**OVERVIEW**

Ankylosing Spondylitis (AS) is an inflammatory condition that usually involves the spine. Unlike rheumatoid arthritis (RA), oral DMARDs (methotrexate, leflunomide, etc) have not been effective in the treatment of AS. NSAIDs (ibuprofen, naproxen, etc) and physical therapy are first-line treatment. In patients who are symptomatic despite NSAID treatment, treatment with TNF biologics are recommended. This review will examine the treatment guidelines of AS, the currently available AS drug products, and their coverage criteria.

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Generic Name (Brand Name)</th>
<th>Available Strengths</th>
<th>Fml Limits</th>
<th>Cost/ Month</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biologics</strong></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Adalimumab (Humira, Humira CF)</td>
<td>20mg/0.4ml, 40mg/0.8ml</td>
<td>PA; PL; SP</td>
<td>$5,371.99</td>
<td>Reserved for treatment failure to 2 NSAIDs tried within the last 30-60 days.</td>
</tr>
<tr>
<td></td>
<td>Etanercept (Enbrel)</td>
<td>50mg/ml, 25mg/ml</td>
<td>PA; PL; SP</td>
<td>$4,948.98</td>
<td>Reserved for treatment failure to 2 NSAIDs tried within the last 30-60 days.</td>
</tr>
<tr>
<td></td>
<td>Infliximab-dyyb (Inflectra) Infliximab-abda (Renilex)</td>
<td>100mg IV vial</td>
<td>PA; PL; SP</td>
<td>--</td>
<td>Reserved for treatment failure to 2 NSAIDs tried within the last 30-60 days.</td>
</tr>
<tr>
<td></td>
<td>Infliximab (Remicade)</td>
<td>100mg IV vial</td>
<td>NF</td>
<td>--</td>
<td>Non-Formulary</td>
</tr>
<tr>
<td></td>
<td>Golimumab (Simponi)</td>
<td>50mg/0.5ml, 100mg/ml</td>
<td>PA; PL; SP</td>
<td>$4,610.15</td>
<td>Reserved for treatment failure to either Adalimumab, Etanercept, or Infliximab.</td>
</tr>
<tr>
<td></td>
<td>Certolizumab (Cimzia)</td>
<td>200mg/ml</td>
<td>PA; PL; SP</td>
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<td>Reserved for treatment failure to either Adalimumab, Etanercept, or Infliximab.</td>
</tr>
<tr>
<td></td>
<td>Secukinumab (Cosentyx)</td>
<td>150mg/ml</td>
<td>PA; PL; SP</td>
<td>$5,261.11</td>
<td>Reserve for treatment failure to two 1st line agents OR one 1st line agent and one 2nd line agent</td>
</tr>
</tbody>
</table>

PL = Prescriber Limit, (Must be prescribed by Rheumatologist); PA = Prior Authorization Required; NF = Non-Formulary; SP = Specialty
**EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION**

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

### Biologics

**1st line—Adalimumab (Humira, Humira CF), Etanercept (Enbrel), Infliximab (Inflectra, Renflexis)**

- **Coverage Criteria:** Reserved for documented symptomatic AS despite treatment with NSAIDs (unless NSAID-intolerant). An adequate trial is defined as at least 2 different NSAIDs tried over 1 month or 2 different NSAIDs over 2 months.
- **Limits:** None
- **Required Information for Approval:** Prescription history showing at least 2 NSAIDs tried.
- **Other Notes:** Medication is to be dispensed by HPSJ’s designated specialty pharmacy. Must be initiated by a rheumatologist. Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.
- **Non Formulary:** Remicade

**2nd line—Certolizumab (Cimzia), Golimumab (Simponi)**

- **Coverage Criteria:** Reserved for treatment failure to Adalimumab, Etanercept, or Infliximab.
- **Limits:** None
- **Required Information for Approval:** Prescription history showing at least 3 month trial of one first line agent (Adalimumab, Etanercept, or Infliximab).
- **Other Notes:** Medication is to be dispensed by HPSJ’s designated specialty pharmacy. Must be initiated by a rheumatologist. Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.

**3rd line—Secukinumab (Cosentyx)**

- **Coverage Criteria:** Reserved for treatment failure/documented intolerance to two 1st line agents (adalimumab, etanercept, infliximab) OR one 1st line agent (adalimumab, etanercept, infliximab) and one 2nd line agent (certolizumab, golimumab). Must be prescribed by rheumatologist.
- **Limits:** None
- **Required Information for Approval:** Prescription history showing at least 3 month trial of [1] adalimumab, etanercept, or infliximab AND/OR [2] certolizumab or golimumab.
- **Other Notes:** Medication is to be dispensed by HPSJ’s designated specialty pharmacy. Must be initiated by a rheumatologist. Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.
**CLINICAL JUSTIFICATION**

The goals of treatment are to reduce symptoms to maintain body function and quality of life. The 2015 American College of Rheumatology (ACR)/Spondylitis Association of America (SAA)/Spondyloarthritis Research and Treatment Network (SRTN) Guidelines recommends the following:

**Active AS**
- NSAIDs and physical therapy are first-line treatment.
  - The guidelines define "adequate trial" as "lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete responses to at least 2 different NSAIDs over 2 months."
- In patients who are symptomatic despite NSAID treatment, treatment with TNF biologics are recommended.
  - There is insufficient evidence to favor one TNF biologic over another. However, experts agreed that in patients with AS and inflammatory bowel disease, infliximab or adalimumab is preferred over etanercept due to lower rates of iritis.
  - For patients with active AS despite treatment with TNF biologic, the guidelines recommend switching to another TNF biologic (as opposed to adding a DMARD).
- Methotrexate and Leflunomide have shown to have minimal benefit and are associated with side effects. The benefits did not outweigh the risks and, therefore, are generally not recommended.
  - Sulfasalazine was shown to have a small benefit on pain relief and may be an option for patients who cannot use TNF biologics.
  - DMARDs are preferred over non-TNF biologics (abatacept, tocilizumab, ustekinumab, etc) due to questionable efficacy and study bias.
- Systemic glucocorticoids are not recommended due to lack of strong safety and efficacy data.

**Stable AS**
- Patients with stable AS or on stable treatment regimen, experts recommend using NSAIDs on an as-needed basis.
- Patients with stable AS receiving both a TNF biologic and NSAIDs or a TNF biologic with DMARDs, may consider discontinuing the NSAID or DMARD and continuing on TNF biologic as monotherapy.

The efficacy between TNF biologics do not differ significantly but the cost may vary due to differences in administration frequency (twice monthly vs. weekly vs. monthly, and so forth). Therefore, HPSJ’s order of preference of the biologic therapies are based on the cost-benefit ratio where the first-line biologics are agents associated with the lowest cost-benefit ratio.
REFERENCES


**REVIEW & EDIT HISTORY**

<table>
<thead>
<tr>
<th>Document Changes</th>
<th>Reference</th>
<th>Date</th>
<th>P&amp;T Chairman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creation of Policy</td>
<td>Biological Response Modifiers Review 2-19-08.doc</td>
<td>2/2008</td>
<td>Allen Shek, PharmD</td>
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<tr>
<td>Updated Policy</td>
<td>Biologic Response Modifiers 2010 final.doc</td>
<td>5/2010</td>
<td>Allen Shek, PharmD</td>
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<tr>
<td>Updated Policy</td>
<td>TNF MUE summary 2-21-2012.doc</td>
<td>2/2012</td>
<td>Allen Shek, PharmD</td>
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<tr>
<td>Updated Policy</td>
<td>Psoriatic Arthritis &amp; Ankylosing Spondylitis.doc</td>
<td>10/2014</td>
<td>Jonathan Szkotak, PharmD</td>
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<td>Updated Policy</td>
<td>Class Review- Biologics, Apremilast, and Tofacitinib in Inflammatory Joint, Skin, and Bowel Diseases.doc</td>
<td>2/2016</td>
<td>Johnathan Yeh, PharmD</td>
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<tr>
<td>Updated Policy</td>
<td>Class Review- Biologics, Apremilast, and Tofacitinib in Inflammatory Joint, Skin, and Bowel Diseases.doc</td>
<td>02/2017</td>
<td>Johnathan Yeh, PharmD</td>
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<tr>
<td>Updated Policy</td>
<td>HPSJ Coverage Policy – Rheumatology – Ankylosing Spondylitis 2018-02.doc</td>
<td>02/2018</td>
<td>Johnathan Yeh, PharmD</td>
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<tr>
<td>Updated Policy</td>
<td>HPSJ Coverage Policy – Rheum &amp; Immuno – Ankylosing Spondylitis 2019-05.doc</td>
<td>05/2019</td>
<td>Matthew Garrett, PharmD</td>
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</tbody>
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*Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy*