Specialist Pharmacy Service

NICE Bites

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A summary of prescribing recommendations from NICE guidance

Spondyloarthritis in over 16s: diagnosis and management

NICE NG65; 2017

This guideline covers the diagnosis and management of suspected or confirmed spondyloarthritis in adults ≥16 years.

Definition of terms

NSAID	non-steroidal anti-inflammatory drug
TNF-alpha inhibitor	tumor necrosis factor-alpha inhibitor
DMARDs	disease modifying anti-rheumatic drugs
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
PsARC	Psoriatic Arthritis Response Criteria
PASI	Psoriasis Area and Severity Index
VAS	visual analogue scale
PAS	patient access scheme

- Spondyloarthritis is a group of inflammatory conditions that have a range of manifestations and may be predominantly:
  - **axial;** which mainly causes pain and stiffness in the back,
  - **peripheral**; which mainly causes pain, stiffness and swelling in the hands, feet arms and legs.
- People with predominantly axial spondyloarthritis may have additional peripheral symptoms and vice versa.
- Axial presentations of spondyloarthritis are often misdiagnosed as mechanical low back pain, leading to delays in accessing effective treatments. Peripheral presentations are often seen as unrelated joint/tendon problems, and can be misdiagnosed as problems can move around between joints.

Spondyloarthritis

Axial:	Peripheral:
♦ Radiographic (ankylosing spondylitis)	♦ Psoriatic arthritis
♦ Non-radiographic	♦ Reactive arthritis
	♦ Enteropathic spondyloarthritis

Recognition and diagnosis

- Spondyloarthritis can have diverse symptoms and be difficult to identify, which can lead to delayed or missed diagnoses. Signs and symptoms may be musculoskeletal (e.g. inflammatory back pain, enthesitis and dactylitis) or extra-articular (e.g.uveitis and psoriasis [including psoriatic nail symptoms]). Risk factors include recent genitourinary infection and a family history of spondyloarthritis/psoriasis.
- Be aware that axial and peripheral spondyloarthritis may be missed, even if onset is associated with established comorbidities (e.g. uveitis, psoriasis, inflammatory bowel disease or a gastrointestinal or genitourinary infection).
- Be aware that axial spondyloarthritis:
  - affects a similar number of women as men,
  - can occur in people who are human leukocyte antigen B27 (HLA-B27) negative,
  - may be present despite no evidence of sacroiliitis on plain film X-ray.
- In specialist care settings, consider using validated spondyloarthritis criteria to guide clinical judgement when diagnosing spondyloarthritis. See NICE pathway.
- **Do NOT** rule out a diagnosis of spondyloarthritis:
  - solely on the basis of a negative HLA-B27 result,
  - if a person's C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are normal.

Referral criteria – see NICE pathway for suspected spondyloarthritis.

Treatment and management

Axial spondyloarthritis

Non-pharmacological treatment

- Refer to a specialist physiotherapist to start an individualised, structured exercise programme. See NICE pathway.
- Consider referral to hydrotherapy for pain or other specialist therapists for people having difficulties with everyday activities.

Pharmacological treatment

NSAIDs

- Offer NSAIDs at the lowest effective dose to people with pain associated with axial spondyloarthritis. Consider appropriate clinical assessment, ongoing monitoring of risk factors, and use of gastroprotective treatment.
- If an NSAID taken at the maximum tolerated dose for 2 to 4 weeks does not provide adequate pain relief, consider switching to another NSAID.

Biological DMARDs

TNF-alpha inhibitors. See NICE TA383.

- In adults whose disease has responded inadequately to, or who cannot tolerate, NSAIDs:
  - adalimumab*, certolizumab pegol*, etanercept*, golimumab* and infliximab* are recommended as options for treating **severe active ankylosing spondylitis**.
  - adalimumab*, certolizumab pegol* and etanercept* are recommended as options for treating **severe non-radiographic axial spondyloarthritis**.
- Infliximab is recommended only if treatment is started with the least expensive product. People currently receiving infliximab should be able to continue with the same product until they and their NHS clinician consider it appropriate to stop.
- Choice of treatment should be made after discussion between clinician and patient about advantages and disadvantages of treatments available. This may include considering associated conditions such as extra-articular manifestations. Of available suitable treatments choose the least expensive (taking into account administration costs and PAS).
- Assess response to TNF-alpha inhibitors 12 weeks after the start of treatment. Only continue treatment if there is clear evidence of response**.
- Treatment with another TNF-alpha inhibitor is recommended for people who cannot tolerate, or whose disease has not responded to the first TNF-alpha inhibitor, or whose disease has stopped responding after an initial response.

Interleukin inhibitor: secukinumab. See NICE TA407

- Secukinumab* is recommended as an option for treating **active ankylosing spondylitis** in adults whose disease has responded inadequately to conventional therapy (NSAIDs or TNF-alpha inhibitors) only if the company provides it with the discount agreed in the PAS.
- Assess response after 16 weeks of treatment. Only continue if there is clear evidence of response**.

* within its marketing authorisation

** response is defined as: a reduction in the BASDAI*** score to 50% of the pre-treatment value or by ≥2 units, **AND** a reduction in the spinal pain VAS*** by ≥2 cm.

*** when using BASDAI, and spinal pain VAS scores, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect responses and make any adjustments they consider appropriate.

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Spondyloarthritis in over 16's: diagnosis and management continued ……

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Peripheral spondyloarthritis

Pharmacological treatment

- Consider local corticosteroid injections as monotherapy for non-progressive monoarthritis.

Standard DMARDs

- Offer **standard** DMARDs to people with:
  - peripheral polyarthritis,
  - oligoarthritis,
  - persistent or progressive monoarthritis associated with peripheral spondyloarthritis.
- When deciding which DMARD to offer, take into account:
  - the person's needs, preferences and circumstances (such as pregnancy planning and alcohol consumption),
  - comorbidities such as uveitis, psoriasis and inflammatory bowel disease,
  - disease characteristics,
  - potential side effects.
- If a **standard** DMARD taken at the maximum tolerated dose for at least 3 months does not provide adequate relief from symptoms, consider switching to or adding another DMARD.

NSAIDs

- Consider NSAIDs as an adjunct to **standard** or **biological DMARDs** to manage symptoms. Use oral NSAIDs at the lowest effective dose for the shortest possible period of time. Consider appropriate clinical assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment.
- If NSAIDs do not provide adequate relief from symptoms, consider steroid injections (local or intramuscular) or short-term oral steroid therapy as an adjunct to **standard** DMARDs or **biological** DMARDs to manage symptoms.
- If extra-articular disease is adequately controlled by an existing **standard** DMARD but peripheral spondyloarthritis is not, consider adding another **standard** DMARD.

Psoriatic arthritis

Phosphodiesterase type-4 inhibitor: apremilast

- Apremilast, alone or in combination with DMARDs, is recommended as an option for treating active psoriatic arthritis in adults only if:
  - they have peripheral arthritis with ≥3 tender joints and ≥3 swollen joints, **AND**
  - their disease has not responded to adequate trials of at least 2 **standard** DMARDs, given either alone or in combination, **AND**
  - the company provides apremilast with the discount agreed in the PAS. See NICE TA433
- Stop apremilast at 16 weeks if psoriatic arthritis has not shown an adequate response using the PsARC[α]

Biological DMARDs

TNF-alpha inhibitors. See NICE TA199, TA220

- Etanercept*, infliximab*, adalimumab* and golimumab* are recommended for the treatment of adults with **active and progressive psoriatic arthritis**:
  - who have peripheral arthritis with ≥3 tender joints and ≥3 swollen joints, **AND**
  - their disease has not responded to adequate trials of at least 2 **standard** DMARDs, given alone or in combination,
  - golimumab; the company provides the 100mg dose at the same cost as the 50mg dose.
- Start treatment with the least expensive drug taking into account administration costs, dose and price per dose.
- Assess response at 12 weeks. Only continue if there is an adequate response using the PsARC[α].

Interleukin inhibitor: ustekinumab. See NICE TA340.

- Ustekinumab is recommended as an option alone or in combination with methotrexate for treating **active psoriatic arthritis** in adults only when:
  - TNF-alpha inhibitors would be considered but are contraindicated, **OR** the person has had treatment with ≥1 TNF-alpha inhibitors, **AND**
  - the company provides it in accordance with the PAS.
- Assess response at 24 weeks. Only continue if there is an adequate response using the PsARC[α].
- Patients already on apremilast or ustekinumab may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

[α]defined as improvement in at least 2 of the 4 PsARC [α α] criteria (one of which has to be joint tenderness or swelling score) with no worsening in any of the 4 criteria. People whose disease has a PASI 75 response but whose PsARC does not justify treatment continuation, should be assessed by a dermatologist.

[α α] when using PsARC, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect responses and make any adjustments they consider appropriate.

Reactive arthritis

- For reactive arthritis caused by gastrointestinal or genitourinary infection, antibiotics are **NOT** recommended
- After treating the initial infection, **DO NOT** offer long-term (≥4 weeks) treatment with antibiotics solely to manage reactive arthritis caused by a gastrointestinal or genitourinary infection.

Managing flares

- Manage flares in either specialist care or primary care depending on the person's needs.
- When managing flares in primary care, seek advice from specialist care as needed, particularly for people who:
  - have recurrent or persistent flares,
  - are taking biological DMARDs,
  - have comorbidities that may affect treatment or management of flares.
- Consider developing a flare management plan tailored to the person's individual needs, preferences and circumstances. Provide information on:
  - access to care during flares (including details of a named person to contact e.g. a specialist rheumatology nurse),
  - self-care e.g. exercises, stretching and joint protection,
  - pain and fatigue management,
  - potential changes to medicines,
  - managing the impact on daily life and ability to work.
- Be aware that uveitis can occur during flare episodes. See NICE pathway.

Managing long-term complications

- Take into account adverse effects associated with NSAIDs, standard DMARDs and biological DMARDs when monitoring spondyloarthritis in primary care.
- Advise people that there may be a greater risk of skin cancer in people treated with TNF-alpha inhibitors.
- Discuss risk factors for cardiovascular comorbidities with all people with spondyloarthritis.
- Consider regular osteoporosis assessments (every 2 years) for people with axial spondyloarthritis. See NICE pathway.
- Advise people with axial spondyloarthritis that they may be prone to fractures, and should consult a healthcare professional following falls or physical trauma, particularly in the event of increased musculoskeletal pain.

Referral for surgery – see NICE pathway

Coordinating care – see NICE pathway

Resources

Infographic –identifying and referring spondyloarthritis
http://www.bmj.com/content/bmj/suppl/2017/02/28/bmj.j839.DC1/mcak020217.wi.pdf

Clinical knowledge summary - DMARDS
https://cks.nice.org.uk/dmards

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