MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Ankylosing Spondylitis (AS)	**P&T DATE:**	06/20/2023
CLASS:	Rheumatology/Anti-inflammatory Disorders	**REVIEW HISTORY** (*month/year*)	11/22, 05/21, 02/08, 05/10, 02/12, 10/14, 02/16, 02/17, 02/18, 05/19, 05/20
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/MVHP Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit https://medi-calrx.dhcs.ca.gov/home/ for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit.
All medical claims require that an NDC is also submitted with the claim. If a physician administered medication has a specific assigned CPT code, that code must be billed with the correlating NDC. If there is not a specific CPT code available for a physician administered medication, the use of unclassified CPT codes is appropriate when billed with the correlating NDC.

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. The purpose of this coverage policy is to review the available agents (Table 1) and distinguish where the medications may be billed to. For agents listed for coverage under the medical benefit, this coverage is specific to outpatient coverage only (excludes emergency room and inpatient coverage).

Table 1. Available Ankylosing Spondylitis Agents *(Current as of 4/2023)*

CPT Code	Generic Name (Brand Name)	Available Strengths	Pharmacy Benefit	Outpatient Medical Benefit (Restrictions)
TNF-inhibitors				
J0135	Adalimumab (Humira, Humira CF)	20mg/0.4ml, 40mg/0.8ml 40mg/0.4ml	Yes	No
--	Adalimumab-atto (Amjevita)	40 mg/0.8 mL, 20 mg/0.4 mL	Yes	No

J1438	Etanercept (Enbrel)	50mg/ml, 25mg/ml,	Yes	No
Q5103	Infliximab-dyyb (Inflectra)	100mg IV vial	Yes	Yes (PA)
Q5104	Infliximab-abda (Renflexis)			
J1745	Infliximab (Remicade)			
Q5121	Infliximab-axxq (Avsola)			
J1602	Golimumab (Simponi)	50mg/4ml IV vial, 100mg/ml, 50mg/0.5ml auto-injector, 50mg/0.5ml 100mg/ml prefilled syringe	Yes	Yes, for vials (PA)
J0717	Certolizumab (Cimzia)	200mg	Yes, for pre-filled syringes	Yes, for lyophilized solutions (PA)
IL-17 Inhibitors				
--	Secukinumab (Cosentyx)	150mg/ml	Yes	No
--	Ixekizumab (Taltz)	80mg/ml	Yes	No
JAK Inhibitors				
--	Tofacitinib (Xeljanz)	5mg IR, 11mg ER tablet	Yes	No
--	Upadacitinib (Rinvoq)	15mg tablet	Yes	No

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for agents with medical benefit restrictions. This coverage criteria has been reviewed and approved by the HPSJ/MVHP Pharmacy & Therapeutics (P&T) Advisory Committee. For agents that do not have established prior authorization criteria, HPSJ/MVHP will make the determination based on Medical Necessity criteria as described in HPSJ/MVHP Medical Review Guidelines (UM06).

Biologics

1st line—Infliximab (Inflectra, Renflexis, Remicade, Avsola)

- ❒ **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:** Must be initiated by a rheumatologist.

2nd line— 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:** Must be initiated by a rheumatologist.

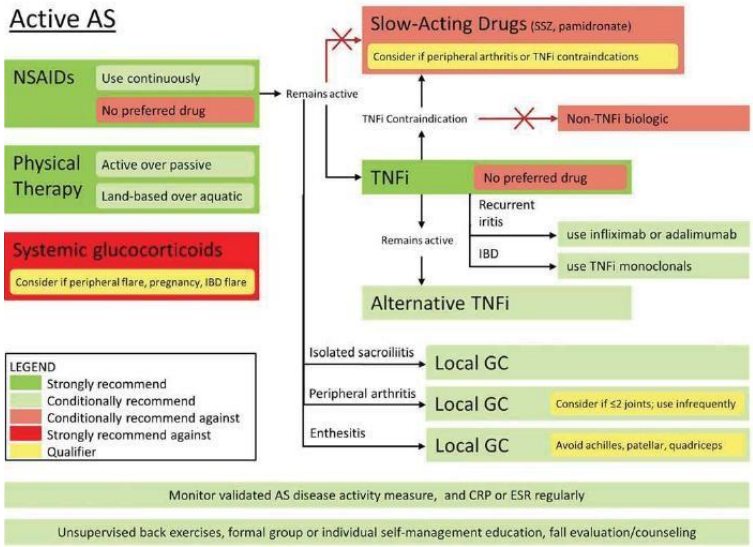
2nd line— Certolizumab (Cimzia)

- ❒ **Coverage Criteria:** Reserved for treatment failure to Adalimumab, Etanercept, or Infliximab OR women that are currently pregnant or breastfeeding.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** Prescription history showing at least 3 month trial of one first line agent (Adalimumab, Etanercept, or Infliximab) OR pregnancy/breastfeeding status.
- ❒ **Other Notes:** Must be initiated by a rheumatologist.

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:

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



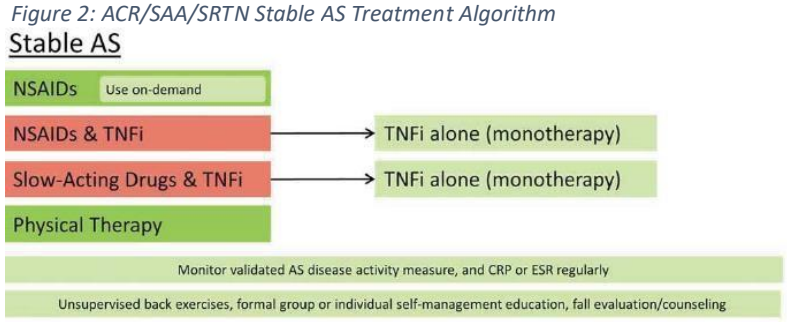
Active AS

- 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).

- According to the *2019 ACR/SAA/SRTN Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis* guidelines, the guidelines recommend for the consideration of the use of biological disease-modifying antirheumatic drugs (bDMARDs) in patients with persistently high disease activity despite conventional treatments, with a preference for TNFi therapy over interleukin-17 inhibitors (IL-17i).[28]
- 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.

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



Stable AS

- For 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 the 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/MVHP'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.

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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 – Ankylosing Spondylitis 2018-02.docx	02/2018	Johnathan,Yeh, PharmD
Updated Policy	HPSJ Coverage Policy – Rheum & Immuno – Ankylosing Spondylitis 2019-05.docx	05/2019	Matthew Garrett, PharmD

Updated Policy	Ankylosing Spondylitis.docx	05/2020	Matthew Garrett, PharmD
Updated Policy	Ankylosing Spondylitis.docx	05/2021	Matthew Garrett, PharmD
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Updated Policy	Ankylosing Spondylitis.docx	6/2023	Matthew Garrett, PharmD

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