or certolizumab pegol are recommended in those who have not responded to treatment with a corticosteroid or an immunosuppressive agent

- Use of infliximab concomitantly with an immunomodulator is more efficacious than monotherapy with either agent in individuals naïve to these medications
• Vedolizumab with or without use of an immunomodulator should be considered for induction of remission in individuals with moderately to severely active Crohn’s disease with evidence of active disease
• Natalizumab should be a consideration for induction of symptomatic response and remission in active Crohn’s disease
• Natalizumab should be used to maintain natalizumab-induced remission of Crohn’s disease only if antibodies are negative to John Cunningham (JC) virus
• Ustekinumab should be used in individuals with moderate to severe Crohn’s disease who have not responded to corticosteroids, thiopurines, methotrexate or anti-TNF inhibitors, or who are anti-TNF naïve

Severe/fulminant disease
• Infliximab, adalimumab, and certolizumab pegol may be used to treat severely active Crohn’s disease
• Infliximab may be used to treat fulminant Crohn’s disease

Perianal/fistulizing disease
• Infliximab should be considered for treatment of perianal fistulas in Crohn’s disease
• Infliximab should be a consideration for treatment of enterocutaneous and rectovaginal fisulas in Crohn’s disease
• Adalimumab and certolizumab pegol should be a consideration to treat perianal fistulas in Crohn’s disease

Maintenance Therapy of Luminal Crohn’s Disease
• Anti-TNF therapy should be used for maintenance therapy of anti-TNF induced remission (specifically Infliximab, adalimumab and certolizumab pegol)
• Although monotherapy with anti-TNFs is efficacious in maintaining anti-TNF induced remissions, consideration should be given to concomitant use with azathioprine/6-mercaptopurine or methotrexate due to the risk for immunogenicity and loss of response
• Vedolizumab therapy should be utilized to maintain vedolizumab-induced remissions of Crohn’s disease
• Natalizumab therapy should be a consideration for maintenance of natalizumab-induced of remissions in Crohn’s disease if John Cunningham (JC) virus is negative
• Ustekinumab therapy should be used to maintain ustekinumab-induced remissions of Crohn’s disease (Lichtenstein, 2018)

American Gastroenterological Association (AGA) Guideline on the Use of Thiopurines, Methotrexate, and Anti–TNF-α Biologic Drugs for the Induction and Maintenance of Remission in Inflammatory Crohn’s Disease
The AGA provides recommendations for the induction and maintenance of remission in inflammatory Crohn’s disease. Specifically addressing biologic therapy, the recommendations are as follows:

Induction of Remission in patients with moderately to severely active Crohn’s disease:
• Anti-TNF biologics are recommended.
• If monotherapy is utilized, anti-TNF biologics are preferred over thiopurine monotherapy.
• If combination therapy is utilized, anti-TNF biologics combined with thiopurines is the suggested regimen.

Maintenance of Remission
• It is recommended to use an anti-TNF biologic to maintain remission which was induced by corticosteroids or an anti-TNF biologic.
• The AGA is neutral regarding use of combination therapy of an anti-TNF biologic plus a thiopurine compared to either class alone to maintain remission which was achieved by use of a combination of these classes. (Terdiman, 2013)

European Evidence-based Consensus (ECCO) on the Diagnosis and Management of Crohn’s Disease
The third ECCO evidence based consensus group stated guidelines were, in part, revisited in order to recognize the Crohn’s Disease indication for vedolizumab along with its clinical data. Several recommendations were provided by the ECCO guidelines on the use of vedolizumab in the treatment of Crohn’s Disease. They are as follows:

- Moderately active localised ileocaecal Crohn’s disease: Treat with budesonide or with systemic corticosteroids; Anti-TNFs could be used as an alternative for those patients that are steroid-refractory or intolerant; In patients refractory to steroids or Anti-TNFs, vedolizumab is an alternative (Gomollón, 2017)
- Active colonic Crohn’s Disease: Treat with systemic corticosteroids; Anti-TNFs is appropriate in those who have relapsed; In patients refractory to steroids or Anti-TNFs, vedolizumab is an alternative (Gomollón, 2017)

If remission has been achieved with the combination then maintenance with the same regimen is recommended. Therefore, maintenance treatment with vedolizumab is appropriate in patients achieving remission with vedolizumab. (Gomollón, 2017)

**Hidradentitis Suppurativa**

European guidelines for hidradenitis suppurative and acne inversa suggest surgery or laser procedures for locally recurring lesions. In cases where lesions are more widespread, treatment options include medical monotherapy or in combination with more radical surgery. Medical therapies mentioned include antibiotics (clindamycin plus rifampicine, tetracycles), acitretin and biologics (adalimumab, infliximab). (Zouboulis, 2014)

In a randomized, double-blind, placebo-controlled, crossover trial of 38 individuals, infliximab (5 mg/kg on weeks 0, 2, and 6) was compared to placebo infusions. An open-label phase followed, where individuals in the infliximab arm had maintenance infusions of infliximab at weeks 14 and 22, while the individuals in the placebo arm were allowed the option to receive infliximab to receive infliximab per the same treatment protocol. Evaluation at week 8 did not demonstrate a significant difference between the infliximab and placebo arms for the primary endpoint of a greater than or equal to 50 percent decrease in an unvalidated disease severity score. Patient quality of life, pain and physician global assessments did demonstrate statistically significant improvements in the infliximab group. (Grant, 2010).

**Juvenile Idiopathic Arthritis**

American College of Rheumatology (ACR) 2013 Update of the 2011 Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications (Ringold, 2013)

Systemic JIA Treatment Recommendations:

**Initial treatment in patients with the following: active systemic features and varying degrees of synovitis**

- Systemic monotherapy with a glucocorticoid (either oral or intravenous) is recommended for a maximum of two weeks for patients with an MD global < 5 and Active Joint Count > 4 and for all patients with an physician global assessment (MD) ≥ 5 irrespective of the Active Joint Count.
- Initiating monotherapy with an NSAID in a patient without prior treatment is recommended as an option for patients with an MD global < 5 irrespective of the Active Joint Count.

**Treatment in patients with active systemic features and varying degrees of synovitis, with continued disease activity**

- Glucocorticoid monotherapy is recommended as a treatment option after failure of NSAID monotherapy for patients with an MD global < 5 and Active Joint Count > 0 and for patients with an MD global ≥ 5 (irrespective of the Active Joint Count).
- Intraarticular glucocorticoid injection is recommended as adjunct therapy at any time.
- Methotrexate (or leflunomide) is recommended for patients with an MD global < 5 and Active Joint Count > 0 after treatment with the following: glucocorticoid monotherapy, tocilizumab, or an IL-1 inhibitor. Methotrexate (or leflunomide) is recommended for patients with an MD global ≥ 5 and Active Joint Count > 0 (only after a trial of an IL-1 inhibitor or tocilizumab).
- Initiation with a TNF inhibitor is recommended for patients with Active Joint Count > 4 that is irrespective of the MD global after a trial of an IL-1 inhibitor or tocilizumab.
• Initiation with a TNF inhibitor is recommended for patients with Active Joint Count > 0 irrespective of the MD global after a trial of both an IL-1 inhibitor and tocilizumab sequentially.
• The use of a TNF inhibitor for patients with an MD global <5 and Active Joint Count = 0 is inappropriate, with the following exception: in patients who had tried both an IL-1 inhibitor and tocilizumab sequentially or a DMARD plus either an IL-1 inhibitor or tocilizumab (in which case it is uncertain).
• The use of a TNF inhibitor for patients with an MD global ≥ 5 and Active Joint Count = 0 is inappropriate, with the following exception: in patients who had tried an IL-1 inhibitor or tocilizumab (in which case it is uncertain).

Initial treatment in patients without active systemic features and varying degrees of synovitis
• Intraarticular glucocorticoid injection is recommended as an initial treatment in patients with Active Joint Count ≤ 4.
• Initiation of methotrexate (or leflunomide) is recommended in patients with Active Joint Count > 4.
• Initiation of NSAID monotherapy in patients without prior treatment for a maximum of one month is recommended as a treatment approach for patients with Active Joint Count > 0. Note: Continuing NSAID monotherapy for longer than two months for patients with continued disease activity is inappropriate.

Treatment in patients without active systemic features and varying degrees of synovitis, with continued disease activity
• The use of methotrexate (or leflunomide) is recommended as a treatment option for Active Joint Count > 0 following treatment with the following: intraarticular injection, NSAID monotherapy, an IL-1 inhibitor, or tocilizumab.
• Initiation of a TNF inhibitor is recommended in patients with Active Joint Count > 0 after treatment with the following: methotrexate (or leflunomide), anakinra, or tocilizumab.
• When continued disease activity is present after DMARD and NSAID use, the following are options when continued therapy is required: Abatacept, Anakinra, TNF inhibitor, Tocilizumab

Initial treatment in patients with features concerning for MAS (macrophage activation syndrome)
• The use of systemic glucocorticoid monotherapy (administered by either oral or IV) is also recommended as a therapeutic option for patients with features concerning for MAS.

NOMID
There are no published guidelines for the treatment of NOMID.

Psoriasis and Psoriatic Arthritis
American Academy of Dermatology (AAD)
The AAD updated their 2008 published guidelines for the care and treatment of psoriasis and psoriatic arthritis in July 2011. Psoriasis severity is defined by both the extent of body surface area (BSA) involvement (<5% considered mild, > 5% but <10% moderate, and > 10% severe), and the involvement of the hands, feet, facial, or genital regions. The majority of psoriasis patients have involvement defined as less than 5% BSA and can effectively treated with topical agents. Psoriasis patients who are candidates for ultra-violet based or systemic therapy (which include oral and biologic agents) have more significant disease, defined as affecting more than 5% of the BSA, or may have less than 5% BSA affected but have psoriasis in vulnerable areas such as the face, genitals, hands and feet (palmoplantar disease), scalp, or intertriginous areas and have disease that adversely affects their quality of life.

Despite the introduction of current and future biologic agents, topical medications, phototherapy, photochemotherapy, and traditional systemic drugs continue to play an essential role in the therapeutic armamentarium of psoriasis. Topical therapies are the mainstay for mild disease either as monotherapy or combination therapy, and are also commonly used in conjunction with phototherapy, traditional systemic agents, or biologic agents for moderate to severe disease. Phototherapy, photochemotherapy, and traditional systemic agents are generally used for individuals with moderate or severe disease and in situations in which topical therapy is ineffective or otherwise contraindicated. Phototherapy and photochemotherapy are effective and economical without many of the potential toxicities of traditional and biologic systemic therapies. However, inconvenience, lack of availability, and reimbursement issues do limit their feasibility, with home ultraviolet (UV) phototherapy an attractive alternative for the appropriate patient. In general, traditional systemic agents
(methotrexate [MTX], acitretin, cyclosporine, and others) have been available far longer than biologics (MTX was approved for psoriasis in 1971), with short- and long-term toxicity profiles that are well known from clinical practice in spite of the absence of formal long-term studies in patients with psoriasis. Traditional systemic agents are given orally (MTX may also be given by injection) and are also less expensive than injectable biologic agents. Biologic agents, including adalimumab, etanercept, and infliximab, are routinely used for moderate to severe psoriasis when one or more traditional systemic agents fail to produce an adequate response, are not tolerated because of adverse effects, or are unsuitable because of the presence of comorbidities.

For patients with moderate to severe PsA, MTX, TNF-alfa blockade, or the combination of these therapies is considered first-line treatment. However, it is appropriate to initiate MTX treatment for patients with moderate to severe PsA who have no contraindications to MTX therapy. If after 12 to 16 weeks of MTX therapy with appropriate dose escalation there is minimal improvement in the signs and symptoms of PsA, it is very appropriate to either add or switch to a TNF-alfa inhibitor, with all of the TNF-alfa inhibitors approved for PsA (adalimumab, etanercept, golimumab, and infliximab) being equally reasonable choices. Because of the lack of sufficient data, however, it is difficult for the clinician to make definitive recommendations regarding the proper sequence or duration of therapies that should be used to treat patients with moderate to severe PsA.

(Menter, 2008; Menter, 2009[a]; Menter, 2009[b]; Menter, 2010; Menter, 2011)

European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update

Refer to guidelines for Strength of Evidence details.

EULAR recommendations for treatment in Psoriatic Arthritis patients

- NSAIDs may be used to relieve musculoskeletal signs and symptoms (Strength of Evidence: 1b, A).
- In active disease (particularly including the following: numerous swollen joints, structural damage in the presence of inflammation, high erythrocyte sedimentation rate/C-reactive protein and/or clinically relevant extraarticular manifestations), treatment with DMARDs (methotrexate, sulfasalazine, or leflunomide) should be considered (Strength of Evidence: 1b, B) at an early stage (Strength of Evidence: 3, B), with MTX given priority for patients with skin involvement (Strength of Evidence: 1b, B).
- Local corticosteroid injections should be considered as adjunctive therapy (Strength of Evidence: 3b, C); systemic glucocorticoids may be used with caution at the lowest effective dose (Strength of Evidence: 4, C)
- In patients with an inadequate response to at least one synthetic DMARD, therapy with a biologic, which is usually a TNF inhibitor, should be started (Strength of Evidence: 1b, B).
- In patients with peripheral arthritis and an inadequate response to at least one synthetic DMARD, in whom TNF inhibitors are not appropriate (for example, demyelinating disease), biologic DMARDs targeting IL12/23 or IL17 pathways may be considered (Strength of Evidence: 1b, B)
- In patients with peripheral arthritis and an inadequate response to at least on synthetic DMARD, in whom biologic DMARDs are not appropriate, a targeted synthetic DMARD such as a PDE-4 inhibitor may be considered (Strength of Evidence: 1b, B)
- In patients with active enthesitis or dactylitis and insufficient response to either NSAIDs or corticosteroid injections, biologics should be considered. The current practice being the use of a TNF inhibitor (Strength of Evidence: 1b, B).
- In patients with predominantly axial disease which is active and has insufficient NSAID response, a biologic should be considered. The current practice being the use a TNF inhibitor (Strength of Evidence: 1b, B).
- In patients who have failed to respond to biologics, switching to another biologic should be considered. This includes switching between TNF inhibitors (Strength of Evidence: 1b, B). (Gossec, 2016; Ramiro, 2016)

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) provides recommendations for the treatment of Plaque Psoriasis which includes the following: topical therapies, phototherapy, DMARDs, antiTNFs, IL-12/23 inhibitors, IL-17 inhibitors, and PDE-4 inhibitors. The GRAPPA recommendations for Psoriatic Arthritis vary based on the domain which is involved: peripheral arthritis, axial disease, enthesitis, dactylitis, skin, and nails. (Coates, 2016)

Treatment for psoriatic arthritis is based on peripheral or axial disease and prior therapies. Recommendations include DMARDs, NSAIDs, simple analgesics, antiTNFs, IL-12/23 inhibitors, or PDE-4 inhibitors. (Coates, 2016)
Treatment for nail disease in psoriatic arthritis is based on data from the psoriasis clinical studies. For mild disease, treatment options could include topical agents, corticosteroid injections or nonbiologic DMARDs. For moderate to severe nail psoriasis disease, GRAPPA recommends antiTNFs agents based on available data. In addition, GRAPPA further recommends that ustekinumab and IL-17 inhibitors should be considered alternative biologic therapy to antiTNFs. (Coates, 2016)

Rheumatoid Arthritis

American College of Rheumatology (ACR) 2015 Guideline for the Treatment of Rheumatoid Arthritis

In the ACR guidelines, anti–tumor necrosis factor (anti-TNF) biologics include the following: Cimzia (certolizumab), Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab), and Simponi (golimumab). Non-TNF biologics include the following: Actemra (tocilizumab), Ocrevus (abatacept), and Rituxan (rituximab). DMARD agents include the following: methotrexate, leflunomide, sulfasalazine, and hydroxychloroquine (excludes azathioprine, cyclosporine, minocycline, and gold).

Early disease recommendations (defined as less than 6 months)

For patients with low disease activity and in those who have not taken a DMARD, the guidelines recommend to use DMARD monotherapy (Methotrexate preferred) over double therapy or triple therapy (Recommendation: strong; Level of evidence: Low). If the disease activity remains moderate or high despite monotherapy with a DMARD, use combination DMARDs or use a TNF inhibitor or a non-TNF inhibitor biologic (all options are with or without methotrexate and given in no preference order) rather than continuing monotherapy with a DMARD (Recommendation: strong; Level of evidence: Low). If the disease activity remains moderate or high despite DMARDs, the guidelines suggest use of monotherapy with a TNF inhibitor over monotherapy with tofacitinib (Level of evidence: Low) or use a TNF inhibitor with methotrexate over tofacitinib with methotrexate (Level of evidence: Low).

Established disease recommendations (defined as greater than 6 months)

For patients with low disease activity and those who have not taken a DMARD, the guideline recommends use of monotherapy with a DMARD (methotrexate preferred) over a TNF inhibitor (Recommendation: Strong; Level of evidence: Low). If the disease activity remains moderate or high despite monotherapy with a DMARD, use combination traditional DMARDs or add a TNF inhibitor or a non-TNF inhibitor biologic (all options are with or without methotrexate and given in no preference order) rather than continuing monotherapy with a DMARD (Recommendation: Strong; Level of evidence: Moderate to very low). If the disease activity remains moderate or high despite TNF inhibitor in patients who are not currently on a DMARD, add one or two DMARDs to a TNF inhibitor rather than continuing monotherapy with a TNF inhibitor (Level of evidence: High).

Conditional recommendations for established RA disease:

- If the disease activity remains moderate/high despite the use of non-TNF biologic, use another non-TNF biologic (with or without methotrexate) over tofacitinib (with or without methotrexate) (Level of evidence: Very low).
- If the disease activity remains moderate/high despite use of multiple (defined as 2+) sequential TNF inhibitors, use tofacitinib (with or without methotrexate) over another TNF inhibitor (with or without methotrexate) if the use of a non-TNF biologic is not a treatment option (Level of evidence: Low).
- If the disease activity remains moderate/high despite use of a TNF inhibitor and at least one non-TNF biologic, the guideline recommends to first use another non-TNF biologic (with or without methotrexate) over tofacitinib or use tofacitinib (with or without methotrexate) over another TNF inhibitor agent (Level of evidence: Very low).

Recommendations for specific high-risk conditions:

- Congestive Heart Failure (CHF): ACR guidelines recommend using combination DMARDs or a non-TNF biologic agent or tofacitinib over TNF inhibitors (conditional recommendation; Level of evidence: Moderate to very low). If there is CHF worsening on a current TNF inhibitor, ACR recommends use of a combination DMARD or non-TNF biologic or tofacitinib over another TNF inhibitor (conditional recommendation; Level of evidence: Very low).
• Previously treated lymphoproliferative disorder: ACR guidelines recommend using rituximab over TNF inhibitor (Recommendation: Strong; Level of evidence: Very low) or use combination DMARD or abatacept or tocilizumab over TNF inhibitor (conditional recommendation; Level of evidence: Very low).
• Previous serious infection: ACR guidelines recommend using combination DMARD over TNF inhibitor or use abatacept over TNF inhibitor (conditional recommendation; Level of evidence: Very low).

(Singh, 2016)

European League Against Rheumatism (EULAR): Management Of Rheumatoid Arthritis With Synthetic And Biological Disease-Modifying Antirheumatic Drugs: 2013 Update
This EULAR guideline recommends that methotrexate should be used as part of a first treatment strategy in active rheumatoid arthritis and, if methotrexate is contraindicated/not tolerated, treatment with sulfasalazine or leflunomide should be considered. In patients with inadequate response to methotrexate and/or other conventional synthetic DMARDs, biologic DMARDs (TNF inhibitors, abatacept or tocilizumab) should be started with methotrexate. The guideline states that if the patients fails the first biologic DMARD, consider treatment with another biologic DMARD; if the first TNF inhibitor therapy has failed, the patient may receive another TNF inhibitor or a biological agent that has different mechanism of action. (Smolen, 2014)

European League Against Rheumatism: The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation
Considerations for Pregnancy:
• Biologic DMARDs (such as the following: rituximab, anakinra, tocilizumab, abatacept, and ustekinumab) have limited documentation on safe use in pregnancy. Therefore, should be replaced before conception by other medication. They should be used during pregnancy only when there are no other pregnancy compatible drug that can effectively control maternal disease (Grade of recommendation: D).
• Continuation of TNF inhibitors during the first part of pregnancy should be considered among the biologic DMARDs. Two agents, etanercept and certolizumab, may be considered for use throughout pregnancy due to low rate of transplacental passage (Grade of recommendation: B).

Considerations for Lactation:
• Biologic DMARDs with no data on breast feeding (such as the following: rituximab, anakinra, ustekinumab, tocilizumab, and abatacept) should be avoided during lactation if other therapy is available to control the disease. Lactation should not be discouraged when using these agents, if no other options are available, based on the pharmacological properties of biologic DMARDs. (Götestam Skorpen, 2016)
• For infliximab, adalimumab, etanercept, and certolizumab, there has been shown a low transfer to breast milk. The continuation of TNF inhibitors should be considered as compatible with breast feeding (Grade of recommendation: D). (Götestam Skorpen, 2016)

Systemic Juvenile Idiopathic Arthritis (SJIA)
American College of Rheumatology (ACR): 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis
In 2013, the ACR updated their 2011 guidelines for the treatment of Juvenile Idiopathic arthritis, of which sJIA is a subtype. Kineret is recommended for initial treatment of SJIA with features concerning macrophage activation syndrome (MAS). Kineret also has a place in the treatment of SJIA patients with and without active systemic features and varying degrees of synovitis in patients who have continued disease activity.

Kineret is recommended within the guideline in the following situations (not inclusive): (1) Kineret is recommended for initial treatment of SJIA with features concerning macrophage activation syndrome (MAS). Kineret also has a place in the treatment of SJIA patients with and without active systemic features and varying degrees of synovitis in patients who have continued disease activity. (2) Anakinra was recommended as one initial therapeutic option for patients with an MD global > 5 irrespective of the AJC, or an MD global < 5 and an AJC > 0 (level C). (3) Anakinra was recommended for patients with continued disease activity after treatment with GC monotherapy (level A) or NSAID monotherapy (level C). (4) Anakinra was recommended as a therapeutic option for patients with an AJC > 4 following failed intraarticular injection or NSAID monotherapy (level B). Use of anakinra was also recommended for patients with an AJC > 0 following treatment with MTX or leflunomide (level B).
Ulcerative Colitis
American College of Gastroenterology (ACG) Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee

ACG guidelines for ulcerative colitis recommend the use of infliximab for all forms of the disease. These guidelines were developed prior to approval of adalimumab and golimumab for the disease. Goals of treatment are induction and maintenance of remission of symptoms to provide an improved quality of life, reduction in need for long-term corticosteroids, and minimization of cancer risk. (Kornbluth, 2010) The recommendations are as follows:

Management of Mild-Moderate Distal Colitis:
- First-line therapy includes aminosalicylates, topical mesalamine, or topical steroids (topical mesalamine agents are superior to topical steroids or oral aminosalicylates) where combination oral and topical aminosalicylates are more effective than either alone
- Patients refractory to oral aminosalicylates or topical corticosteroids may find mesalamine enemas or suppositories effective
- Patients refractory to all of the above agents in maximal doses or those systemically ill may require treatment with oral prednisone in doses up to 40–60 mg per day or infliximab with an induction regimen of 5 mg/kg at weeks 0, 2, and 6

Maintenance of Remission in Distal Disease:
- Mesalamine enemas and compounds, sulfasalazine, and balsalazide are effective (combination oral and topical mesalamine is more effective than either one alone)
- Thiopurines (6-mercaptopurine [6-MP] or azathioprine) and infliximab, but not corticosteroids, are effective when all the other treatments fail

Mild-Moderate Extensive Colitis: Active Disease:
- Oral sulfasalazine or an aminosalicylate
- Oral steroids for those refractory to oral aminosalicylates in combination with topical therapy or symptoms that demand rapid improvement
- 6-MP and azathioprine when there is no response to oral steroids
- Infliximab for patients who are steroid refractory or steroid dependent despite adequate doses of a thiopurine or who are intolerant of these medications

Mild-Moderate Extensive Colitis: Maintenance of Remission:
- Sulfasalazine, olsalazine, mesalamine, and balsalazide are all effective in reducing relapses
- Azathioprine or 6-MP may be useful as steroid-sparing agents for steroid-dependent patients and for maintenance of remission not adequately sustained by aminosalicylates
- Infliximab is effective in maintaining improvement and remission in the patients responding to the infliximab induction regimen

Management of Severe Colitis:
- Infliximab 5 mg/kg if urgent hospitalization is not necessary and patient is refractory to maximal oral prednisone, oral aminosalicylate drugs, and topical medications
- Infliximab may be effective in avoiding colectomy in patients failing IV steroids (long-term efficacy unknown in this setting) (Kornbluth, 2010)

Biosimilars
According to the FDA, a biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product. There may be minor differences in clinically inactive components of the product. (FDA, 2017)

In the ACR guidelines for treatment of Crohn’s disease, the organization states that biosimilar forms of infliximab and adalimumab effectively treat moderate to severe Crohn’s disease and may be used in both initial induction and maintenance phases of treatment. Furthermore, the guideline mentions the current lack of evidence
supporting the safety and efficacy of changing from one biosimilar to another of the same biosimilar molecule in individuals who have stable disease and are in maintenance phase (Lichtenstein, 2018). According to The Task Force on the Use of Biosimilars to Treat Rheumatological Disorders, participation by prescribers and patients is important in the decision to switch between biosimilars (Kay, 2018).

Clinical Efficacy

**Ankylosing Spondylitis (reactive arthritis and undifferentiated spondyloarthropathy)**

Reactive arthritis is an inflammatory arthropathy which happens in response to several characteristic infections; with typical involvement including peripheral oligoarticular arthritis generally prominent in the lower extremities and usually accompanied by sacroiliitis. Undifferentiated arthritis is used to describe inflammatory arthritides which do not belong into any known category. These patients usually have rheumatoid factor negative mono or oligoarthritis that resembles Reactive Arthritis, however it is absent of an infection. (Meador, 2002). A few case series exist for adalimumab, etanercept, and infliximab in Reactive Arthritis patients. (Flagg, 2005, Meyer 2011) Their use is supported by their effectiveness in the treatment of other spondyloarthopathies, including axial and peripheral SpA and the various forms of psoriatic arthritis. (Yu, 2016)

**Crohn’s Disease**

Van Assche et al published results of a prospective, randomized switch trial. The trial evaluated the effect of switching to adalimumab in patients with Crohn’s disease controlled by maintenance infliximab. The results stated that elective switching of a Crohn’s disease patient from infliximab to adalimumab is associated with the loss of efficacy and tolerance within one year. The data suggests that patients who have achieved a sustained response with infliximab should be maintained on infliximab and not switched to an alternative anti TNF agent because switching in this situation is associated with worse clinical outcomes. (Van Assche, 2012)

Singh et al (2014) and Hazlewood et al (2015) published the results of two network meta-analysis providing comparative efficacy data of biologic therapy in biologic-naïve Crohn disease patients. The results stated that infliximab and adalimumab but not certolizumab were more likely to induce remission. However, in the absence of head to head trials comparing these agents, the confidence of these results are low and future comparative studies are needed.

**Plaque Psoriasis**

**Clinical Efficacy: Comparative Trials**

**Stelara versus Enbrel**

The ACCEPT trial was a 64 week, Phase 3, multicenter, randomized controlled trial in 903 patients comparing Enbrel and Stelara in patients with plaque psoriasis for greater than or equal to six months. The treatment interventions were (1) Stelara 45 mg SC at weeks 0 and 4, (2) Stelara 90 mg at SC weeks 0 and 4, and Enbrel 50 mg SC twice weekly for 12 weeks. Patients in the Enbrel treatment group that did not have a response at week 12 received 90 mg of Stelara at week 16 and week 20; while those patients who did not respond to Stelara received one additional dose. In this study, a higher proportion of patients with plaque psoriasis achieved PASI 75 at week 12 with Stelara 45 mg (67.5%) and Stelara 90 mg (73.8%) compared to Enbrel 50 mg (56.8%; P=0.01 versus Stelara 45 mg; P < 0.001 versus Stelara 90 mg). In this trial, therapy with Enbrel was associated with a greater risk of erythema at the injection site (14.7% vs 0.7% of all ustekinumab patients) (Griffiths, 2010).

**Cosentyx versus Enbrel**

The FIXTURE study by Langley was a 52 week, Phase 3, multicenter, double blind, placebo controlled, randomized controlled trial comparing Cosentyx versus Enbrel in 1,306 patients with moderate to severe plaque psoriasis. The treatment interventions were (1) Cosentyx 300 mg at weeks 0, 1, 2, 3 and 4, then every 4 weeks, (2) Cosentyx 150 mg at weeks 0, 1, 2, 3 and 4, then every 4 weeks, (3) Enbrel 50 mg twice weekly for 12 weeks then 50 mg once weekly, and (4) placebo. The proportion of patients achieving PASI 75 was 62.5% Cosentyx 300 mg, 51.1% with Cosentyx 150 mg, 44% with Enbrel, and 4.9% with placebo. The rate of serious adverse events was low and comparable in active treatment groups and placebo. (Langley, 2014)

**Cosentyx versus Stelara**

The CLEAR study (n=676) was a head to head trial that compared secukinumab 300 mg to ustekinumab 45 mg or 90 mg based on body weight. The primary endpoint was the proportion of patients achieving PASI 90 at week...
16. PASI 90 was achieved in 79% of patients in the secukinumab group and 57.6% in the ustekinumab group. The study’s other endpoints also favored secukinumab over ustekinumab, including the following: PASI 75, PASI 100, investigator’s global assessment (IGA) 0 or 1. The endpoints were assessed at weeks 4, 12, and 16. (Thaçi et al 2015)

Siliq versus Stelara
AMAGINE-2 and AMAGINE-3 were Phase 3, double blind, randomized controlled trials and compared brodalumab 210 mg, brodalumab 140 mg, ustekinumab, and placebo (Lebwohl 2015). The dosing schedule was as follows: brodalumab at weeks 0, 1, and 2, followed by every 2 weeks through week 10; ustekinumab given in weight-based doses per its FDA-approved labeling. For both of these studies, primary endpoints included a comparison of brodalumab 210 mg vs ustekinumab for the proportion of patients achieving PASI 100 at week 12. For AMAGINE-2, the proportion of patients achieving PASI 75 was 86% for brodalumab 210 mg, 67% brodalumab 140 mg, 70% for ustekinumab, and 8% for placebo. The proportion of patients achieving PGA success was 79% brodalumab 210 mg, 58% brodalumab 140 mg, 61% ustekinumab, and 4% placebo. The proportion of patients achieving PASI 100 was 44% brodalumab 210 mg, 26% brodalumab 140 mg, 22% ustekinumab, and 1% placebo, respectively. (Lebwohl 2015) For AMAGINE-3, the proportion of patients achieving PASI 75 was 85% brodalumab 210 mg, 69% brodalumab 140 mg, 69% ustekinumab, and 6% placebo. The proportion of patients achieving PGA success was 80% brodalumab 210, 60% brodalumab 140 mg, 57% ustekinumab, and 4% placebo. The proportion of patients achieving PASI 100 in AMAGINE -3 was 37% brodalumab 210 mg, 27% brodalumab 140 mg, 19% ustekinumab, and 0.3% placebo. (Lebwohl 2015)

Taltz versus Enbrel
The UNCOVER trials was a Phase 3, double blind, placebo control, multicenter, randomized controlled trial in 1,224 patients with moderate to severe plaque psoriasis. The treatment interventions were (1) Taltz 160 mg SC starting dose followed by 80 mg SC every 2 weeks, (2) Taltz 160 mg SC starting dose followed by 80 mg SC every 4 weeks, and Enbrel 50 mg SC twice weekly. After 12 weeks for UNCOVER-2, Taltz responders (patients achieving PGA 0 or 1) were re-randomized to receive Taltz every 4 weeks, Taltz every 12 weeks, or placebo for 48 weeks. There was two primary endpoints (1) the proportion of patients achieving PASI 75 and (2) the proportion of patients achieving a PGA 0 or 1 at week 12. The proportions of patients achieving PASI 75 were 89.7% in the Taltz every 2 week group, 77.5% in the Taltz every 4 week group, 41.6% for Enbrel, and 2.4% for placebo (P<0.0001 for all active treatments vs placebo and for both ixekizumab arms vs etanercept). The proportions of patients achieving PGA 0 or 1 were 83.2% in the Taltz every 2 week group, 72.9% in the Taltz every 4 week group, 36% for Enbrel, and 2.4% for placebo (P<0.0001 for all active treatments vs placebo and for both ixekizumab arms vs etanercept). Rates of serious adverse events and discontinuations due to adverse events were comparable across study groups, and no deaths were recorded. For UNCOVER-3, the PASI 75 at week 12 were 87.3% for Taltz (2 week), 84.2% for Taltz (4 weeks) and 53.4% for Enbrel (p < 0.0001 for all active treatments vs. placebo and for both Taltz arms vs. Enbrel). (Griffiths, 2015)

Taltz versus Stelara
The IXORA-S study (N = 676) directly compared ixekizumab (160 mg LD, then 80 mg every 2 weeks for 12 weeks, then 80 mg every 4 weeks) to ustekinumab (45 mg or 90 mg weight-based dosing per label). The primary endpoint results demonstrated the PASI 90 response at week 12 was achieved by 72.8% of individuals in the ixekizumab arm and 42.2% of patients in the ustekinumab arm (p < 0.001). Ixekizumab’s superior efficacy was maintained through week 24. In addition, response rates for PASI 75, PASI 100, and PGA 0 or 1 also favored ixekizumab over ustekinumab (adjusted p < 0.05). (Reich, 2017 [b]).

Tremfya versus Humira
Individuals in the VOYAGE 1 and 2 studies were randomized to receive Tremfya (100 mg at weeks 0,4, then every 8 weeks), Humira (80 mg at week 0, 40 mg at week 1, then every 2 weeks) or placebo. Studied endpoints included the proportion of patients achieving an IGA (investigator’s global assessment) of 0 or 1 at week 16 and the proportion of individuals who attained PASI 90 at week 16. Evaluations between Tremfya and Humira were studied as secondary endpoints at the 16, 24 an 48 week time points. These studies yielded data of up to 48 weeks of favorable efficacy data with Tremfya. (Baluvent, 2017; Reich 2017). Additional studies are necessary to evaluate and confirm the long-term safety and efficacy information of Tremfya.

Demyelinating disorders

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In a review of demyelinating disorders secondary to tumor necrosis factor (TNF)-inhibitor use in psoriasis, the incidence in clinical trials was found to be exceedingly rare. For example, of 6990 individuals who received etanercept there was a single reported case of multiple sclerosis. There are a few case reports, outside of clinical trials, of incidents of demyelinating disorders secondary to use of tumor necrosis factor-inhibitors. The authors state that TNF-inhibitors are not recommended when there is a history of a demyelinating disorder. (Zhu, 2016)

Drug labels approved by the FDA for the TNF-inhibitors include language to exercise caution in individuals with preexisting or recent-onset of demyelinating disorders and to consider discontinuation if any demyelinating disorder occurs.

**Nail and Scalp Psoriasis**

**Clinical Efficacy**

A Phase 3, double blind, randomized, placebo controlled study evaluated the efficacy of Humira in 217 adult patients with moderate to severe fingernail psoriasis and moderate to severe chronic plaque psoriasis. Subjects had to have chronic plaque psoriasis of at least moderate severity on the Physician Global Assessment scale, fingernail involvement of at least moderate severity on a 5-point Physician's Global Assessment of Fingernail Psoriasis scale (PGA-F), a Modified Nail Psoriasis Severity Index score (mNAPSI) for the target nail of greater than or equal to 8, and either a Body Surface Area (BSA) involvement of at least 10% or a BSA involvement of at least 5% with a total mNAPSI score for all fingernails of greater than or equal to 20. Subjects were given an initial dose of Humira 80mg followed by 40mg every other week or placebo for 26 weeks followed by open label Humira for 26 additional weeks. The purpose of the study was to evaluate the percent of subjects who achieved an assessment of clear or minimal with at least a two grade improvement on the PGA-F scale and the percent who achieved improvement at week 26 of at least a 75% from baseline in the mNAPSI score. The study found a higher percent for Humira than in the placebo group achieved the PGA-F endpoint at week 26. (Humira PI, 2017)

In the apremilast trials ESTEEM 1 and ESTEEM 2, 66.1% and 64.7% had nail psoriasis and 66.7% and 65.5% had moderate to very severe scalp psoriasis at baseline, respectively. At week 16, the Nail Psoriasis Severity Index (NAPSI) score demonstrated greater improvement with apremilast treatment compared to placebo. In addition, apremilast demonstrated greater NAPSI-50 response, which is defined as a 50% reduction from baseline in target nail NAPSI score. In addition, the Scalp Physician Global Assessment response was greater with apremilast compared to placebo. Over 52 weeks, improvements in outcomes were generally maintained in patients who experienced a PASI response at week 32 in the study. (Rich, 2016)

**Rheumatoid Arthritis**

**Clinical Efficacy: Comparative Trials**

**TNF versus non-TNF Biologic**

A 52 week multicenter, pragmatic, open-label randomized clinical trial evaluated non–TNF targeted biologic agent versus a second Anti-TNF to treat Rheumatoid Arthritis in patients with an insufficient response to a first Anti-TNF agent. Patients were randomly assigned 1:1 to receive a non-TNF or an anti-TNF that was different from the previous treatment. The non-TNF could be: (1) abatacept: 500 to 1000 mg IV, dosed according to the patient’s weight, every 14 days until week 4 and once monthly thereafter, (2) Rituximab: 1 g infusion IV followed by another 2 weeks later, (3) tocilizumab: 8mg/kg monthly IV. The Anti-TNF (that differed from their initial treatment) could be: (1) adalimumab: 40 mg SQ every 14 days, (2) certolizumab: 400 mg SQ every 14 days until week 4, then 200mg every 14 day, (3) Etanercept: 50 mg SQ every 7 days, (4) infliximab: 3 mg/kg IV initially (with the possibility of ascending doses at weeks 2 and 6 and every 8 weeks thereafter). At week 24, 69% in the non-TNF group and 52% in the second anti-TNF group achieved a EULAR response which was defined as “good” or “moderate”. The authors concluded that in patients with rheumatoid arthritis that were previously treated with anti-TNFs but with an inadequate primary response, non-TNFs were more effective in achieving a good or moderate disease activity response at 24 weeks than was the 2nd anti-TNF. (Gottenberg, 2016)

**Cimzia versus Humira**

The EXXELERATE study examined Cimzia versus Humira in rheumatoid arthritis. This study was a 104-week, randomized, single-blind (double-blind until week 12 and then investigator blind after), parallel-group, head-to-head superiority study. Treatment interventions included Cimzia 400 mg weeks 0, 2, and 4, then 200 mg once every 2 weeks plus MTX or Humira 40 mg once every 2 weeks plus MTX. The results demonstrated no
significant difference between Cimzia and Humira in combination with MTX in either short-term (12-week) or long-term (2-year) efficacy. Over 2 years, the safety profile was comparable (including serious and opportunistic infections). The authors noted the importance of the ability to make a clinical decision at week 12 and by doing this one can maximize the potential benefit of a TNF inhibitor for a specific patient. This approach allows early identification of an inadequate responder that might benefit from utilizing treatment of a difference mechanism of action. (Smolen, 2016)

Humira versus Actemra
The ADACTA study was a double blind, multicenter, Phase 4, randomized control trial that examined Actemra 8 mg/kg IV every 4 weeks plus placebo SQ every 2 weeks versus Humira 40 mg SQ every 2 weeks plus placebo IV every 4 weeks in patients with severe asthma who could not take methotrexate. Results demonstrated that patients in the Actemra group had a significantly greater improvement in DAS28 at week 24 then patients in the Humira group; the change in DAS28 from baseline to week 24 for Actemra was -3.3 versus Humira -1.8 (95% CI, -1.8 to -1.1; p < 0.0001). Incidences of adverse events were similar in the Actemra and Humira group (Actemra: 82.1% versus Humira 82.7%). (Gabay, 2013)

Orencia versus Humira
The AMPLE study by Schiff et al was a multicenter, investigator blind, randomized controlled trial examining Orencia (125 mg SQ once weekly) directly compared to Humira (40 mg SQ every other week) in RA patients with an inadequate response to methotrexate. The proportions achieving ACR 20 responses were comparable between the Orencia and Humira treatment groups after two years (59.7 and 60.1%, respectively; difference 1.8%; 95% CI, -5.6 to 9.2%). (Schiff, 2014)

Other Covered Uses

Anakinra: SJIA
The efficacy of Kineret in patients with systemic-onset juvenile idiopathic arthritis (SJIA) was evaluated in the multi-center, randomized, double-blind placebo controlled ANAJIS trial. The primary endpoint was to evaluate the efficacy of a one month treatment with anakinra (at a dose 2 mg/kg SQ daily, maximum: 100 mg) compared to placebo between two groups. Each group had 12 patients with SJIA. Response was defined as a 30% improvement of the pediatric American College of Rheumatology (ACR) criteria for JIA, resolution of systemic symptoms and a decrease of at least 50% of both C-reactive protein and erythrocyte sedimentation rate when compared to baseline values. After month 1, patients taking placebo were switched to treatment with anakinra. At month 1, 8 out of 12 responders were receiving anakinra treatment and 1 responder receiving placebo. 10 patients from the placebo group switched to anakinra and nine were responders at month 2. Between month 1 and month 2, 6 patients discontinued treatment due to an adverse event (n=2), lack of efficacy (n=2) or because of a disease flare (n=2). (Quartier, 2011)

Etanercept: Graft versus Host Disease
First and Second Line Systemic Treatment of Acute Graft versus Host Disease: Recommendations of the American Society of Blood and Marrow Transplantation
The guidelines recommend that the use of 6-methylprednisolone or prednisone alone is the standard of care for initial treatment of acute Graft-versus-Host Disease. From studies combining the use of other immunosuppressive agents combined with glucocorticoid therapy, survival and response data do not support this approach as standard of care. The guideline further states for second line therapy that the evaluation of six month survival estimates does not support the choice of any specific agent. The guidelines lists as second line option include (not all inclusive): etanercept, daclizumab plus etanercept, daclizumab plus infliximab, daclizumab plus etanercept plus horse antithymocyte globulin. Furthermore, results provide no evidence that any specific agent should be avoided for secondary therapy of Graft versus Host Disease. There are few prospective comparative studies that have been conducted to determine the efficacy and safety of second line therapy for Graft versus Host Disease. The guideline states that this leads clinicians to rely on reports of retrospective studies and single arm phase II studies to evaluate the benefits of treatment; and further states the comparison between these studies is complicated due to the lack of standardized endpoints and due to the small numbers of patients within the studies. (Martin, 2012)

Diagnosis and management of acute Graft Versus Host Disease from the British Society of Hematology Guidelines and British Society of Blood and Marrow Transplant
The management of Grade I Graft versus Host Disease should include topical therapy and optimized calcineurin inhibitors levels without the need for additional systemic immunosuppression.

For the first line treatment of Grade II through IV disease, systemic corticosteroids are recommended for first line therapy for Grade II through IV Graft versus Host Disease. For second line treatment, the following agents are suggested for use in the second line treatment of steroid-refractory acute Graft versus Host Disease: anti-tumor necrosis factor alpha antibodies, extracorporeal photopheresis, mammalian target of rapamycin inhibitors, mycophenolate mofetil, interleukin-2 receptor antibodies. Lastly, for third line treatment, the following agents are suggested in acute steroid-refractory Graft versus Host Disease as third line agent: alemtuzumab, pentostatin, mesenchymal stem cells and methotrexate. (Dignan, 2012)

**Experimental, Investigational, Unproven Uses**

**Adalimumab**
There are case reports for the treatment of pyoderma gangrenosum using adalimumab. At this time, however, there is insufficient published data in terms of safety and efficacy to support its use for this indication.

**Anakinra**
Treatment of Recurrent Idiopathic Pericarditis, AIRTRIP, was a double blind, placebo controlled, multicenter, randomized withdrawal trial conducted among 21 corticosteroid dependent patients. During the six month treatment phase, pericarditis recurrence was observed in 18% in the Kineret group and 90% of the placebo group. The authors stated that in this preliminary study in patients with recurrent pericarditis with colchicine resistance and corticosteroid dependence, the use of Kineret reduced the risk of recurrence over a median of 14 months compared to placebo. Additional studies are needed to further evaluate efficacy as well as to examine safety. (Brucato, 2016)

Anakinra has also been studied for use in adult Still's disease, ankylosing spondylitis, gout, gouty arthritis, inflammatory bowel disease arthritis, and reactive arthritis. At this time, however, there is insufficient published data in terms of safety and efficacy to support its use in these indications.

**Apremilast**
Apremilast has been studied for use in ankylosing spondylitis. At this time, however, there is insufficient published data in terms of safety and efficacy to support its use for this indication.

**Etanercept**
Melikoglu et al conducted a randomized trial (N=40) in patients in Behcet's disease, in order to determine the effect of etanercept on the pathergy and monosodium urate status and on the mucocutaneous and articular manifestations of patients with Behcet's disease. Results demonstrated there were no decreases in the pathergy and monosodium urate responses in the etanercept group compared to the placebo group at any time. However, mean numbers of oral ulcers, nodular lesions, and papulopustular lesions were less with etanercept compared to placebo at all weekly evaluations (except for papulopustular lesions in the second week). (Melikoglu, 2005)

Etanercept has been studied in individuals with moderate to severe Crohn's disease. Patients received subcutaneous etanercept 25 mg or placebo twice weekly. In the primary outcome, at week 4, 39% of patients taking etanercept had a clinical response as compared with 45% with placebo. Findings demonstrated that etanercept at the dose studied was not effective for the treatment of patients with moderate to severe Crohn's disease. (Sandborn, 2001)

Wegener's Granulomatosis Etanercept Trial (WGET) Research Group evaluated etanercept plus standard therapy for Wegener's granulomatosis. The primary outcome was sustained remission which was defined in this study as a Birmingham Vasculitis Activity Score for Wegener's Granulomatosis of zero for at least six months. Patients did receive glucocorticoids plus cyclophosphamide or methotrexate in addition to active treatment or placebo. There were no significant differences between the etanercept and control groups in the rates of sustained remission, sustained periods of low-level disease activity, or the time required to achieve those measures. The research group determined that etanercept is not effective for the maintenance of remission in patients with Wegener's granulomatosis. (WGET, 2005)
There are case reports for the treatment of pyoderma gangrenosum using etanercept. At this time, however, there is insufficient published data in terms of safety and efficacy to support its use for this indication.

**Tocilizumab**

There is insufficient evidence in the peer-reviewed published scientific literature to support safety and efficacy of tocilizumab in uveitis.

**Tofacitinib**

Therapies for alopecia areata (AA) are addressed in the British Association of Dermatologists’ guidelines for the management of alopecia areata. According to the guidelines, mild forms of alopecia areata have high rates of spontaneous remission, which makes evaluation of treatment difficult. In the severe form of the condition, there are low spontaneous remission rates, and these individuals often do not respond to any type of treatment. The organization states that there many case studies of treatments, but overall, there is a lack of randomized controlled trials (the exception being contact immunotherapy) and publications demonstrating long-term outcomes. Despite reports of various therapies which can promote hair growth in alopecia areata, none are capable of modifying the long-term course of the condition. The guidelines further state that use of anti-tumor necrosis factor (anti TNF) drugs are ineffective, and cites a number of reports where alopecia areata has happened in individuals receiving these drugs for other diseases. (Messenger, 2012)

Tofacitinib was studied retrospectively in 90 individuals with AA and at least 40% loss of scalp hair. The primary endpoint was the percent change in the Severity of Alopecia Tool (SALT) score. Prospective responders to treatment were described as individuals with alopecia totalis or alopecia universalis with a duration of current disease of 10 years or less, or alopecia areata. Seventy-seven percent of the prospective responders had a clinical response, with 58% of the individuals reaching a greater than 50% change in SALT score over 4-18 month duration of treatment. Those with the highest percentage in SALT score change tended to be those with AA, compared to those with alopecia totalis or alopecia universalis. Limitations of the study include retrospective data, small sample size and no control group. The authors state that although efficacy was seen for AA in the short-term, there is no long term data and randomized controlled trials are needed. (Liu, 2017a)

There are reports of anti-TNF drugs being used in a topical formulation, however, these drugs are not FDA approved for topical application. (Iorizzo, 2018; Luzhou, 2014)

A small case series of 10 individuals with vitiligo were treated with JAK inhibitors. Five subjects achieved some repigmentation at sites of either sunlight exposure or low dose nbUVB light. The authors stated that JAK monotherapy does not seem to be effective, but appears to need concurrent nbUVB phototherapy or sunlight exposure. The authors concluded that prospective clinical trials are necessary to evaluate the use of JAK inhibitors in vitiligo. This study was limited by small sample size, retrospective design and no control group. (Liu, 2017b)

In a review of JAK inhibitor use in dermatology found the strongest evidence for the use of these drugs is in treating psoriasis. The authors reference data regarding the potential efficacy of these drugs in alopecia areata and vitiligo but further study is necessary, particularly head to head studies of the JAK inhibitors compared to current standard therapies. (Ciechanowicz, 2018)

In October 2015, the manufacturer of tofacitinib received a Complete Response Letter from the FDA denying its supplemental New Drug Application (sNDA) for treatment of adults with moderate to severe chronic plaque psoriasis.

The use of tofacitinib was evaluated in adults with moderate-to-severe active Crohn’s disease (Crohn’s Disease Activity Score [CDAI] of 220-450). The primary endpoint was clinical response at 4 weeks (defined as a reduction in CDAI score of at least 70 points from baseline). Results demonstrated There was not a significant difference between any of the tofacitinib dose groups and placebo in clinical response. In addition, a secondary endpoint of clinical remission (defined as a CDAI score of less than 150 at 4 weeks) was not significantly different between the treatment groups and placebo. (Sandborn, 2014)
Coding/ Billing Information

Note: Oral and subcutaneous immunomodulators are typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions.

Tildrakizumab-asmn (Ilumya) and ustekinumab intravenous (Stelara) require medical drug coding and are listed as follows:

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J3245</td>
<td>Injection, tildrakizumab, 1 mg</td>
</tr>
<tr>
<td>J3358</td>
<td>Ustekinumab, for intravenous injection, 1 mg</td>
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References


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64. Sanofi-Aventis U.S. Kevzara (sarilumab) [product information]. Bridgewater NJ: Sanofi-Aventis; April 2018.


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