A Specialty Networks Company

CLINICAL PRACTICE GUIDELINE

Axial Spondyloarthritis (axSpA)

Version 1.1.2023
February 2023

Table of Contents

List of Tables

List of Figures

Abbreviations

ACR	American College of Rheumatology
AS	Ankylosing spondylitis
ASAS	Assessment of SpondyloArthritis International Society
axSpA	Axial spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
COX-2	Cyclooxygenase-2
CRP	C-reactive protein
csDMARD(s)	Conventional synthetic disease-modifying anti-rheumatic drug(s)
CVD	Cardiovascular disease
ESR	Erythrocyte sedimentation rate
EULAR	European League Against Rheumatism
FDA	Food and Drug Administration

HLA-B27	Human leukocyte antigen B27
IBD	Inflammatory bowel disease
IBP	Inflammatory back pain
IL-17i	Interleukin-17 inhibitor
JAK	Janus kinase
MDA	Moderate disease activity
MRI	Magnetic resonance imaging
NICE	National Institute for Health and Care Excellence
nr-axSpA	Non-radiographic axial spondyloarthritis
NSAID(s)	Non-steroidal anti-inflammatory drug(s)
QoL	Quality of life
RA	Rheumatoid arthritis
r-axSpA	Radiographic axial spondyloarthritis
SI	Sacroiliac
SpA	Spondyloarthritis
T2T	Treat to target
TNFi	Tumor necrosis factor inhibitor
UC	Ulcerative colitis

Introduction

Axial spondyloarthritis (axSpA) is an inflammatory rheumatic disease of the spine, sacroiliac (SI) joints and, sometimes, peripheral joints. Most patients are under 45 years of age and present with chronic inflammatory back pain. Other complaints include uveitis, peripheral arthritis, enthesitis, dactylitis, inflammatory bowel disease (IBD) and psoriasis. Classifications have been proposed that divide axSpA into three general categories: radiographic axSpA (r-axSpA), which is also called ankylosing spondylitis (AS), non-radiographic axSpA (nr-axSpA)[1, 2] and peripheral SpA.

There is no known single etiology for axSpA. Genetics along with environmental and immunologic factors are thought to contribute to disease development. The disease, which tends to cluster in families and affects young adults (under 45 years of age), negatively impacts their quality of life (QoL).

One of the most important QoL issues for patients with axSpA and peripheral SpA is an increase in functional or physical disability resulting from decreased ability to perform activities of daily living secondary to pain, stiffness, bone fusion in the spine and sacroiliac joints, fatigue, poor sleep, side effects of medications, as well as a negative body image. Often these patients cannot adequately perform household chores and participate in social or leisure activities. Some even require aides to assist them. Employed patients with SpA and significant functional disabilities are concerned about the future, especially the ability to maintain full-time employment. These patients often have diminished productivity at work and more lost workdays than their peers. Some patients are forced to change employment to a less physically demanding environment, and some are forced to retire at an early age.[3-6]

A 2011 study estimated the mean annual medical cost of caring for a patient with AS was approximately $17,728.[7] Another study published in 2018 compared the direct cost of caring for patients with AS to a control group, which was matched for age, gender, and location.[8] The inpatient admission rate was two times greater for the AS group as compared with the control group. Visits to the emergency department, outpatient visits and pharmacy costs were also greater for the AS group. The total cost of medical care was $24,978 per person for the AS group and only $2,139 per person in the control group. The pharmacy costs for the AS group were $14,074 and $1,737 for the control group. Neither of these studies included the cost of care for patients with nr-axSpA or peripheral SpA (see classification below). The implications of these high medical expenditures become more urgent when they are considered in the context of prevalence rates. AS is one of the most common rheumatologic diseases in the US, almost equal to rheumatoid arthritis (RA; Figure 1).[9-11]

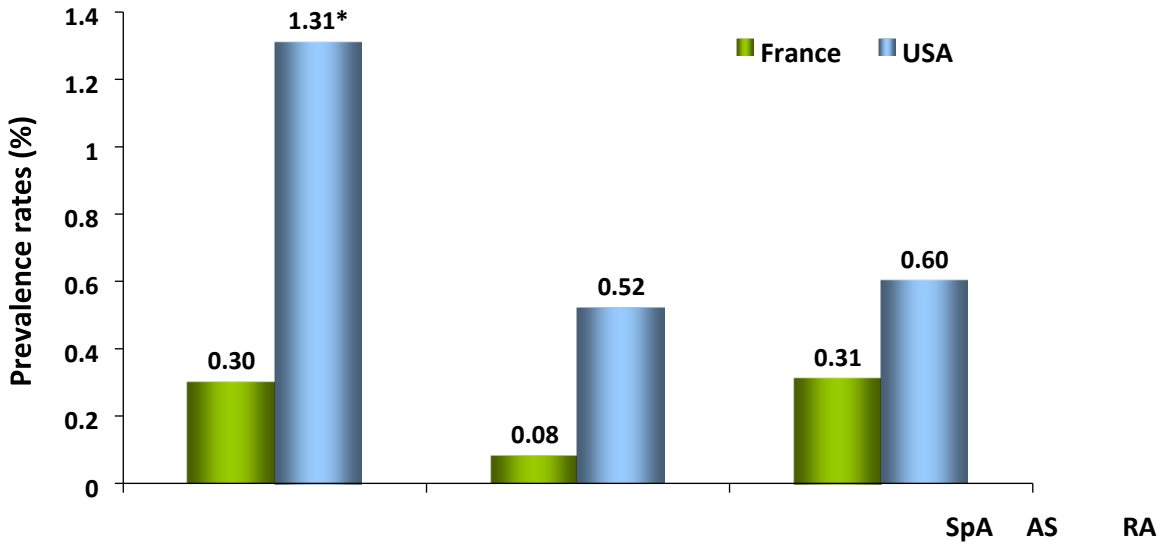

Figure 1. Prevalence of SpA, AS, and RA in France and the US

*Prevalence estimate ranged from 0.345% to 1.310%.

AS, ankylosing spondylitis; RA, rheumatoid arthritis; SpA, spondyloarthritis

Guillemin F, et al. Ann Rheum Dis 2005;64:1427-1430.[9] Saraux A, et al. Ann Rheum Dis 2005; 64:1431-1435.[10] Helmick CG, et al. Arthritis Rheum 2008; 58:15-25.[11]

Diagnosis

The diagnosis of axial SpA , or peripheral SpA is established by correlating the results of a detailed medical history and physical examination with the results of imaging and laboratory tests (see discussion of Classification below). As the disease progresses, enthesitis may develop in the spine, which in turn may lead to the formation of syndesmophytes, and eventually, fusion of the vertebrae and apophyseal joints. Enthesitis commonly occurs in the heel at the insertion of the Achilles tendon and at the insertion of the plantar fascia. Deformities of the spine such as flattening of the normal lumbar lordosis, kyphosis of the thoracic spine, hyperextension of the cervical spine;[12] and fusion of the SI joints can occur.

Classification

As stated above, SpA can be divided into radiographic axSpA (ankylosing spondylitis or AS), nonradiographic axSpA (nr-axSpA) and peripheral SpA. It has been postulated that AS and nr-axSpA may represent different points on a spectrum of the same disease as some patients with nr-axSpA eventually develop AS.[13] Both AS and nr-axSpA are considered to be predominantly axial disease. Peripheral SpA involves much fewer patients and the dominant complaints are usual peripheral (arthritis, enthesitis, dactylitis).

In 2009, the Assessment of SpondyloArthritis International Society (ASAS) published criteria for the classification of spondyloarthritis (SpA).[1, 14] Although these classification criteria were designed to be used for clinical trials, they are often used in clinical practice.

According to the ASAS classification criteria, patients <45 years of age with ≥3 months of back pain with or without peripheral complaints can be classified as having AS, if they have sacroiliitis on X-rays of the SI joints and ≥1 of the SpA findings listed in

Table

1. Patients can be classified as having nr-axSpA, if they are <45 years of age with ≥3 months of back pain, no X-ray signs of sacroiliitis and magnetic resonance imaging (MRI) findings of sacroiliitis plus one finding of SpA listed in Table 1 or are human leukocyte antigen B27 (HLA-B27) positive and have ≥2 of the findings listed in

Table

1 and Figure 2.[1, 14]

MRI findings in the sacroiliac joints are divided into 5 grades which is similar to the New York Criteria for x-ray diagnosis of sacroiliitis. Grade 0 is considered to be normal; grade 1 has suspicious changes of the SI joint(s); grade 2 shows minimal changes unilaterally with sclerosis of the joint, small erosions and no change in joint width; grade 3 images show definite abnormalities of the SI joint(s) with severe erosions, sclerosis on both sides of the joint, and either widening or narrowing of the joint and/or partial fusion of the SI joint (these changes can be unilateral or bilateral)**;** and grade 4 images show fusion and sclerosis of the joint(s) (unilaterally or bilaterally)**.*[15]*** MRI of the sacroiliac joint is considered to be positive for sacroiliitis if the patient has grade 2 MRI changes bilaterally or grade 3 or 4 changes either unilaterally or bilaterally.***[1, 14]***

The category of peripheral SpA includes patients primarily presenting with peripheral complaints such as peripheral arthritis in the legs, enthesitis, dactylitis, reactive arthritis, inflammatory bowel disease and arthritis and undifferentiated SpA. These patients may have a remote history of back pain but usually do not present with it.

Table

1. Clarification of the additional findings required to establish a diagnosis of axSpA

Additional Findings	Comments
IBP	At least four of the following must be present to establish the diagnosis of IBP: • Age <40 years old • Insidious onset • Improves with exercise • Does not get better with rest • Pain at night that improves upon getting up
Peripheral oligoarthritis mostly in the lower extremities	Past or present active synovitis diagnosed by a physician
Enthesitis (heel)[1, 14]	Past or present pain or tenderness at the insertion of the Achilles tendon or plantar fascia at the calcaneus
Uveitis	Past or present diagnosis by an ophthalmologist
Dactylitis	Past or present diagnosis by a physician
Psoriasis	Past or present diagnosis by a physician
IBD (Crohn's disease or UC)	Past or present diagnosis by a physician
Family history of SpA	Presence of AS, psoriasis, acute uveitis, reactive arthritis,[a] or IBD in first-degree[b] or second-degree[c] relative
HLA-B27	Positive
CRP	Elevated

Table

[a]Reactive arthritis, previously known as Reiter's syndrome [b]First-degree relative: mother, father, sister, or brother

[c]Second-degree relative: maternal and paternal grandparents, aunts, uncles, nieces, or nephews

AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; IBD, inflammatory bowel disease; IBP, inflammatory back pain; SpA, spondyloarthritis; UC, ulcerative colitis

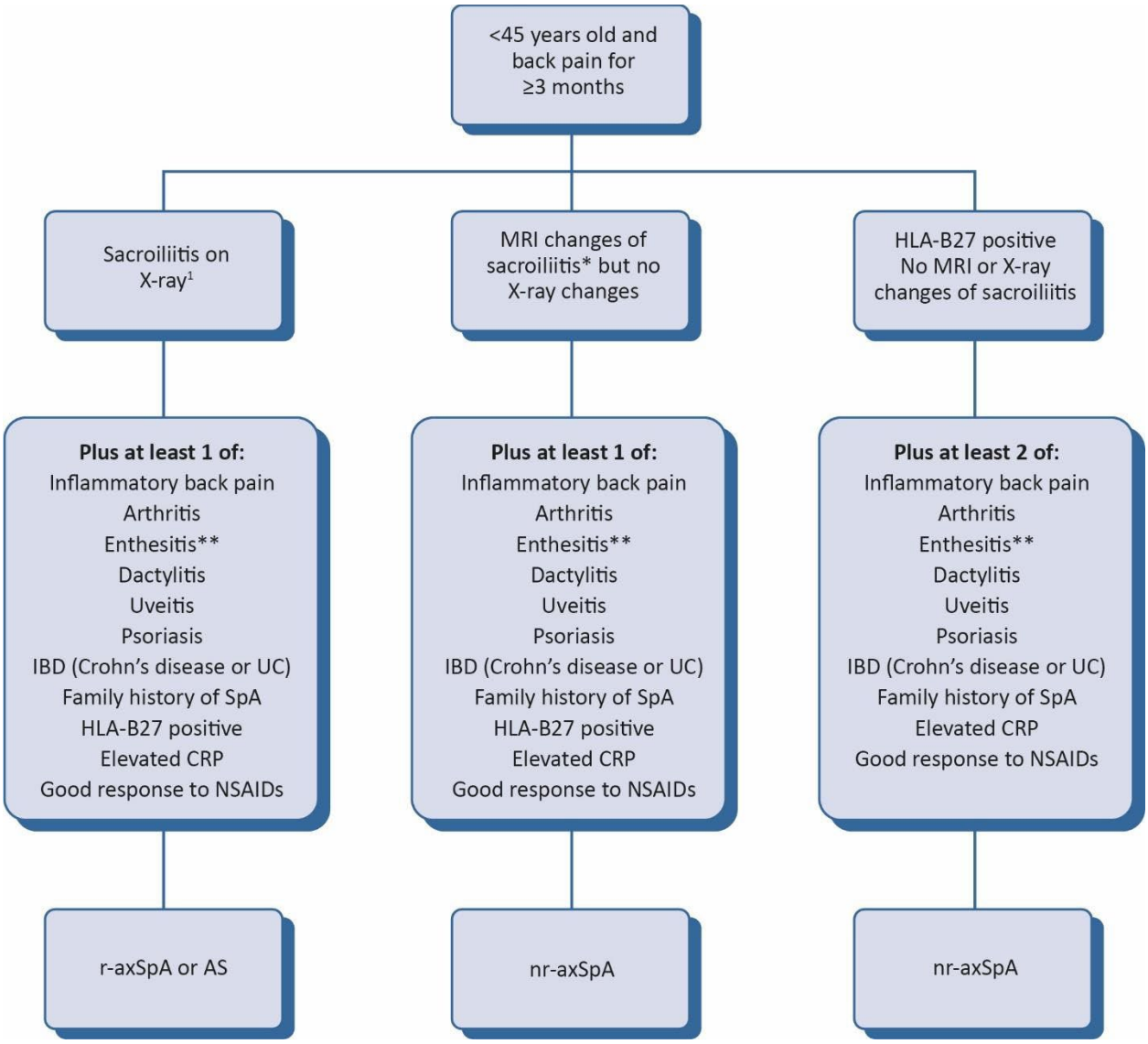

Figure 2. Chart demonstrating the ASAS classification system for axSpA

*MRI findings of active inflammatory lesions of the SI joints with bone marrow edema and/or osteitis suggestive of sacroiliitis
**Only enthesitis of the heel is acceptable[1, 14] AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis international Society; axSpA, axial spondyloarthritis; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; IBD, inflammatory bowel disease; MRI, magnetic resonance imaging; nr-axSpA, non-radiographic axSpA; NSAIDs, non-steroidal anti-inflammatory drugs; r-axSpA, radiographic axSpA; SI, sacroiliac; SpA, spondyloarthritis; UC, ulcerative colitis

This classification system is used in clinical practice as diagnostic criteria for axSpA despite the fact they were not meant to be diagnostic criteria.[16] According to Robinson et al.,[17] it is important providers understand that:

> *…. the above are all classification criteria for use in clinical research and are not diagnostic criteria. As such, these criteria should not simply be applied in a clinical setting as making a diagnosis of nr-axSpA requires*

exclusion of other potential causes for the presenting symptoms or findings (both clinical and imaging). (Page 166).

Boonen et al.,[18] reported that women develop nr-axSpA more often than men. The clinical complaints and functional impairments of patients with nr-axSpA are often equal to those found in patients with AS. Despite the differences in imaging findings women report more functional limitations as compared to men. Women also report a family history of axSpA more frequently than men.[19]

Some patients with nr-axSpA can develop AS over time, while others remain stable or may even report regression of symptoms. Patients with longer disease duration, high C-reactive protein (CRP) levels and more extensive bone marrow edema on MRI and are usually male are more likely to progress to AS. The identification of patients with nr-axSpA is important because they may benefit from treatment as much as patients with AS[16] since they may have the same burden of disease activity.

The ASAS classification was found to have considerably better sensitivity and specificity than prior classification systems. Using this system, Strand et al.[20] 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.

Often, there is up to an 8- to 12-year delay between the onset of symptoms, establishment of the diagnosis of SpA,[21] and the start of appropriate therapy. A common reason for this delay is failure of primary care providers, to recognize the early signs and symptoms of SpA. In the early stages of the disease, X-rays are often normal. However, negative radiographs do not exclude early nr-axSpA and as a result, at-risk patients may not be referred for a rheumatologic evaluation early in the course of their disease. Delays in diagnosis can negatively impact the ultimate outcome of the disease and the earlier treatment is initiated the better the outcome.

Recent advances in drug therapy can slow disease progression and limit structural damage, improving the patient's QoL and pain. Patients presenting with a history of at least 3 months of chronic back pain who are younger than 45 years of age should be evaluated carefully to determine if they have inflammatory back pain (IBP) (see Inflammatory Back Pain below). If a patient has IBP, then X-rays of the SI joints and/or an HLA-B27 blood test should be performed. A patient with IBP who has sacroiliitis on X-ray whether or not they are HLA-B27 positive[22, 23] should be referred for rheumatologic evaluation; those that are HLA-B27 positive with negative X-rays should be referred for an MRI of the SI joints and a rheumatologic evaluation.[12,13]

In 2011, the ASAS published an additional set of classification criteria for patients with predominantly peripheral disease).[24] This group of patients usually presented without back pain, a clinical suspicion of SpA and one or more of the following before age 45:

- Peripheral arthritis
- Enthesitis • Dactylitis.

Patients with peripheral symptoms were divided into 2 groups (See Figure 3 below).

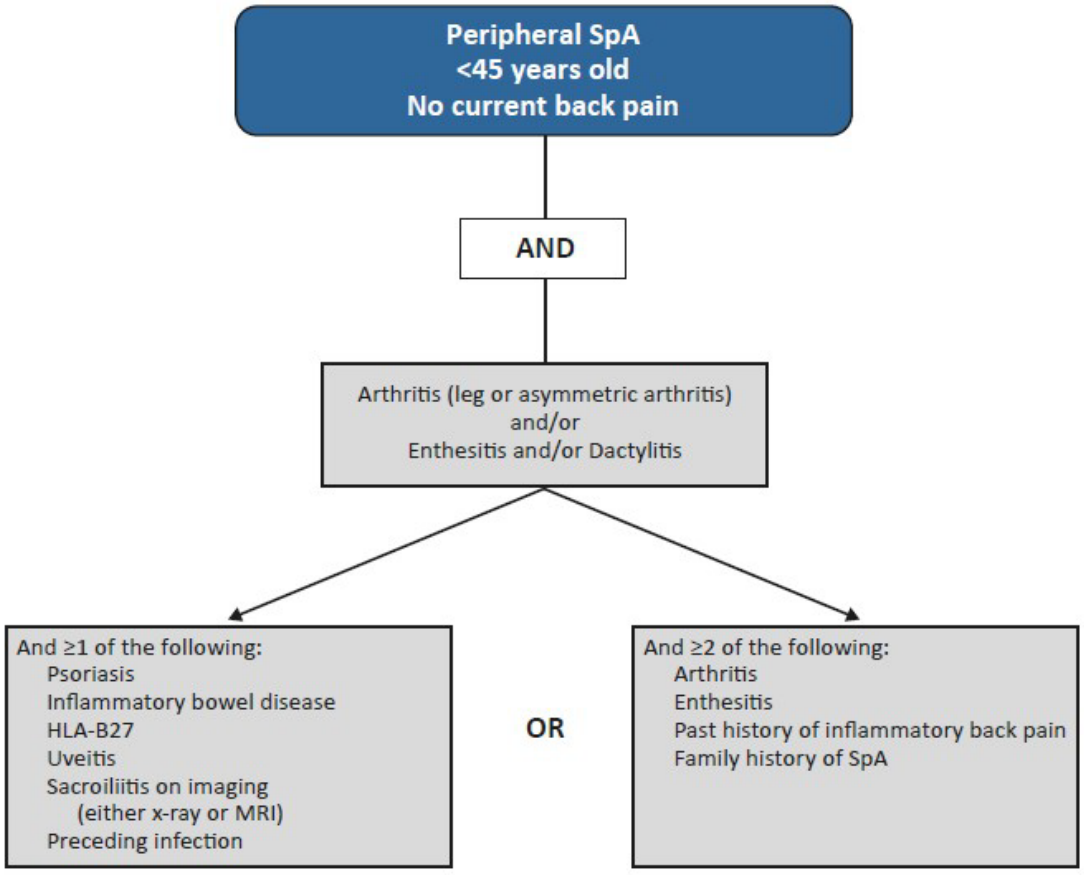

Figure 3. Classification criteria for peripheral SpA

HLA-B27, human leukocyte antigen B27; MRI, magnetic resonance imaging, SpA, spondyloarthritis

Inflammatory Back Pain

Back pain is one of the most common reasons people seek medical attention. Approximately 19.2% of the US population between 20 and 69 years of age, have 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*.[25] 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 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), 28% to 38% met the criteria for IBP.

Seventy to 80% of patients with axSpA have IBP. To identify patients at risk for axSpA, providers must be able to recognize IBP. 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:[1]

- 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

Comorbidities that have been identified in patients with axSpA include pulmonary fibrosis in the apex of the lungs (has not been reported in women), renal amyloidosis, cardiovascular disease (CVD), aortic insufficiency, cardiac conduction changes, asthma, hyperlipidemia, multiple sclerosis, uveitis, diabetes, hypertension, sleep apnea, spinal fractures, and psoriasis.[26, 27]

Initial Laboratory Testing

More than 90% of patients with axSpA test positive for HLA-B27.[28] Therefore, an HLA-B27 test should be performed as part of the initial work-up of patients considered at risk for this condition, if it has not already been done. Erythrocyte sedimentation rate (ESR) or CRP (preferred) are both non-specific measures of inflammation, but baseline levels should be obtained as they may be useful later for monitoring response to treatment. According to the National Institute for Health and Care Excellence (NICE),[29] a negative HLA-B27 or a normal CRP or ESR does not rule out the diagnosis of SpA.

Imaging for the Diagnosis of axSpA

The European League Against Rheumatism (EULAR) recommends plain films of the SI joints as the initial imaging test for patients whose history, physical exam, and laboratory findings suggest SpA.[30] The radiographs must show evidence of bilateral sacroiliitis grade 2–4 or unilateral sacroiliitis grade 3–4 to be consistent with AS. The grades of sacroiliitis on X-ray are as follows:[31]

- Grade 0 Normal
- Grade 1 Suspicious changes
- Grade 2 Minimum abnormality (normal joint space with minor erosions or sclerosis
- Grade 3 Unequivocal abnormality (moderate to advanced sacroiliitis with erosions, sclerosis and either widening, narrowing or partial fusion)
- Grade 4 Severe abnormality with complete ankylosis of the joint

According to the ASAS MRI working group,[32] if X-ray films do not show evidence of SI joint disease and the clinical suspicion for axSpA is high, MRI of the SI joints should be obtained. MRI can demonstrate early signs of sacroiliitis not detected on X-rays.[33] The finding of bone marrow edema without structural changes is consistent with nr-axSpA in the appropriate clinical setting[32] as are other MRI findings described above. If there is a high clinical suspicion of axSpA, negative X-rays and negative MRI, then the patient is managed

as having nr-axSpA if HLA-B27 is positive and at least two clinical findings consistent with axSpA are present (see Table 1).

Information about appropriate MRI techniques and findings can be found in papers by Schueller-Weidekamm et al.[34] and Lambert et al.[32] Plain films and MRI are the only imaging studies recommended by EULAR, with the possible very rare exception of computed tomography if the plain films are negative or MRI is contraindicated[30] or unavailable.

Progression of Disease

It can take years to develop the radiographic changes in the SI joints that are consistent with AS. The delay between the onset of symptoms and X-ray changes of the SI joint(s), which usually appear before changes in the spine, can be up to 12 years. As in other rheumatic diseases, the earlier treatment is started the better the outcome. However, in the case of a patient with normal X-rays of the SI joint(s), treatment may be delayed because of the absence of radiographic changes. Patients with a high clinical degree of suspicion of axSpA and negative X-rays may have nr-axSpA and these patients should have an MRI of their SI joints. Some have minimal changes of inflammation in the SI joints on MRI and with appropriate clinical findings can be diagnosed with nr-axSpA. Others with no X-ray or MRI changes of sacroiliitis may fit the description of nr-axSpA if they have a positive test for HLA-B27, and two other appropriate clinical findings (Table 1). Some patients with nr-axSpA can progress to AS over time.

Treatment

Goals of Therapy

According to the ASAS-EULAR recommendations for axSpA published in 2017,[35] "*The primary goal of treating the patient with axSpA is to maximize health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalization of function and social participatio*n" (Page 981).

A treat-to-target (T2T) approach has been advocated for the treatment of many chronic diseases (diabetes, CVD, RA, etc.)[20] and can also be used for the management of axSpA. Targets for the management of axSpA were first established in 2014 by an international Task Force, and were based primarily on a systematic review of the literature and the consensus of Task Force participants.[36] The Task Force noted that the literature available at the time was weak, but they did publish both principles and recommendations for treating axSpA 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.[36]

The recommendations for a T2T strategy in patients with axSpA were reviewed again in 2017.[37] 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. According to these recommendations, treatment should aim at providing the best care possible, using a combination of pharmacologic and non-pharmacologic interventions individualized for each patient.[35] The treatment plan should also consider the patient's general medical status, drug risks, existing comorbidities, current

medications, and psychosocial factors (Table 2). Care for patients with comorbidities should be coordinated with the appropriate medical specialists. ***Table 2. Treatment goals in patients with axSpA***

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

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

The recommended target for the management of axSpA is complete remission (absence of clinical or laboratory evidence of inflammation, including normal values of acute-phase reactants ESR and/or CRP and the absence of extra-articular disease). The target should always be documented in the medical record even though it is not always met.

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).[37] 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.

The Task Force noted that treatment of axSpA is expensive with high medical and societal costs, which must be considered when developing a plan for each patient.[35] They also recommended that any changes in management be the result of a joint decision based on a discussion between the patient and the provider.

For those patients with non-rheumatologic comorbidities, care should be coordinated with the appropriate medical specialists. Controlling symptoms and limiting inflammation is important to prevent further bone destruction and disability. Maximizing QoL and minimizing comorbidities is also important.

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:[38]

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

The BASDAI score, which has a minimum score of 0 and a maximum of 10, is calculated according to the following formula:

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

Scores of ≥4 suggest suboptimal control and patients with these scores are good candidates for a change in their medical therapy. The BASDAI score can also be calculated using the Medal online service or the *British Columbia Ministry of Health Form*.

The interpretation of BASDAI scores is important. They can tell the provider if the patient is improving, unchanged or worsening and may help in making treatment decisions. According to van der Heijde et al.[39] BASDAI scores can be evaluated as follows:

- <2 Low disease activity
- ≥2 to <4 Moderate disease activity
- ≥4 to ≤6 High disease activity
- >6 Very high disease activity

Since the BASDAI does not include the results of any acute phase reactants, if a patient's score is under 2, a CRP level should be obtained.[39, 40]

Non-pharmacologic Management of axSpA

In the 2010 and 2016 updates of their joint recommendations for the management of axSpA, the ASAS and EULAR provided the following general non-pharmacologic recommendations that should be used for every patient:[35, 41]

- Education is very important so that the patient can make informed decisions about his/her health care
- Encourage a regular exercise program ○ This includes physical therapy and:[29]
    - Stretching and strengthening exercises
    - Postural exercises

- Spinal extension exercises
- Aerobic exercise
- Range-of-motion exercises for the spine ○ Supervised exercises, on land or in the water, are preferred to home exercises, because they have been found to be more effective

○ If supervised exercise is not an option, then a home exercise program can be initiated ○ Supervised water exercise therapy in a hydrotherapy pool (water temperature between 32°C and 36°C) is encouraged[42]

- Patients may find joining patient associations and self-help groups to be useful
- Extra-articular manifestations should be managed collaboratively with the appropriate medical specialists
- Patients should be educated about the increased risk for both CVD and osteoporosis
- Patients with axSpA should be encouraged to stop smoking. It has been shown that there is an association between smoking and disease activity.

The exercise program, whether supervised or at home, should consist of functional exercises aimed at maintaining current mobility and strength, preventing or stabilizing spinal deformities, improving symptoms and function, and improving the patient's QoL. The program should also improve cardiopulmonary health.[43]

It should be stressed to the patient that these non-pharmacologic treatments are essential for obtaining optimal results. However, using only these methods will not provide maximum disease control.

Pharmacologic Treatment

Axial SpA

All drugs currently used for the treatment of axSpA are listed in Table 3. No difference in efficacy has been shown between different tumor necrosis factor inhibitor (TNFi) medications. However, in patients with IBD or recurrent uveitis, infliximab or adalimumab are preferred (Currently the only TNFi drug which is FDA approved for use in patients with nr-axial SpA is certolizumab pegol.

Table 3).[44] Interleukin 17 inhibitor (IL-17i) drugs should not be used in patients with ulcerative colitis (UC) or Crohn's disease. Currently the only TNFi drug which is FDA approved for use in patients with nr-axial SpA is certolizumab pegol.

Table 3. Drugs used to manage axSpA

Medication	Comments
NSAIDs including Coxibs	• 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 must be considered when choosing one of these drugs
TNFi[1] **Infliximab** **Certolizumab pegol** **Golimumab** **Adalimumab** **Etanercept**	• Certolizumab pegol is approved for use in nr-axSpA[45, 46] and AS. No other TNFi drugs are currently approved for use in nr-axSpA • There are no data to support the use of one TNFi drug over another for AS except if the patient has IBD or recurrent uveitis • In the presence of IBD or recurrent uveitis, infliximab or adalimumab are preferred
IL-17i[2] **Secukinumab** **Ixekizumab**	• Can be used as the first line drug • If there is a contraindication to TNFi drugs, use an IL-17i drug as first-line treatment • Do not use in patients with IBD • Both secukinumab and ixekizumab are FDA approved for use in nr-axSpA
JAK inhibitor **Tofacitinib**	• Use instead of IL-17i for patients with UC

[1] Currently the only TNFi agent approved by the FDA for treatment of nr-axSpA is certolizumab pegol

[2]Both secukinumab[47] and ixekizumab[48] may be used for nr-axSpA

AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; Coxibs, cyclooxygenase-2 (COX-2) inhibitors; CVD, cardiovascular disease; IBD, inflammatory bowel disease; IL-17i, interleukin-17 inhibitor; JAK, Janus Kinase; nr-axSpA, non-radiographic axSpA; NSAIDs, non-steroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor; UC, ulcerative colitis

Active axSpA

The initial drug of choice for patients with axSpA is a non-steroidal anti-inflammatory drug (NSAID; Figure 4A). The ASAS/EULAR recommendations state that NSAIDs should be given continuously up to the maximum dose and not on an "as needed" basis.[35] However, the physician should be aware of the gastrointestinal, cardiovascular, and renal risks of these medications and make the appropriate modifications in dosage when needed. The latest American College of Rheumatology (ACR) treatment recommendations published in 2019[49] also recommend continuous NSAIDs as the initial treatment for patients with active axSpA, suggesting any NSAID can be used over a 4 week period and if the patient does not improve, a different NSAID might be tried for another 4 weeks (Figure 4A). The ACR treatment

recommendations published in 2016 state that the benefits of NSAIDs at full dose “far outweighed” (Page 6) the risks.

If there is inadequate improvement with NSAIDs or a trial of a second anti-inflammatory is not desired (Figure 4B), a TNFi or IL-17i drug should be started with or without an NSAID. For nraxSpA there are only 3 drugs which are currently approved by the FDA; the TNFi drug certolizumab pegol; and the IL-17i drugs secukinumab and ixekizumab. Patients should be reevaluated after 2–4 months of treatment, to determine if they have reached their target or low disease activity. All TNFi drugs are considered to be equally effective, so for most patients with AS any one of them may be used. However, in patients with IBD or recurrent uveitis, infliximab or adalimumab are preferred (Currently the only TNFi drug which is FDA approved for use in patients with nr-axial SpA is certolizumab pegol.

Table 3).[44] If the patient has UC or Crohn’s disease then tofacitinib could be tried. In some cases, providers may decide to continue NSAIDs when a TNFi agent is used.

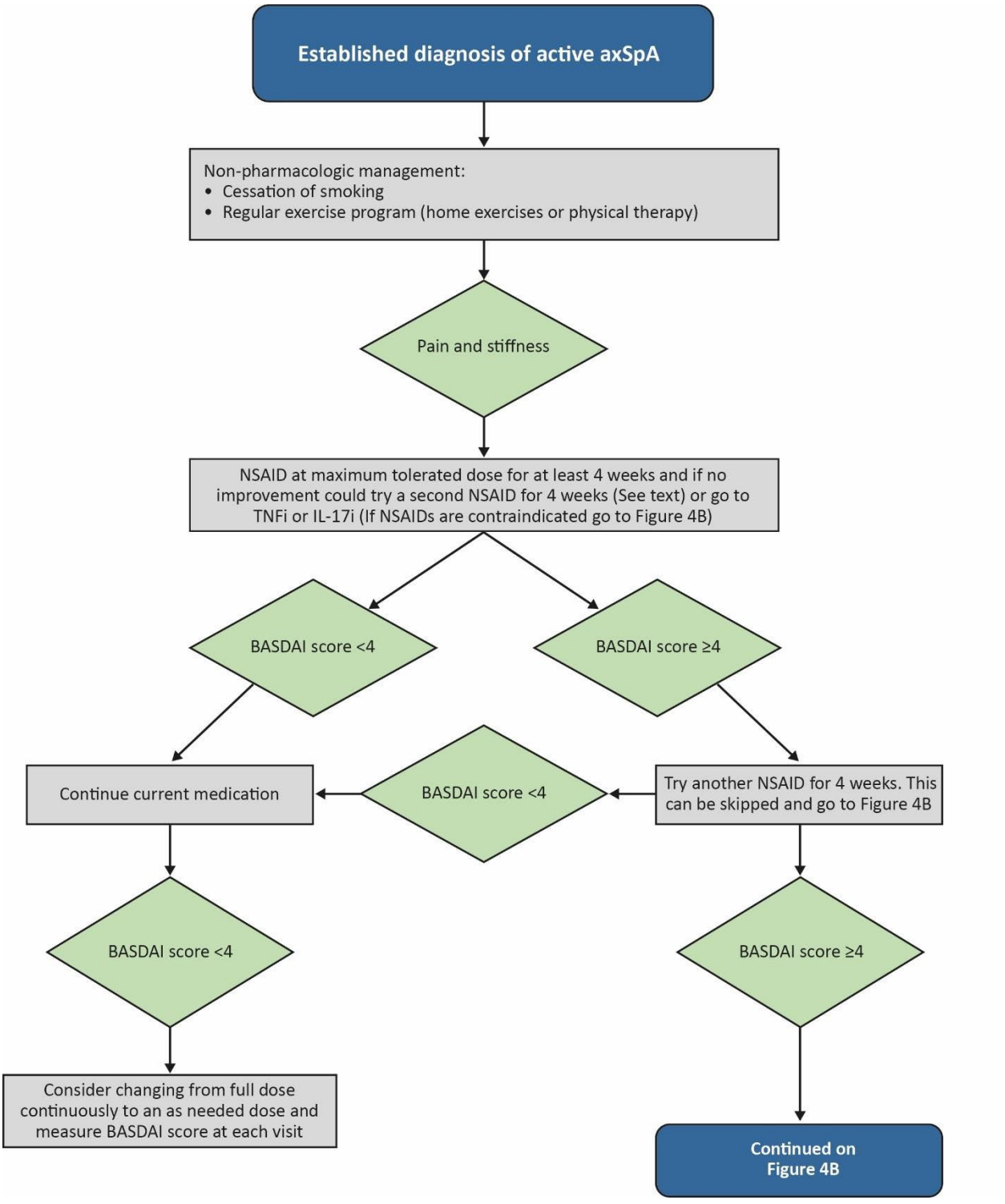

Figure 4A. Management of patients with active axSpA

axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IL-17i, Interleukin-17 inhibitor; NSAID, nonsteroidal anti-inflammatory drug; TNFi tumor necrosis factor inhibitor

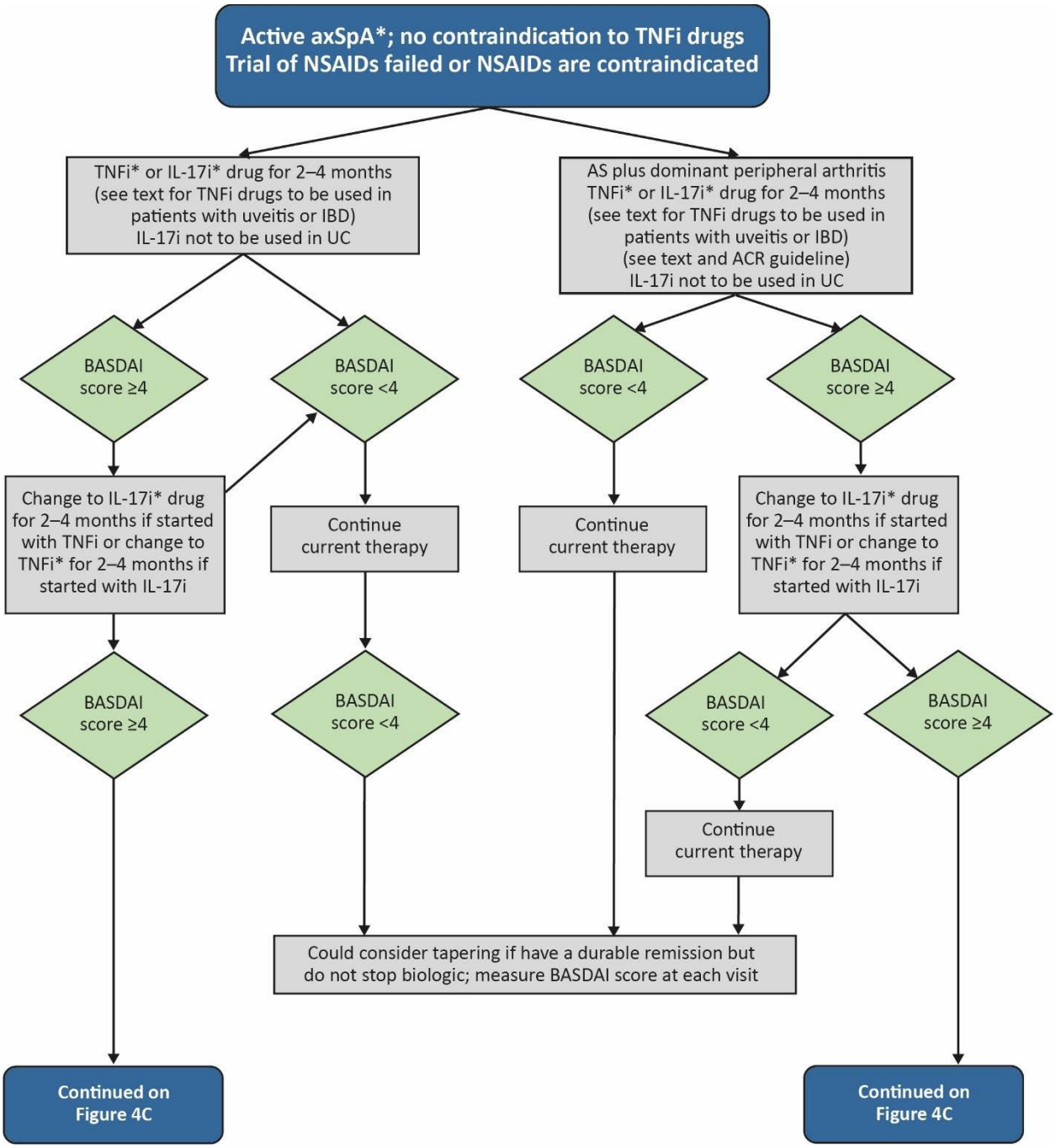

Figure 4B. Management of patients with active axSpA and poor response to NSAIDs or NSAIDs contraindicated; no contraindication of TNFi drugs

ACR, American College of Rheumatology; AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IBD, inflammatory bowel disease; IL-17i, interleukin-17 inhibitor; NSAIDs, non-steroidal antiinflammatory drugs; TNFi, tumor necrosis factor inhibitor; UC, ulcerative colitis

Conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), such as methotrexate and sulfasalazine, have little if any role in the treatment of patients with axSpA except perhaps in one clinical scenario:[41, 44, 49] patients with peripheral arthritis dominant axSpA. In these patients, if NSAIDs fail, sulfasalazine or methotrexate could be considered but TNFi or IL-17i agents are preferred. The results of treatment with csDMARDs should be evaluated after 3 months and if the patient fails to adequately respond to either of these drugs, a TNFi or IL-17i drug could be started. In the unlikely situation that a patient with axSpA and peripheral arthritis has a good response of axial symptoms to a TNFi or IL-17i drug but a poor response of their peripheral symptoms, the ACR suggests adding sulfasalazine to the biologic. If a patient with active axSpA does not respond to a TNFi drug, a biosimilar of that **reference drug should not be used**.[49]

Patients with an inadequate response to the initial TNFi drug could be changed to an IL-17i and re-evaluated after 2–4 months; those initially treated with an IL-17i drug should be switched to a TNFi drug and also re-evaluated in 2–4 months.[49] For patients with IBD or recurrent uveitis, infliximab or adalimumab are preferred (Currently the only TNFi drug which is FDA approved for use in patients with nr-axial SpA is certolizumab pegol.

Table 3).[44] If the patient has UC then tofacitinib could be tried. In addition, some providers may decide to continue NSAIDs when a TNFi drug is used.

Patients who have failed to adequately improve on the first TNFi drug or the first IL-17i drug should be started on a drug with a different mode of action for 2–4 months and then re-evaluated (

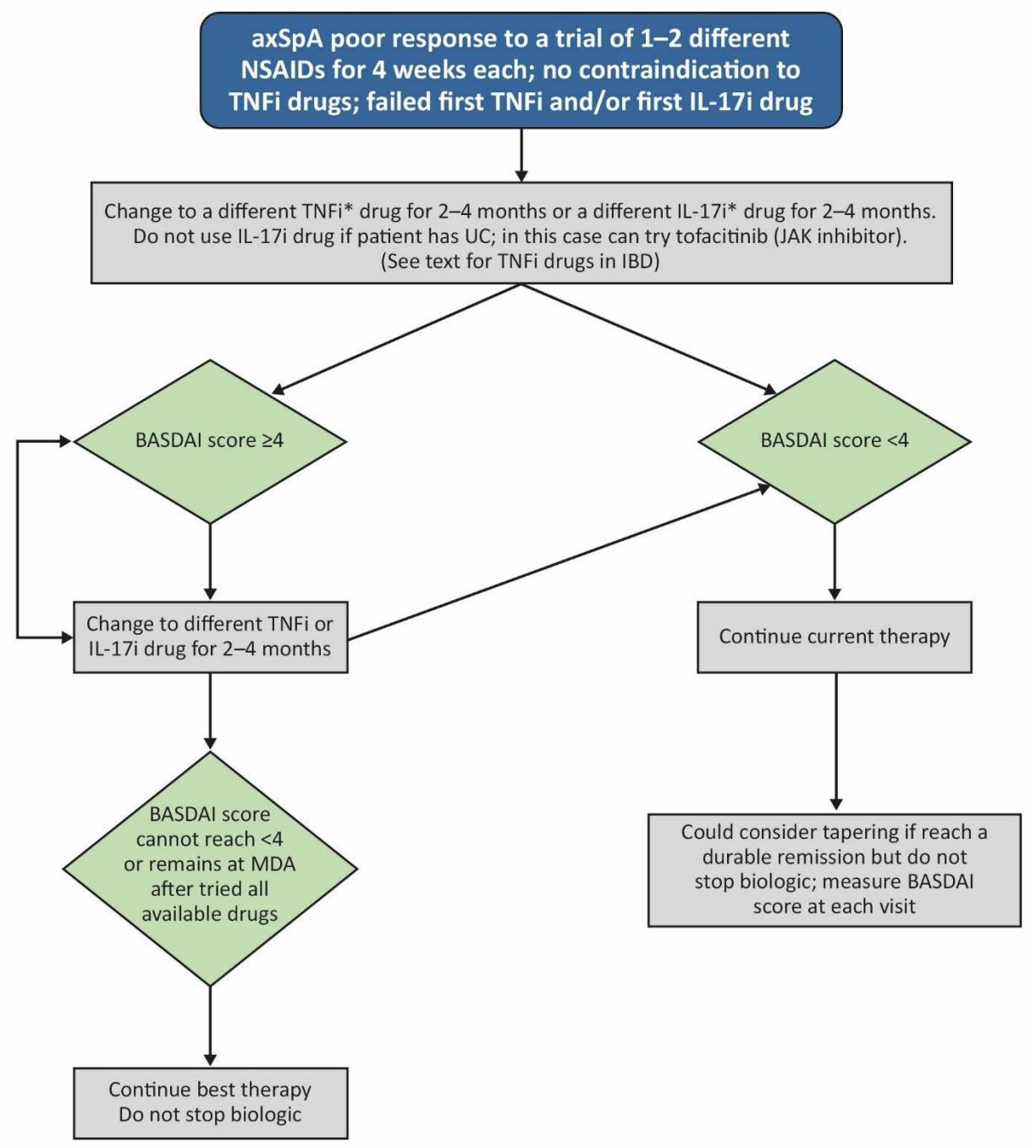

Figure 4C). For patients with IBD or recurrent uveitis, infliximab or adalimumab are preferred (Currently the only TNFi drug which is FDA approved for use in patients with nr-axial SpA is certolizumab pegol.

Table 3).[26] If the patient has UC, then tofacitinib could be tried. Patients who have contraindications to the use of a TNFi agent could be given an IL-17i drug initially if NSAIDs do not achieve the desired result, except for patients with IBD. If the first IL-17i fails to achieve a BASDAI score of <4 a different IL-17i agent could be tried. Patients with UC could be treated with tofacitinib (

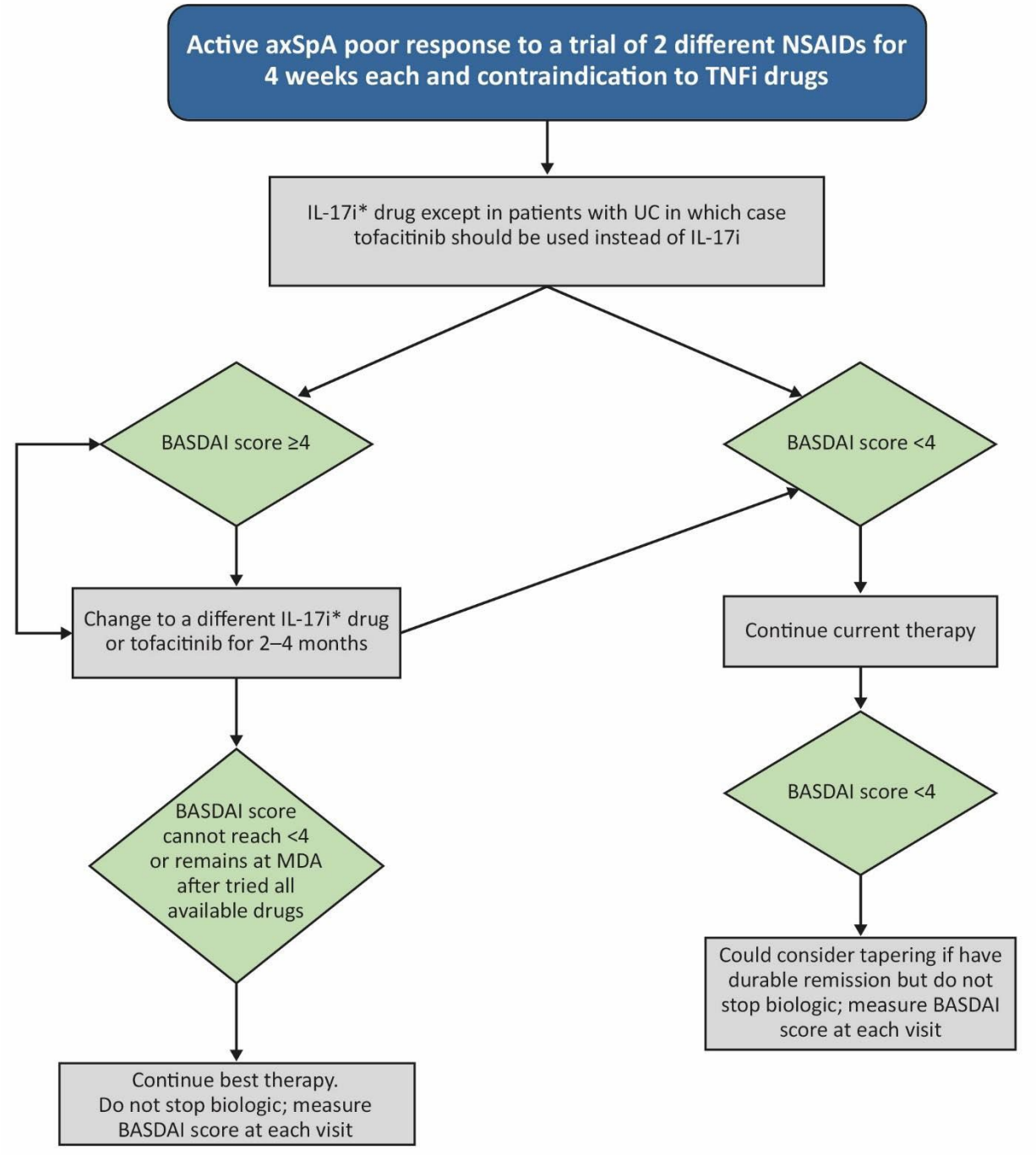

Figure 4).[49] If a patient with axSpA initially responds well to a TNFi agent and then relapses, the ACR recommends changing to a different TNFi drug (Figure 4E).[49]

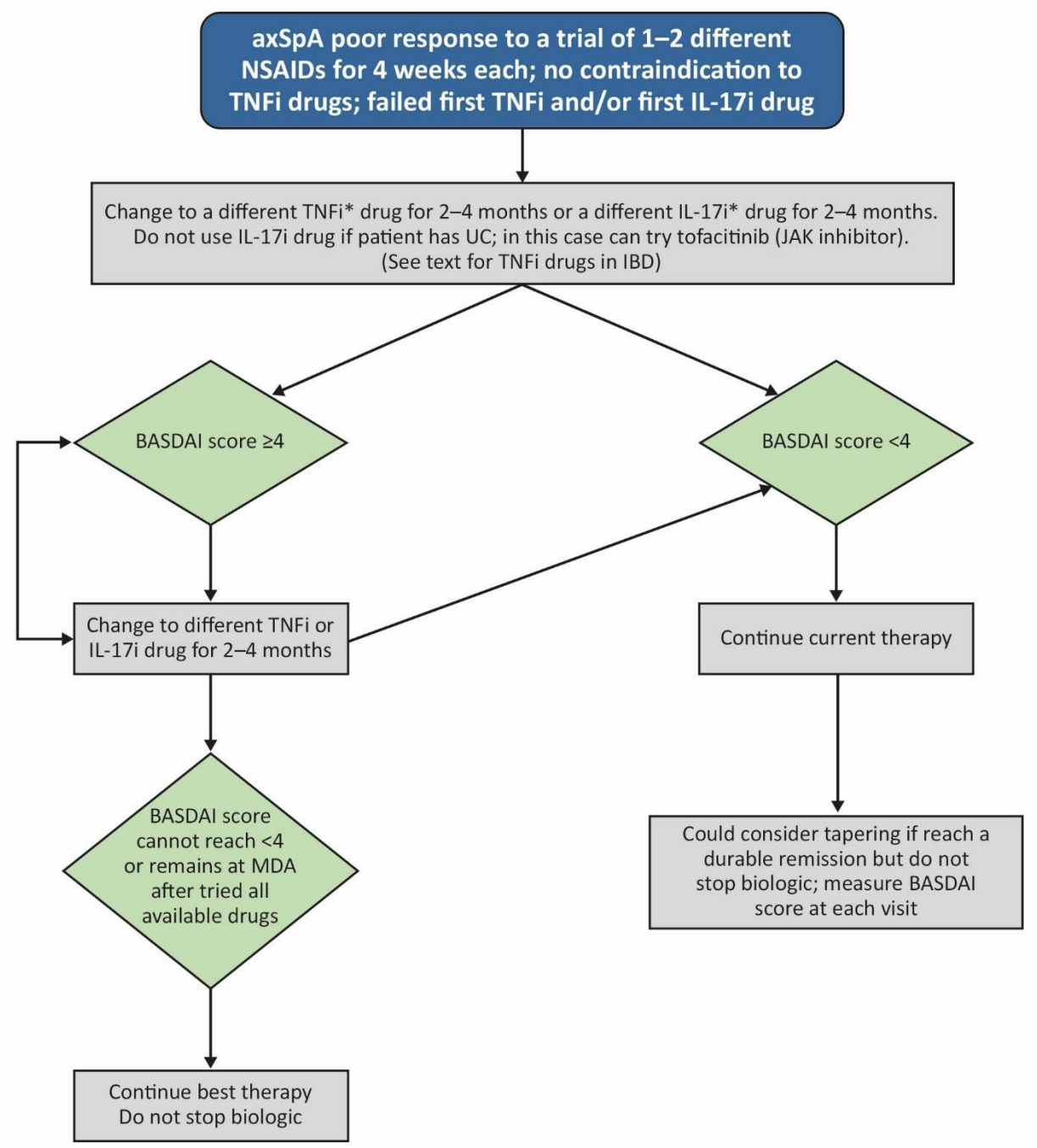

Figure 4C. Management of patients with active axSpA; poor response to NSAIDS; poor response to first TNFi drug and first IL-17i drug

axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IBD, inflammatory bowel disease; IL17i, interleukin-17 inhibitor; JAK, Janus kinase; MDA, moderate disease activity; NSAIDS, non-steroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor; UC, ulcerative colitis

* For nr-axSpA patients the only TNFi drug which is currently FDA approved is certolizumab pergol. The approved IL-17 drugs for nr-axSpA are secukinumab and ixekizumab.

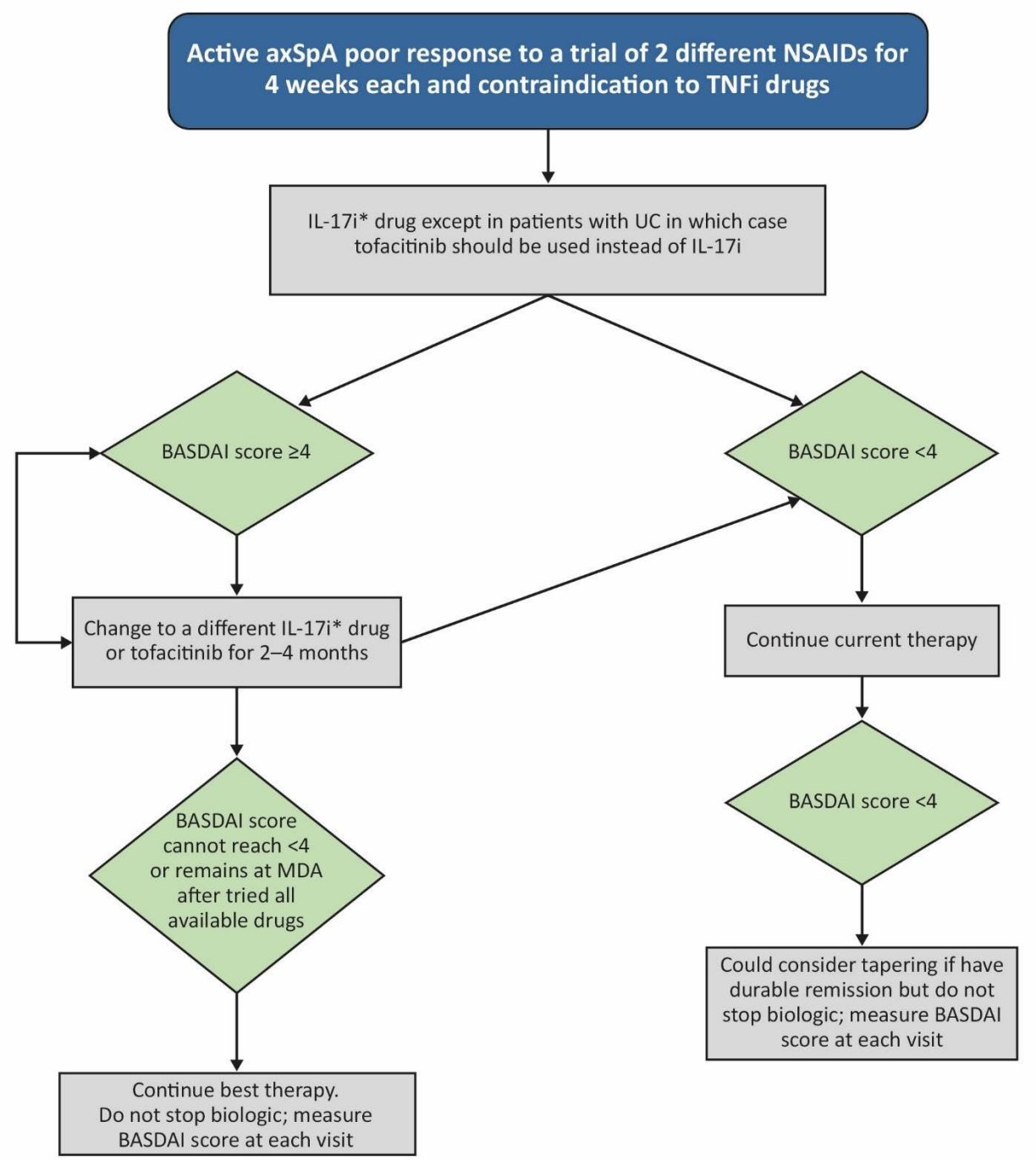

Figure 4D. Management of patients with active axSpA and contraindications to TNFi drugs

axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IL-17i, interleukin-17 inhibitor; MDA, moderate disease activity; NSAIDs, non-steroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor; UC, ulcerative colitis.

* For nr-axSpA patients the approved IL-17i drugs are secukinumab and ixekizumab.

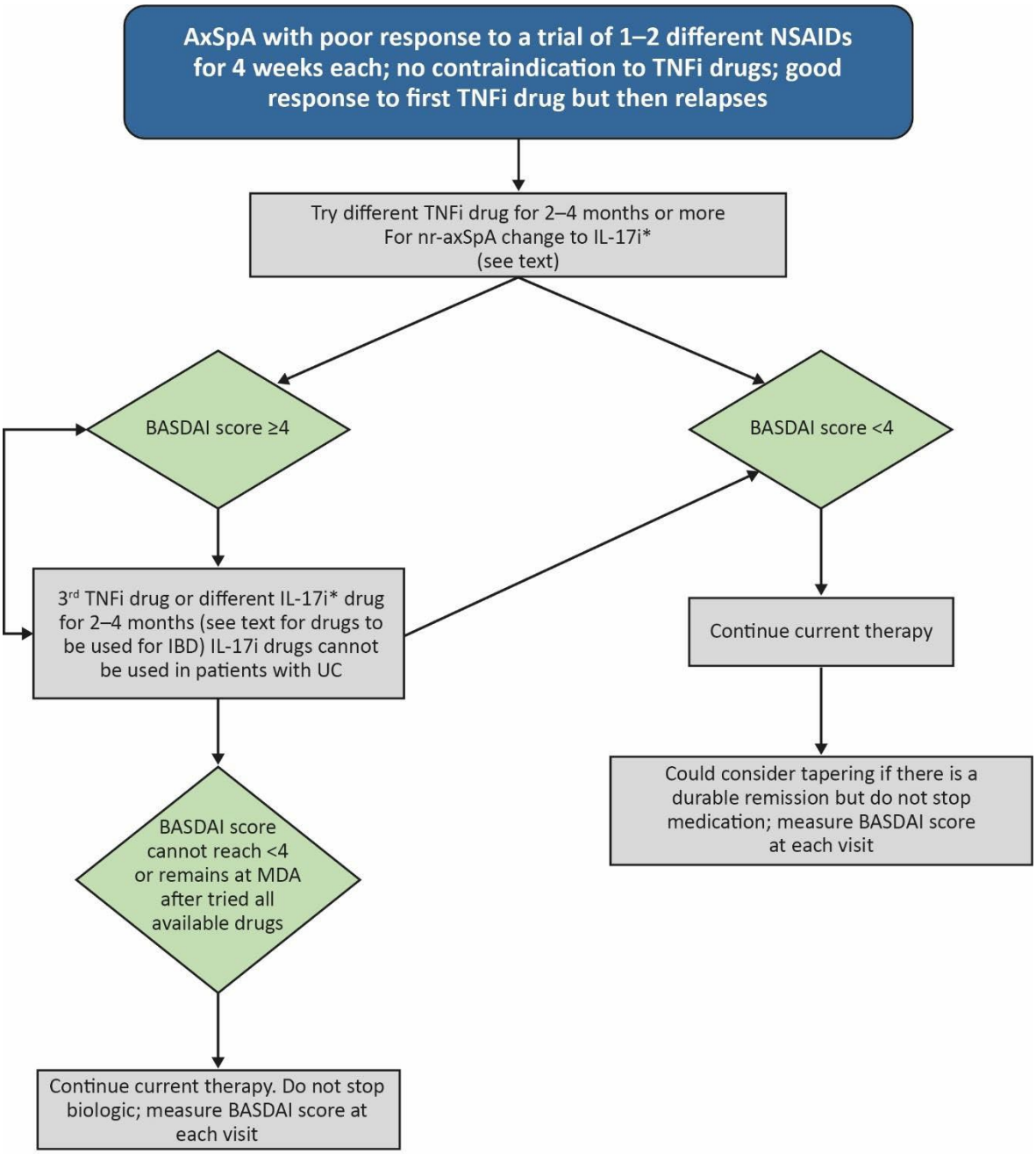

Figure 4E. Management of patients with active axSpA and poor response to NSAIDs; no contraindication to TNFi drugs; initially did well on a TNFi drug then relapsed

axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; FDA, Food and Drug Administration; IBD, inflammatory bowel disease; IL-17i, interleukin-17 inhibitor; MDA, moderate disease activity; nr-axSpA, non-radiographic axial spondyloarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor; UC, ulcerative colitis

* For nr-axSpA patients the only TNFi drug which is currently FDA approved is certolizumab pergol. The approved IL-17 drugs for nr-axSpA are secukinumab and ixekizumab.

The ACR does not recommend the use of systemic glucocorticoids.[49] Glucocorticoid injections into the SI joints can be considered if the patient's only symptom is sacroiliitis. If a patient has stable axial disease and active enthesitis local injections can be given but not into or around the Achilles, patellar and quadriceps tendons (see Currently the only TNFi drug which is FDA approved for use in patients with nraxial SpA is certolizumab pegol.

Table 3).

In addition to pharmacologic treatment; the ACR, EULAR, and ASAS recommend total hip arthroplasty for patients with refractory pain or disability and structural damage to the hip.[35, 44]

Stable axial SpA (AS and nr-axSpA)

For patients with stable disease treated with only NSAIDs, the provider may change from continuous to as needed NSAIDs. Patients who are treated with NSAIDs and a TNFi agent could stop the NSAID and continue the TNFi. If a patient has stabilized on a regimen of a TNFi agent plus a csDMARD the latter could be discontinued. Tapering of biologics (TNFi or IL-17i) can be considered if a patient has a durable remission but the biologic should not be stopped. The decision to taper a drug should be a shared decision made by the provider with input and agreement of the patient (Figure 5).[49]

Long-term systemic glucocorticoids should not be used for patients with stable AS.[35, 44, 49]

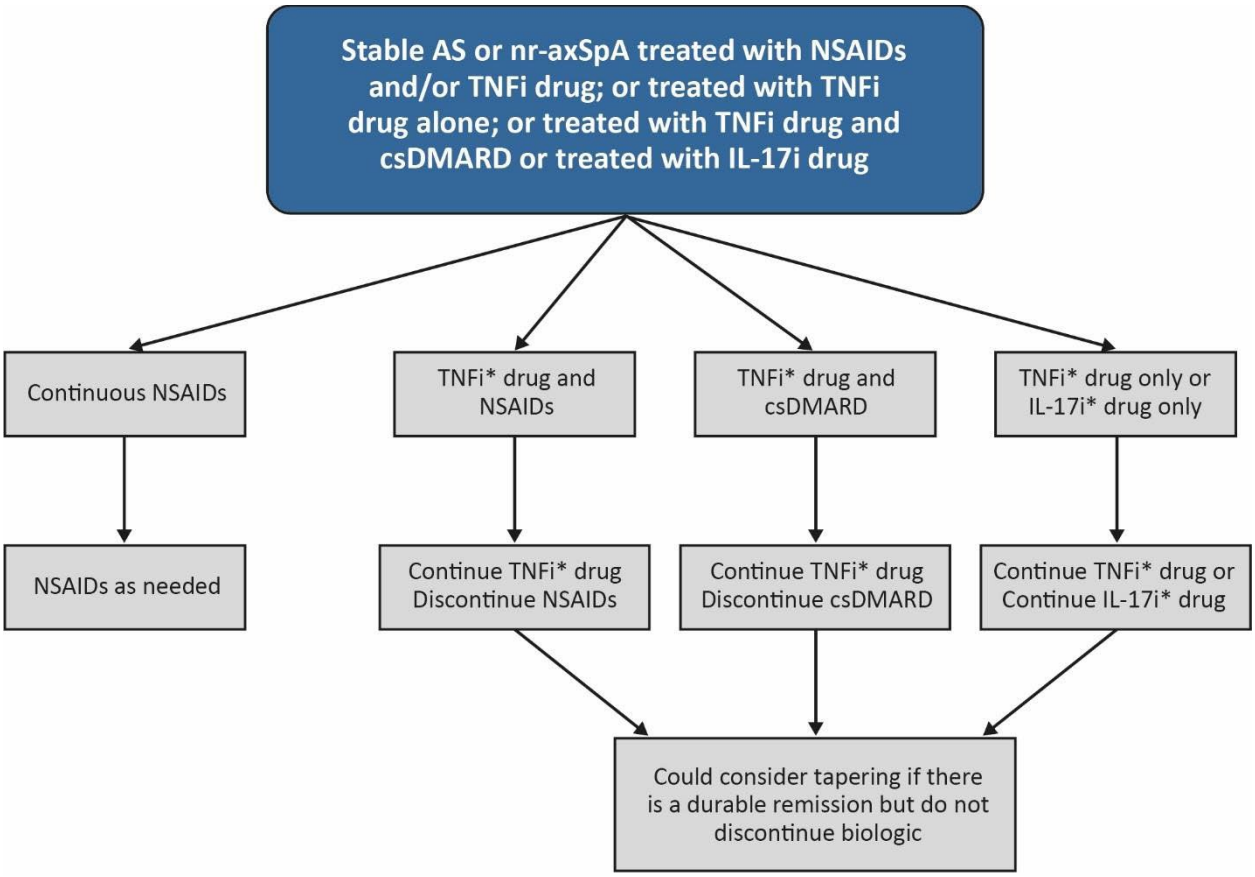

Figure 5. Management of stable axSpA

AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; csDMARD; conventional synthetic disease-modifying antirheumatic drugs; IBD, inflammatory bowel disease; IL-17i, interleukin-17 inhibitor; nr-axSpA, non-radiographic axial spondyloarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor

* For nr-axSpA patients the only TNFi drug which is currently FDA approved is certolizumab pergol. The approved IL-17 drugs for nr-axSpA are secukinumab and ixekizumab

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:[35, 49]

- Clinical findings
- BASDAI score at every visit
- 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
- Based on expert consensus, the ACR also recommends interval blood tests for ESR and/or CRP[44]

- MRI of the pelvis for patients with axSpA treated with a biologic when the activity of disease is uncertain, or findings may influence treatment; MRI of the spine can be substituted for MRI of the pelvis in patients with AS; the spine and pelvis should not be imaged at the same time
- Screening for low bone mass or osteoporosis with a DXA scan should be done at baseline and as indicated but at least every 2 years.

MRI of the pelvis or spine should not be performed in patients who are clinically stable.

Repeat radiographs or MRI of the spine in patients with active or stable axSpA should not be performed routinely. They may be helpful in evaluating a new complaint of spinal pain. According to the ACR guidelines routine imaging of the spine does not improve patient outcomes.[49]

When patients on a biologic drug are in durable remission, the provider could consider drug tapering.[35] 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.[35] 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 together 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 short tau inversion recovery (STIR) images and low-signal on T1 non-contrast images.

Ankylosis Decreased signal intensity on all sequences but may be surrounded by increased signal intensity on T1.

Dactylitis A sausage-shaped digit associated with psoriatic arthritis.

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 in a very high percentage of patients with AS, but it 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:

1. Age <40 years old
2. Insidious onset
3. Back pain that improves with exercise
4. No improvement with rest
5. Pain at night that improves when getting up.

Sacroiliitis Inflammation of the SI joints. For the purposes of the ASAS criteria for axSpA, 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 gadolinium contrast.

References

1. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N, et al. The development of assessment of SpondyloArthritis International Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777-783.
2. Sieper J, van der Heijde D. Nonradiographic axial spondyloarthritis: new definition of an old disease? *Arthritis Rheum* 2013;65:543551.
3. Keat A, Barkham N, Bhalla A, Gaffney K, Marzo-Ortega H, et al. BSR guidelines for prescribing TNF-alpha blockers in adults with ankylosing spondylitis. Report of a working party of the British Society for Rheumatology. *Rheumatology (Oxford)* 2005;44:939-947.
4. Strand V, Singh JA. Patient burden of axial spondyloarthritis. *J Clin Rheumatol* 2017;23:383-391.
5. Osterhaus JT, Purcaru O. Discriminant validity, responsiveness and reliability of the arthritis-specific Work Productivity Survey assessing workplace and household productivity within and outside the home in patients with axial spondyloarthritis, including nonradiographic axial spondyloarthritis and ankylosing spondylitis. *Arthritis Res Ther* 2014;16:R164.
6. Salaffi F, Carotti M, Gasparini S, Intorcia M, Grassi W. The health-related quality of life in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a comparison with a selected sample of healthy people. *Health Qual Life Outcomes* 2009;7:25.
7. Greenberg JD, Palmer JB, Li Y, Herrera V, Tsang Y, Liao M. Healthcare Resource Use and Direct Costs in Patients with Ankylosing Spondylitis and Psoriatic Arthritis in a Large US Cohort. *J Rheumatol* 2016;43:88-96.
8. Walsh JA, Song X, Kim G, Park Y. Healthcare utilization and direct costs in patients with ankylosing spondylitis using a large US administrative claims database. *Rheumatol Ther* 2018;5:463-474.
9. Guillemin F, Saraux A, Guggenbuhl P, Roux CH, Fardellone P, et al. Prevalence of rheumatoid arthritis in France: 2001. *Ann Rheum Dis* 2005;64:1427-1430.
10. Saraux A, Guillemin F, Guggenbuhl P, Roux CH, Fardellone P, et al. Prevalence of spondyloarthropathies in France: 2001. *Ann Rheum Dis* 2005;64:1431-1435.
11. Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum* 2008;58:15-25.
12. Gladman D. Spondyloarthropathies. Educational Review Manual. http://jacobimed.org/public/Ambulatory_files/Educational/Articles/IMRheum_02.pdf. Accessed November 9, 2020.
13. Rudwaleit M, Haibel H, Baraliakos X, Listing J, Marker-Hermann E, et al. The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. *Arthritis Rheum* 2009;60:717-727.
14. Rudwaleit M, Landewe R, van der Heijde D, Listing J, Brandt J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. *Ann Rheum Dis* 2009;68:770-776.
15. SPA-imaging.org. Diagnosis of sacroiliitis by radiography. http://www.spaimaging.org/default.asp?MainMenuId=394& PageId=397. Accessed November 9, 2020.
16. Keat A, Bennett AN, Gaffney K, Marzo-Ortega H, Sengupta R, Everiss T. Should axial spondyloarthritis without radiographic changes be treated with anti-TNF agents? *Rheumatol Int* 2017;37:327-336.
17. Robinson PC, Sengupta R, Siebert S. Nonradiographic axial spondyloarthritis (nraxSpA): advances in classification, imaging

and therapy. *Rheumatol Ther* 2019;6:165177.
18. Boonen A, Sieper J, van der Heijde D, Dougados M, Bukowski JF, et al. The burden of non-radiographic axial spondyloarthritis. *Semin Arthritis Rheum* 2015;44:556-562.
19. Lee W, Reveille JD, Davis JC, Jr., Learch TJ, Ward MM, Weisman MH. Are there gender differences in severity of ankylosing spondylitis? Results from the PSOAS cohort. *Ann Rheum Dis* 2007;66:633-638.
20. Strand V, Rao SA, Shillington AC, Cifaldi MA, McGuire M, Ruderman EM. Prevalence of axial spondyloarthritis in United States rheumatology practices: Assessment of SpondyloArthritis International Society criteria versus rheumatology expert clinical diagnosis. *Arthritis Care Res (Hoboken)* 2013;65:1299-1306.
21. Feldtkeller E, Khan MA, van der Heijde D, van der Linden S, Braun J. Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis. *Rheumatol Int* 2003;23:61-66.
22. Rudwaleit M, Sieper J. Referral strategies for early diagnosis of axial spondyloarthritis. *Nat Rev Rheumatol* 2012;8:262-268.
23. Wendling D, Claudepierre P, Prati C. Early diagnosis and management are crucial in spondyloarthritis. *Joint Bone Spine* 2013;80:582-585.
24. Rudwaleit M, van der Heijde D, Landewe R, Akkoc N, Brandt J, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis* 2011;70:25-31.
25. Weisman MH, Witter JP, Reveille JD. The prevalence of inflammatory back pain: population-based estimates from the US National Health and Nutrition Examination Survey, 2009-10. *Ann Rheum Dis* 2013;72:369-373.
26. Walsh JA, Song X, Kim G, Park Y. Evaluation of the comorbidity burden in patients with ankylosing spondylitis using a large US administrative claims data set. *Clin Rheumatol* 2018;37:1869-1878.
27. Gran JT, Ostensen M. Spondyloarthritides in females. *Baillieres Clin Rheumatol* 1998;12:695-715.
28. Sheehan NJ. The ramifications of HLA-B27. *J R Soc Med* 2004;97:10-14.
29. NICE Guideline. Spondyloarthritis in Over 16s: Diagnosis and Management. 2017. https://www.nice.org.uk/guidance/ng65/resources/spondyloarthritis-in-over-16sdiagnosis-and-management-pdf-1837575441349 2020. . Accessed November 9,
30. Mandl P, Navarro-Compan V, Terslev L, Aegerter P, van der Heijde D, et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. *Ann Rheum Dis* 2015;74:1327-1339.
31. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984;27:361-368.
32. Lambert RG, Bakker PA, van der Heijde D, Weber U, Rudwaleit M, et al. Defining active sacroiliitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI working group. *Ann Rheum Dis* 2016;75:1958-1963.
33. Braun J, Bollow M, Eggens U, Konig H, Distler A, Sieper J. Use of dynamic magnetic resonance imaging with fast imaging in the detection of early and advanced sacroiliitis in spondylarthropathy patients. *Arthritis Rheum* 1994;37:1039-1045.
34. Schueller-Weidekamm C, Mascarenhas VV, Sudol-Szopinska I, Boutry N, Plagou A, et al. Imaging and interpretation of axial spondylarthritis: the radiologist's perspective--consensus of the Arthritis Subcommittee of the ESSR. *Semin Musculoskelet Radiol* 2014;18:265-279.
35. van der Heijde D, Ramiro S, Landewe R, Baraliakos X, Van den Bosch F, et al. 2016 update of the ASAS-EULAR management

recommendations for axial spondyloarthritis. *Ann Rheum Dis* 2017;76:978-991.
36. Smolen JS, Braun J, Dougados M, Emery P, Fitzgerald O, et al. Treating spondyloarthritis, including ankylosing spondylitis and psoriatic arthritis, to target: recommendations of an international task force. *Ann Rheum Dis* 2014;73:6-16.
37. Smolen JS, Schols M, Braun J, Dougados M, FitzGerald O, et al. Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. *Ann Rheum Dis* 2018;77:3-17.
38. Calculate by QxMD. BASDAI. Assess Disease Activity in Ankylosing Spondylitis. https://qxmd.com/calculate/basdai. Accessed November 9, 2020.
39. van der Heijde D, Deodhar A, Fleischmann R, Mease PJ, Rudwaleit M, et al. Early disease activity or clinical response as predictors of long-term outcomes with certolizumab pegol in axial spondyloarthritis or psoriatic arthritis. *Arthritis Care Res (Hoboken)* 2017;69:1030-1039.
40. Ramiro S, van der Heijde D, van Tubergen A, Stolwijk C, Dougados M, et al. Higher disease activity leads to more structural damage in the spine in ankylosing spondylitis: 12-year longitudinal data from the OASIS cohort. *Ann Rheum Dis* 2014;73:1455-1461.
41. Braun J, van den Berg R, Baraliakos X, Boehm H, Burgos-Vargas R, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896-904.
42. Dundar U, Solak O, Toktas H, Demirdal US, Subasi V, et al. Effect of aquatic exercise on ankylosing spondylitis: a randomized controlled trial. *Rheumatol Int* 2014;34:15051511.
43. Reimold AM, Chandran V. Nonpharmacologic therapies in spondyloarthritis. *Best Pract Res Clin Rheumatol* 2014;28:779-792.
44. Ward MM, Deodhar A, Akl EA, Lui A, Ermann J, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations United Rheumatology Clinical Practice Guideline for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol* 2016;68:282-298.
45. Food and Drug Administration. FDA approves treatment for patients with a type of inflammatory arthritis [FDA news release]. May 28, 2019, https://www.fda.gov/newsevents/press-announcements/fda-approvestreatment-patients-type-inflammatoryarthritis. Accessed November 9, 2020.
46. Deodhar A, Gensler LS, Kay J, Maksymowych WP, Haroon N, et al. A fifty-two-week, randomized, placebo-controlled trial of certolizumab pegol in nonradiographic axial spondyloarthritis. *Arthritis Rheumatol* 2019;71:1101-1111.
47. Novartis. Novartis Cosentyx receives FDA approval for new indication to treat active non-radiographic axial spondyloarthritis. https://www.novartis.com/news/mediareleases/novartis-cosentyx-receives-fdaapproval-new-indication-treat-active-nonradiographic-axial-spondyloarthritis. Accessed November 17, 2020.
48. Food and Drug Administration. FDA approves Eli Lilly's Taltz for nonradiographic axial spondyloarthritis. https://www.fdanews.com/articles/197381fda-approves-eli-lillys-taltz-fornonradiographic-axial-spondyloarthritis. Accessed November 17, 2020.
49. Ward MM, Deodhar A, Gensler LS, Dubreuil M, Yu D, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis

Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol* 2019;71:1599-1613.

Document Updates

Document Version	Description of Changes	Approval Date
1.1.2016	Creation of first version	06 Apr 2016
1.1.2017	2017 update	Mar 2017
1.1.2018	2018 update	Mar 2018
1.1.2019	2019 update	Aug 2019
1.1.2021	2021 update- no changes from 2020	March 2021
1.1.2023	2023 Update no change	Feb 2023