MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Ankylosing Spondylitis (AS)	**P&T DATE:**	2/15/2018
CLASS:	Rheumatology/Anti-inflammatory Disorders	**REVIEW HISTORY** (*month/year*)	2/17, 2/16, 10/14, 2/12, 5/10, 2/08
LOB:	Medi-Cal		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Ankylosing Spondylitis (AS) is an inflammatory condition that usually involves the spine.[1] 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.

Available Ankylosing Spondylitis Agents *(Current as of 1/2018)*

Formulary Agents					
Therapeutic Class	**Generic Name (Brand Name)**	**Available Strengths**	**Fml Limits**	**Cost/ Month***	**Notes**
Biologics	Adalimumab (Humira)	20mg/0.4ml, 40mg/0.8ml	PA; PL; SP	$5,846.46	Reserved for treatment failure to 2 NSAIDs tried within the last 30-60 days.
	Etanercept (Enbrel)	50mg/ml, 25mg/ml,	PA; PL; SP	$5,846.40	Reserved for treatment failure to 2 NSAIDs tried within the last 30-60 days.
	Infliximab-dyyb (Inflectra) Infliximab-abda (Renflexis)	100mg IV vial	PA; PL; SP	--	Reserved for treatment failure to 2 NSAIDs tried within the last 30-60 days.
	Infliximab (Remicade)	100mg IV vial	NF	$5605.52	Non-Formulary
	Golimumab (Simponi)	50mg/0.5ml, 100mg/ml	PA; PL; SP	$4853.18 $14,559.55	Reserved for treatment failure to either Adalimumab, Etanercept, or Infliximab.
	Certolizumab (Cimzia)	200mg/ml	PA; PL; SP	$5423.71	Reserved for treatment failure to either Adalimumab, Etanercept, or Infliximab.
	Secukinumab (Cosentyx)	150mg/ml	PA; PL; SP	$5,654.86	Reserve for treatment failure to two 1st line agents OR one 1st line agent and one 2nd line agent

PL = Prescriber Limit, (Must be prescribed by Rheumatologist); PA = Prior Authorization Required; NF = Non-Formulary; SP = Specialty
*Based on pharmacy claims data from 1/2017-12/2017; ^No claims

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), 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.

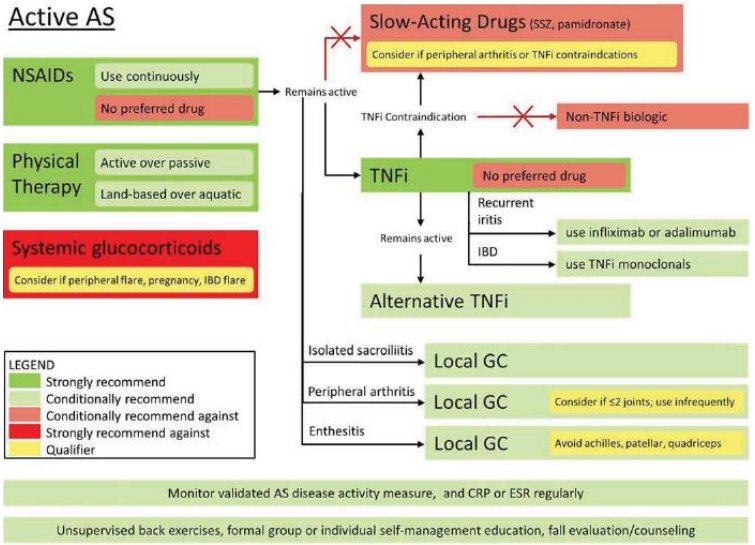
CLINICAL JUSTIFICATION

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*[2] 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).

Figure 1: ACR/SAA/SRTN ctive AS Treatment Algorithm



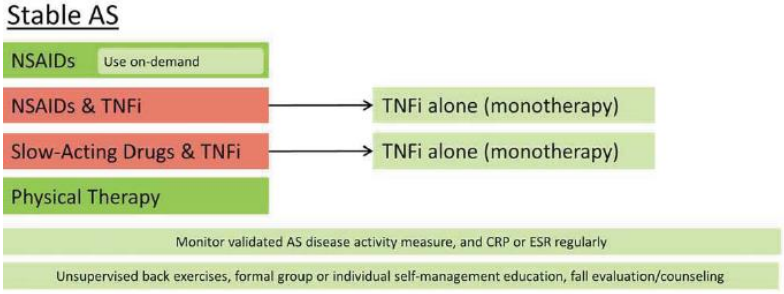
- Methotrexate and Leflunomide have shown to have minimal benefit and are associated with side effects. The benefits did not outweigh the risks and, therefore, are generally, not recommended.
  - Sulfasalazine was shown to have a small benefit on pain relief and may be an option for patients who cannot 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.

Figure 2: ACR/SAA/SRTN Stable AS Treatment Algorithm



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REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Biological Response Modifiers Review 2-19-08.doc	2/2008	Allen Shek, PharmD
Updated Policy	Biologic Response Modifiers 2010 final.docx	5/2010	Allen Shek, PharmD
Updated Policy	TNF MUE summary 2-21-2012.docx	2/2012	Allen Shek, PharmD
Updated Policy	Psoriatic Arthritis & Ankylosing Spondylitis.docx	10/2014	Jonathan Szkotak, PharmD
Updated Policy	Class Review- Biologics, Apremilast, and Tofacitinib in Inflammatory Joint, Skin, and Bowel Diseases.docx	2/2016	Johnathan Yeh, PharmD
Updated Policy	Class Review- Biologics, Apremilast, and Tofacitinib in Inflammatory Joint, Skin, and Bowel Diseases.docx	02/2017	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy – Rheumatology – Anklyosing Spondylitis 2018-02.docx	02/2018	Johnathan,Yeh, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy