Clinical Practice Guideline

Axial Spondyloarthritis

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## Abbreviations

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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACR</td>
<td>American College of Rheumatology</td>
</tr>
<tr>
<td>AS</td>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>ASAS</td>
<td>Assessment of Spondyloarthritis International Society</td>
</tr>
<tr>
<td>axSpA</td>
<td>Axial spondyloarthritis</td>
</tr>
<tr>
<td>BASDAI</td>
<td>Bath Ankylosing Spondylitis Disease Activity Index</td>
</tr>
<tr>
<td>bDMARDs</td>
<td>Biologic disease-modifying antirheumatic drugs</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>DMARD(s)</td>
<td>Disease-modifying antirheumatic drug(s)</td>
</tr>
<tr>
<td>ESR</td>
<td>Erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>EULAR</td>
<td>European League Against Rheumatism</td>
</tr>
<tr>
<td>GI</td>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>Human leukocyte antigen B27</td>
</tr>
<tr>
<td>IBD</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>IBP</td>
<td>Inflammatory back pain</td>
</tr>
<tr>
<td>IL-17i</td>
<td>Interleukin-17 inhibitor</td>
</tr>
<tr>
<td>MDA</td>
<td>Minimal disease activity</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>NSAID</td>
<td>Nonsteroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>PsA</td>
<td>Psoriatic arthritis</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>RA</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>SI</td>
<td>Sacroiliac</td>
</tr>
<tr>
<td>SpA</td>
<td>Spondyloarthritis</td>
</tr>
<tr>
<td>STIR</td>
<td>Short tau inversion recovery</td>
</tr>
<tr>
<td>T2T</td>
<td>Treat to target</td>
</tr>
<tr>
<td>TNFi</td>
<td>Tumor necrosis factor inhibitor</td>
</tr>
<tr>
<td>UC</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
</tr>
</tbody>
</table>
Introduction

Spondyloarthritis (SpA) is a life-long immune-mediated inflammatory arthritis of the spine and sacroiliac (SI) joints and, less commonly, peripheral joints. Patients may also have enthesitis and/or dactylitis. Extra-articular findings include uveitis, inflammatory bowel disease (IBD), and psoriasis.

There is no known single etiology for SpA. It is likely caused by a combination of genetic, environmental, and immunologic factors. Spondyloarthritis is divided into two subcategories, based on whether the symptoms are predominantly spinal (axial SpA or axSpA) or peripheral spondyloarthritis (peripheral SpA), but the two groups have overlapping symptoms and complaints.

In the past, axSpA was divided into radiographic (ankylosing spondylitis or AS) and non-radiographic SpA. However, it has been recognized that both entities represent different points on a spectrum of the same disease. Many, but not all patients with non-radiographic SpA will eventually develop radiographic SpA. Rudwaleit et al. suggest that patients with mostly axial symptoms (radiographic and non-radiographic SpA) be classified as having AS or simply axSpA.

In AS, the entheses of the vertebrae may be inflamed, leading to the formation of syndesmophytes and, eventually, fusion of the vertebrae and apophyseal joints of the spine in some patients. As axSpA progresses, deformities of the spine such as flattening of the normal lumbar lordosis, kyphosis of the thoracic spine, and hyperextension of the cervical spine occur. Fusion of the SI joints may also be seen.

Spondyloarthritis tends to cluster in families, affects young adults, and requires costly lifelong management. The disease negatively impacts the quality of life (QoL) of those affected. The most common problems are stiffness, back pain, fatigue, poor sleep, side effects of medications, negative body image, and concerns about the future; especially the ability to maintain full-time employment. The latter problem also contributes to the high costs associated with caring for these patients.

There are very few estimates of the actual cost of caring for patients with axSpA in the United States (US). A 2011 study estimated the mean annual medical cost of caring for a patient with AS to be approximately $17 728; this did not include costs for those with non-radiographic axSpA. The implications of these high medical expenditures become more urgent when they are considered in the context of prevalence rates. Ankylosing spondylitis is one of the most common rheumatologic diseases in the US, almost equal to rheumatoid arthritis (RA, Figure 1). Helmick et al. estimated the prevalence of SpA (axial and peripheral) in the population to be as high as 1.31%, that of AS to be 0.52%, and that of RA to be 0.60%.
Figure 1. Prevalence of SpA, AS, and RA in France and the US

*Prevalence estimate ranged from 0.345 to 1.310%.
AS, ankylosing spondylitis; RA, rheumatoid arthritis; SpA, spondyloarthritis

Diagnosis

The diagnosis of axSpA is established by integrating a detailed patient history and physical exam with the results of imaging and laboratory tests.

Inflammatory Back Pain

Back pain is one of the most common reasons for people to seek medical attention. Approximately 19.2% of the US population between the ages 20 and 69 years reported a history of axial back pain (cervical, upper thoracic, mid- and lower-back, or SI joint area) for <3 months in the 2009-2010 National Health and Nutrition Examination Survey. In this survey, 40% of the population with axial pain reported that the pain had started before the age of 30, and two thirds reported that it was constant. In addition, using four different sets of criteria for inflammatory back pain (IBP), the report found that between 5% and 6% of 20- to 69-year-olds with back pain met criteria for IBP. However, in the group reporting chronic axial pain (pain for 3 months or more) 28% to 38% met the criteria for IBP.
Seventy percent to 80% of patients with axSpA have IBP. To identify patients at risk for axSpA, providers must be able to recognize when back pain is inflammatory. Back pain is considered to be IBP if it has been present for at least 3 months, and the patient meets four of the following five conditions:

- Age <40 years old
- Insidious onset
- Back pain that improves with exercise
- Back pain that does not improve with rest
- Pain at night that improves when getting up

There is often up to an 8- to 12-year delay between the onset of symptoms, establishment of the diagnosis of axSpA, and the start of appropriate therapy. The most common reason for this delay is that primary care physicians who see these patients initially are not familiar with the early signs and symptoms of axSpA. As a result, they frequently fail to refer at-risk patients for a rheumatology evaluation early in the course of the disease. The delay in diagnosis can negatively impact the course of the disease, especially in view of the recent advances in drug therapy, which can slow disease progression. Primary care physicians must learn to identify patients who are at risk for axSpA. Patients presenting with a history of at least 3 months of chronic back pain and younger than 45 years of age must be evaluated carefully to determine if they have IBP (based on the description above).

If a patient has IBP, then X-rays of the SI joints and/or a human leukocyte antigen B27 (HLA-B27) blood test should be performed. A patient with IBP who has (an) abnormal X-ray of the SI joint(s) or is HLA-B27 positive should be referred for a complete rheumatology evaluation.

**Classification of Spondyloarthritis**

In 2009, the Assessment of Spondyloarthritis International Society (ASAS) published criteria for the classification of SpA. Using this system, Strand et al. demonstrated that approximately 25% of patients meeting the ASAS criteria for axSpA were missed by rheumatologists who used only clinical expertise to make a diagnosis.

The ASAS classification was found to have considerably better sensitivity (79.5%) and specificity (83.3%) than prior classification systems. These criteria should be used to evaluate and classify all patients who potentially have axSpA.

According to the ASAS criteria, patients <45 years of age with ≥3 months of back pain with or without peripheral complaints can be diagnosed with axSpA if they have either sacroilitis on imaging (radiographs or magnetic resonance imaging [MRI]) and ≥1 of the SpA findings listed in Table 1, or test HLA-B27 positive and have ≥2 of the findings in Table 1. The classification system has been put into a simple and easy-to-use algorithm in Figure 2.
<table>
<thead>
<tr>
<th>Additional Findings</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBP</td>
<td>At least four of the following:</td>
</tr>
<tr>
<td></td>
<td>• Age &lt;40 years old</td>
</tr>
<tr>
<td></td>
<td>• Insidious onset</td>
</tr>
<tr>
<td></td>
<td>• Improves with exercise</td>
</tr>
<tr>
<td></td>
<td>• Does not get better with rest</td>
</tr>
<tr>
<td></td>
<td>• Pain at night that improves upon getting up</td>
</tr>
<tr>
<td>Peripheral oligoarthritis mostly in the lower extremities</td>
<td>Past or present active synovitis diagnosed by a physician</td>
</tr>
<tr>
<td>Enthesitis (heel)</td>
<td>Past or present pain or tenderness at the insertion of the Achilles tendon or plantar fascia at the calcaneus</td>
</tr>
<tr>
<td>Uveitis</td>
<td>Past or present diagnosis by an ophthalmologist</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>Past or present diagnosis by a physician</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>Past or present diagnosis by a physician</td>
</tr>
<tr>
<td>IBD (Crohn’s disease or UC)</td>
<td>Past or present diagnosis by a physician</td>
</tr>
<tr>
<td>Good response to NSAIDs</td>
<td>Back pain relieved after 24 to 48 hours of full-dose NSAID</td>
</tr>
<tr>
<td>Family history of SpA</td>
<td>Presence of AS, psoriasis, acute uveitis, reactive arthritis,\textsuperscript{\textdagger} or IBD in first-degree\textsuperscript{\textdaggerdbl} or second-degree\textsuperscript{\textsection} relative</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>Positive test</td>
</tr>
<tr>
<td>CRP</td>
<td>Elevated</td>
</tr>
</tbody>
</table>

\textsuperscript{\textdagger}First-degree relative: mother, father, sister, brother.

\textsuperscript{\textdaggerdbl}Second-degree relative: maternal and paternal grandparents, aunts, uncles, nieces, and nephews.

\textsuperscript{\textsection}Reactive arthritis, previously known as Reiter’s syndrome.

AS, ankylosing spondylitis; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; IBD, inflammatory bowel disease; IBP, inflammatory back pain; NSAID, nonsteroidal anti-inflammatory drug; SpA, spondyloarthritis; UC, ulcerative colitis.

Figure 2. Flow chart demonstrating the ASAS classification system

*MRI findings of active inflammatory lesions of the SI joints with bone marrow edema and/or osteitis suggestive of sacroiliitis.

ASAS, Assessment of SpondyloArthritis International Society; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; IBP, inflammatory back pain; IBD, inflammatory bowel disease; MRI, magnetic resonance imaging; UC, ulcerative colitis

Initial Laboratory Testing

More than 90% of patients with axSpA test positive for HLA-B27. This test should be performed as part of the initial work-up of patients considered at risk for this condition if not already performed. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are both non-specific measures of inflammation, but baseline levels should be obtained as they may be useful in monitoring response to treatment later.

Imaging for the Diagnosis of Axial Spondyloarthritis

Initial Diagnosis

According to the European League Against Rheumatism (EULAR), plain films of the SI joints are the initial imaging test that should be obtained in patients whose history, exam, and laboratory findings (HLA-B27) suggest axSpA. If the films do not show evidence of SI disease and clinical suspicion is high, then MRI of the SI joints should be obtained. The findings on MRI suggesting SpA are:

- Bone marrow edema/osteitis
- Structural abnormalities
  - Bone erosions
  - New bone formation
  - Sclerosis
  - Fatty infiltration

To diagnose sacroiliitis on MRI, the following conditions must be met:

- Active inflammatory lesions of the SI joints must be demonstrated.
  - Bone marrow edema on short tau inversion recovery (STIR) sequences or osteitis on T1 post-contrast images must be present in the subchondral or periarticular marrow.
    - If bone marrow edema/osteitis is seen on only one MRI slice, then more than one lesion must be involved on that slice. If there is only one area of bone marrow edema/osteitis, then it must be seen on at least two contiguous slices.
  - Synovitis, enthesitis, or capsulitis without bone marrow edema/osteitis are insufficient to establish the diagnosis of sacroiliitis.
  - Structural lesions (fat deposition, sclerosis, erosions, bony bridging, or ankylosis) without bone marrow edema/osteitis are insufficient to establish the diagnosis of sacroiliitis.

No other imaging modalities are recommended by EULAR, with the possible rare exception of computed tomography, if the plain films are negative and MRI is contraindicated.

In patients with evidence of sacroiliitis on initial plain films, additional radiographs of the cervical and lumbar spine should be performed. The presence of syndesmophytes on those images predict the future development of additional syndesmophytes.
Magnetic Resonance Imaging Technique for Initial Diagnosis

Magnetic resonance imaging for axSpA should be performed on a 1.5 or higher Tesla whole body magnet with a phased array coil. The images should be oriented in a semi-coronal plane parallel to a line drawn between the upper dorsal aspect of S1 and S3. Semi-axial planes may also be needed, but they are not standard. At times, additional sequences or imaging planes may be needed for clarification.\textsuperscript{16}

MRI sequences should include:\textsuperscript{16}

- T1 without and with intravenous contrast to detect synovitis, capsulitis, enthesitis, and osteitis on post-contrast scans
- STIR to detect bone marrow edema
  - T2 gradient echo sequences should be performed only if better visualization of SI cartilage is required.

Bone marrow edema is best seen on STIR images as an area of increased signal intensity. An area of increased signal intensity in the bone marrow on post-contrast T1 images is called osteitis. Bone marrow edema/osteitis is most commonly seen in periarticular regions of the bone. The presence of bone marrow edema/osteitis is indicative of active sacroiliitis, but it is not limited to axSpA. This can also be seen in areas of structural damage such as sclerosis or erosions.\textsuperscript{16}

Treatment

Goals of Therapy

A treat-to-target (T2T) approach has been advocated for treating many chronic diseases (diabetes, CVD, RA, etc.) including axSpA. When an evidenced-based T2T paradigm is followed, outcomes improve.\textsuperscript{17}

Targets for the management of SpA were first established in 2014. The first recommendations, established by an international Task Force, were based primarily on a systematic review of the literature and the consensus of Task Force participants.\textsuperscript{17} The Task Force noted that the literature available at the time was weak but they did publish both principles and recommendations for treating SpA and psoriatic arthritis (PsA) to target. The members agreed that the target should be either remission or low disease activity. They also encouraged researchers to do better and more complete clinical studies to support this hypothesis.\textsuperscript{17}

The recommendations for a T2T strategy in patients with SpA and PsA were reviewed again in 2017.\textsuperscript{18} The 2017 Task Force was composed of 36 members from both Europe and North America, and included rheumatologists, dermatologists, patients and a non-physician health professional.

Treatment should aim at providing the best care possible, using a combination of pharmacologic and non-pharmacologic interventions that are individualized to the patient.\textsuperscript{19} The plan should also consider the patient’s general medical status, drug risks (especially existing comorbidities), current medications, and psychosocial factors (see Table 2).
Table 2. Treatment goals in axial spondyloarthritis (axSpA)

<table>
<thead>
<tr>
<th>Control Signs and Symptoms</th>
<th>Preserve Function</th>
<th>Minimize Structural Damage</th>
<th>Minimize Socioeconomic Impact</th>
<th>Laboratory Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pain</td>
<td>• Mobility of the spine</td>
<td>• Osteoproliferation and ankylosis</td>
<td>• Decrease or eliminate need for sick days off from work</td>
<td>• Normal ESR and/or CRP</td>
</tr>
<tr>
<td>• Morning stiffness</td>
<td>• Activities of daily living</td>
<td>• Bone destruction</td>
<td>• Decrease or minimize disability claims</td>
<td></td>
</tr>
<tr>
<td>• Fatigue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Extra-articular disease such as uveitis, IBD</td>
<td></td>
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</tbody>
</table>

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IBD, inflammatory bowel disease

The target for the management of axSpA and/or PsA is complete remission (absence of clinical or laboratory evidence of inflammation, including the acute-phase reactants ESR and/or CRP and extra-articular disease). In some individuals, minimal disease activity (MDA) is an acceptable target. The target should always be documented in the medical record.

Disease activity should be measured by a validated measure of “musculoskeletal disease activity and assessment of cutaneous and/or other relevant extra-articular manifestations, should be used in clinical practice to define the target and to guide treatment decisions; the frequency of the measurements depends on the level of disease activity.” (Page 9). Imaging results may be considered in evaluating disease activity but are not encouraged. When the target is reached, it is important that it be maintained throughout the course of the disease.
United Rheumatology recommends the use of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) to measure disease activity in patients with axSpA. With this system, the patient and physician are asked to evaluate the following six parameters (with six questions [Q1-Q6]) on a scale of 1 to 10:20

- Fatigue and/or tiredness experienced by the patient (Q1)
- Spinal pain (Q2)
- Peripheral joint pain or swelling (Q3)
- Enthesitis (Q4)
- Intensity of morning stiffness (Q5)
- Duration of morning stiffness (Q6)

The BASDAI score is calculated according to the following formula:

$$\frac{Q1 + Q2 + Q3 + Q4 + \frac{Q5 + Q6}{2}}{5} = \text{BASDAI}$$

With a minimum score of 0 and a maximum score of 10, scores of 4 or more suggest suboptimal control. Patients with these scores are good candidates for a change in their medical therapy. The BASDAI disease activity score can also be accessed at [https://www.medicalalgorithms.com/basdai-index](https://www.medicalalgorithms.com/basdai-index) or [https://www2.gov.bc.ca/assets/gov/health/forms/5364.pdf](https://www2.gov.bc.ca/assets/gov/health/forms/5364.pdf).

In the evaluation of disease activity in PsA, United Rheumatology recommends the use of MDA (see United Rheumatology Clinical Practice Guideline for PsA).

As in 2014, one important principle for the treatment of axSpA advocated by the Task Force is shared decision making between the patient and the rheumatologist with respect to the treatment target. Another important principle is treating to target, which requires the use of a disease activity measure (see above) and changing treatment as appropriate if the target is not met within a reasonable amount of time. For those patients with non-rheumatologic problems (skin, eyes, gastrointestinal [GI] tract, etc.) care should be coordinated with the appropriate medical specialist. Controlling symptoms and limiting inflammation is important to prevent further bone destruction and disability. Maximizing QoL and minimizing comorbidities are also important. In addition, the Task Force noted that treatment of axSpA is expensive with high medical and societal costs which must be considered when developing a treatment plan.19

**Non-pharmacologic Management**

In the 2010 and 2016 updates of their joint recommendations for the management of axSpA, the ASAS and EULAR provided the following general recommendations:19, 21

- Encourage a regular exercise regimen
  - Supervised exercises, on land or in the water, are preferred to home exercises, because they have been found to be more effective than a home exercise program.
  - If supervised exercise is not an option then a home exercise program should be initiated.
• Patients may find joining patient associations and self-help groups to be useful.
• Extra-articular manifestations should be managed collaboratively by the appropriate medical specialists.
• Patients should be educated about the increased risk for both cardiovascular disease (CVD) and osteoporosis.
• Smoking cessation strategies should be recommended to patients with axSpA, because there has been an association between smoking and disease activity.

Pharmacologic Treatment
The initial drug of choice, for patients with pain and stiffness is a nonsteroidal anti-inflammatory drug (NSAID). The ASAS/EULAR recommendations state that NSAIDs should be given continuously up to the maximum dose and not on an ‘as needed’ basis.\textsuperscript{19} However, the physician should be aware of the GI, cardiovascular, and renal risks of such medications and make the appropriate modifications in dosage, when needed. The latest American College of Rheumatology (ACR) treatment recommendations, published in 2016,\textsuperscript{22} also strongly recommend continuous NSAIDs as the initial treatment, stating that the benefits “far outweighed” (Page 6) the risks. Contraindications to the use of these drugs should always be taken into account.

For adults with pain despite adequate doses of NSAIDs, acetaminophen or opioid-like drugs should be considered. These drugs may also be used if NSAIDs are not well tolerated or are contraindicated (e.g., in patients with IBD).\textsuperscript{19} Glucocorticoid injections into the area of musculoskeletal pain and inflammation may also be considered; however, long-term systemic glucocorticoids should not be used.\textsuperscript{19, 22}

Conventional disease-modifying antirheumatic drugs (DMARDs) are not recommended for the treatment of axSpA.\textsuperscript{21, 22} However, for patients with peripheral arthritis, sulfasalazine may be considered.\textsuperscript{19}

For patients with high disease activity despite treatment with NSAIDs, biological disease-modifying antirheumatic drug (bDMARDs) such as a tumor necrosis factor inhibitor (TNFi) drug should be used. Different patients with the same disease activity may respond differently to the same TNFi drug. Therefore, if a patient fails to improve on a particular TNFi drug after a trial of at least 12 weeks with either no change or an increase in BASDAI, either another TNFi drug or an interleukin-17 inhibitor (IL-17i) should be tried. Conversely, if the patient shows an improvement in the BASDAI score of \( \geq 2 \) after 12 weeks, the current treatment should be continued (Figures 3A and 3B).\textsuperscript{19}
Figure 3A. Management of patients with axSpA

IL-17i, Interleukin-17 inhibitor; NSAID, nonsteroidal anti-inflammatory drug; SpA, TNFi, tumor necrosis factor inhibitor
Figure 3B. Management of patients with axSpA and poor response

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IL-17i, Interleukin-17 inhibitor; NSAIDs, nonsteroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor


No difference in efficacy has been shown between different TNFi medications. However, in patients with IBD or recurrent iritis, infliximab or adalimumab are preferred over etanercept (Table 3).22

If a patient is in sustained remission (no clinical symptoms or evidence of inflammation for 6 months or more), consideration of tapering a bDMARD can be considered, taking into account the predefined treatment target decided upon between the rheumatologist and the patient, as well as future cost considerations. If tapering is considered, either increasing the interval of the dose or decreasing the dose may be considered.
**Table 3. Pharmacologic management of axial spondyloarthritis (axSpA)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **NSAIDs**               | • NSAIDs should be given continuously during the period of active disease.  
• Experts suggest that benefit outweighs the risk.  
• NSAIDs should not be used if there is a contraindication to these drugs.  
• A gastroprotectant should be considered if using traditional NSAIDs continuously.  
• Dose-modification depending on severity of symptoms should be considered.  
• The possible increased risk of CVD with Coxibs must be considered when choosing one of these drugs over traditional NSAIDs. |
| including Coxibs         |                                                                                                                                                                                                                                                                                                                                                                                                       |
| **TNFi**                 | • There is no data to support the use of one TNFi drug over another, except if the patient has IBD or recurrent iritis.  
• In the presence of IBD or recurrent iritis, infliximab or adalimumab are preferred over etanercept.  
• If the response to one agent is not adequate, switch to a different TNFi agent or to an IL-17i.                                                                                                                                                                                |
| Infliximab               |                                                                                                                                                                                                                                                                                                                                                                                                       |
| Certolizumab pegol      |                                                                                                                                                                                                                                                                                                                                                                                                       |
| Golimumab               |                                                                                                                                                                                                                                                                                                                                                                                                       |
| Adalimumab              |                                                                                                                                                                                                                                                                                                                                                                                                       |
| Etanercept              |                                                                                                                                                                                                                                                                                                                                                                                                       |
| **IL-17i**               | • After failure of TNFi or with a contraindication to TNFi drugs, use a first-line treatment.                                                                                                                                                                                                                                                                                                       |
| Secukinumab             |                                                                                                                                                                                                                                                                                                                                                                                                       |

Coxibs, cyclooxygenase-2 (COX-2) inhibitors; CVD, cardiovascular disease; IBD, inflammatory bowel disease; IL-17i, Interleukin-17 inhibitor; NSAIDs, nonsteroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor


The effect of etanercept (a TNFi agent) versus sulfasalazine (a conventional DMARD) on active inflammatory lesions in early axSpA was compared by Song et al.\textsuperscript{23} in a 48-week randomized controlled study. The study showed a 69.2% decrease in MRI-detected inflammation with etanercept, which was almost double that observed in the sulfasalazine group. Half of the TNFi-treated patients experienced a clinical remission, whereas remission was seen in only 19% of the patients treated with sulfasalazine.

In addition to pharmacologic treatment; the ACR, EULAR, and the ASAS recommend total hip arthroplasty for patients with refractory pain or disability and structural damage to the hip.\textsuperscript{19, 22} Based on expert consensus, the ACR also recommends interval blood tests for ESR and CRP.\textsuperscript{22}

**Monitoring**

Frequency of follow-up visits should be individualized and based on the course of symptoms, disease severity, and the prescribed treatment. Monitoring should include:\textsuperscript{19}

- Clinical findings
- Patient Global Assessment
- Patient-reported morning stiffness (severity and duration)
• Fatigue, back pain and/or tenderness
• Peripheral joint pain and/or tenderness
• Swollen joint count
• Results of ESR and CRP, when appropriate
• Imaging as appropriate (Table 4).

Table 4. Recommendations for follow-up imaging

<table>
<thead>
<tr>
<th>Indication</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Disease activity               | Depends on clinical and laboratory results; currently data are insufficient to make a more definitive recommendation | • Value of MRI in follow-up is unclear
• Use selectively may help determine if patient qualifies for bDMARDs
• May find inflammation in patients with clinical remission, but literature is unclear if this should be treated
• STIR imaging only
• No indication for contrast on follow-up |
| Structural damage              | Not more frequently than once every 2 years | • Serial X-rays of the spine are of limited value
• MRI demonstrating extensive bone marrow edema in patients with AS may predict good response to TNFi therapy.
• High CRP |
| Predicting treatment effect    | Prior to start of TNFi therapy |                                                                 |

AS, ankylosing spondylitis; bDMARDs, biologic disease-modifying antirheumatic drugs; CRP, C-reactive protein; MRI, magnetic resonance imaging; STIR, short tau inversion recovery; TNFi, tumor necrosis factor inhibitor

When a patient on a bDMARD drug is in sustained (≥6 months) remission, the provider might consider drug tapering. However, stopping the drug completely is not recommended, because these patients have a heightened incidence of flares. Unfortunately, the 2016 ASAS-EULAR management recommendations do not define “remission” but suggest that “inactive disease” on an activity measure can be used. Tapering can be done by increasing the interval between doses or decreasing the dose at each treatment.

Activity measures are important for tracking a patient’s progress toward the treatment target and are extremely important in monitoring outcomes. They should be recorded at every patient visit along with CRP and/or ESR.
Glossary

**Bone marrow edema**
A lesion* within trabecular bone, with signal characteristics consistent with water content** and often with ill-defined margins.
*May occur alone or surrounding an erosion or other bone abnormalities.
**High-signal intensity and STIR images and low-signal on T1 non-contrast images.

**Bony bridges or ankylosis**
Decreased signal intensity on all sequences, but may be surrounded by increased signal intensity on T1.

**Capsulitis**
Inflammation of the joint capsule, which has increased signal intensity on T1 fat saturated post-contrast images.

**Dactylitis**
A sausage-shaped digit associated with PsA.

**Enthesitis**
Inflammation where tendons, ligaments, or joint capsules attach to bone. In axSpA, this is found at the site of ligamentous insertions to the vertebrae, Achilles tendon and plantar fascial insertion to the calcaneus, patellar tendon insertion on the tibial tubercle, metatarsal heads, superior and inferior borders of the patella, and the base of the 5th metatarsal bone.
On MRI, this has high signal intensity on STIR images and/or contrast-enhanced T1 images. The abnormal signal may extend into the bone marrow or soft tissues.

**Erosions**
On MRI, these are low-signal on T1 images and if they are active they will appear as increased signal intensity on STIR images. They may be seen more clearly on T1 fat saturated images or T2 images.

**HLA-B27**
Also known as human leukocyte antigen with subtypes B 2701-2759. It is a Class I surface antigen detected in blood and found on the surface of white blood cells.
It is positive in 70% to 90% of patients with axSpA and a very high percentage of patients with AS but is also found in patients with IBD, reactive arthritis, uveitis, and psoriasis.

**IBP**
Defined by the ASAS as back pain that has been present for >3 months and meeting four of the following five parameters:
- Age <40 years old
- Insidious onset
- Back pain that improves with exercise
- No improvement with rest
- Pain at night that improves when getting up.

**Periarticular fat deposition**
Seen as increased signal intensity on T1 images.
Sacroiliitis

Inflammation of the SI joints. For the purposes of the ASAS criteria for SpA, the following must be met on MRI:
If bone marrow edema/osteitis in subchondral or periarticular bone is seen on only one MRI slice, then more than one lesion must be involved on that slice. If there is only one area of bone marrow edema/osteitis, then it must be seen on at least two contiguous slices.

Subchondral sclerosis

Sclerosis secondary to axSpA should extend at least 5 mm from the SI joint space. It is of decreased signal intensity on all sequences.

Synovitis

An area in the synovial compartment that shows increased post-gadolinium enhancement* of a thickness greater than the width of the normal synovium.
*Enhancement (signal intensity increase) is judged by comparison between T1 images obtained before and after intravenous Gd contrast.
References


16. Rudwaleit M, Jurik AG, Hermann KG, Landewe R, van der Heijde D, et al. Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by...


## Document Updates

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<tr>
<th>Document Version</th>
<th>Description of Changes</th>
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<tr>
<td>1.1.2016</td>
<td>Creation of first version</td>
<td>06 Apr 2016</td>
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<tr>
<td>1.1.2017</td>
<td>Update with new reference</td>
<td>14 Mar 2017</td>
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<tr>
<td>1.1.2018</td>
<td>2018 literature update</td>
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