### Extracts from Guidance and Guidelines for the Pharmacological Management of Axial SpA (AS or Nr-axSpA)

The following extracts are for consideration in the context of patients with severe axial SpA (AS or nr-axSpA).

This is a summary of the available guidelines and guidance, please refer to the full guidelines and guidance for complete information.

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<td>• If responded inadequately to, or who cannot tolerate, NSAIDs: ◦ Adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are recommended, within their marketing authorisations, as options for treating severe active AS in adults whose disease has responded inadequately to, or who cannot tolerate, non-steroidal anti-inflammatory drugs. Infliximab is recommended only if treatment is started with the least expensive infliximab product. People currently receiving infliximab should be able to continue treatment with the same infliximab product until they and their NHS clinician consider it appropriate to stop (Recommendation 1.1) ◦ Adalimumab, certolizumab pegol and etanercept are recommended, within their marketing authorisations, for treating severe active nr-axSpA in adults whose disease has responded inadequately to, or who cannot tolerate, NSAIDs (Recommendation 1.2)</td>
<td>• Patients should be considered for TNF-alpha inhibitor therapy if they have active axial SpA (Recommendations for treatment eligibility) • Currently there is insufficient evidence to recommend the use of other biologic agents in axial SpA (Recommendations for treatment eligibility) • Active disease is defined as a BASDAI and spinal pain VAS ≥4 despite standard therapy (Recommendations for treatment eligibility) • The BASDAI should be measured on two occasions at least 3–6 months apart (Recommendations for treatment eligibility)</td>
<td>• Biological DMARDs should be considered in patients with persistently high disease activity despite conventional treatments; current practice is to start with TNF-alpha inhibitor therapy (Recommendation 9)</td>
<td>• In adults with active AS: ◦ If intolerance to ≥2 NSAIDs over 1 month or incomplete response to ≥2 NSAIDs over 2 months (PICO 6) In adults with active nr-axSpA: ◦ If inadequate response to NSAIDs (PICO 3B)</td>
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**Appraised biosimilars**

Remsima® and Inflectra® were included in the appraisal. In severe, active AS, infliximab is recommended only if treatment is started with the least expensive infliximab product. People currently receiving infliximab should be able to continue treatment with the same infliximab product until they and their NHS clinician consider it appropriate to stop* (Recommendation 1.1)

| **TNF-alpha inhibitor response** |
| • The response to adalimumab, certolizumab pegol, etanercept, golimumab or infliximab treatment should be assessed 12 weeks after the start of treatment. Treatment should only be continued if there is clear evidence of response, defined as: ◦ A reduction in the BASDAI score to 50% of the pre-treatment value or by 2 or more units and ◦ A reduction in the spinal pain VAS by 2 cm or more (Recommendation 1.4) | • Initial efficacy response should be assessed following 3–6 months of therapy and responders should then be reassessed every 6 months (Recommendations for assessment of response) • Response is defined as a reduction of the BASDAI and spinal pain VAS ≥2 units from baseline (Recommendations for assessment of response) | | |

| **Sequential use of TNF-alpha inhibitor** |
| • Treatment with another TNF-alpha inhibitor is recommended for people who cannot tolerate, or whose disease has not responded to, treatment with the first TNF-alpha inhibitor, or whose disease has stopped responding after an initial response (Recommendation 1.5) | • In the event of TNF-alpha inhibitor failure due to inefficacy or adverse event, an alternative TNF-alpha inhibitor should be offered if clinically appropriate (Recommendation for switching drugs) | • If TNF-alpha inhibitor therapy fails, switching to another TNF-alpha inhibitor or IL-17 inhibitor therapy should be considered (Recommendation 10) | • In adults with active AS despite treatment with the first TNF-alpha inhibitor used: ◦ Conditionally recommend treatment with a different TNF-alpha inhibitor over adding a SAARD (PICO 9) ◦ Conditionally recommend treatment with a different TNF-alpha inhibitor over treatment with a non-TNF-alpha inhibitor biologic agent (PICO 10) |

* NICE will consider similar biological medicinal products notified to it by the National Institute for Health Research Horizon Scanning Centre for referral to the Technology Appraisal topic selection process. These products will usually be considered in the context of a Multiple Technology Appraisal in parallel with their reference products in the indication under consideration.

This Back in Focus resource was developed in collaboration with the Back in Focus Steering Committee, for UK healthcare professionals only, organised and funded by AbbVie Ltd.

January 2019 | UK-HUM-180130

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**Back in Focus**

Fighting the whole of axial spondyloarthritis

For UK health care professionals only

This resource is intended for UK healthcare professionals only

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**Pharmacological Management of Axial SpA (AS or Nr-axSpA)**

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- The response to adalimumab, certolizumab pegol, etanercept, golimumab or infliximab treatment should be assessed 12 weeks after the start of treatment. Treatment should only be continued if there is clear evidence of response, defined as:
  - A reduction in the BASDAI score to 50% of the pre-treatment value or by 2 or more units and
  - A reduction in the spinal pain VAS by 2 cm or more (Recommendation 1.4)

- Treatment with another TNF-alpha inhibitor is recommended for people who cannot tolerate, or whose disease has not responded to, treatment with the first TNF-alpha inhibitor, or whose disease has stopped responding after an initial response (Recommendation 1.5)

- In the event of TNF-alpha inhibitor failure due to inefficacy or adverse event, an alternative TNF-alpha inhibitor should be offered if clinically appropriate (Recommendation for switching drugs)

- If TNF-alpha inhibitor therapy fails, switching to another TNF-alpha inhibitor or IL-17 inhibitor therapy should be considered (Recommendation 10)

- In adults with active AS despite treatment with the first TNF-alpha inhibitor used:
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<td><strong>NSAIDs</strong></td>
<td>¹ 1st line therapy for axial SpA (Recommendations 1.1 and 1.2)</td>
<td>¹ Patients suffering from pain and stiffness should use an NSAID as first-line drug treatment up to the maximum dose, taking risks and benefits into account. For patients who respond well to NSAIDs continuous use is preferred if symptomatic otherwise (Recommendation 5)</td>
<td>³ 1st line therapy for axial SpA</td>
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<td>² In adults with active AS:</td>
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<td>² Strongly recommend treatment with NSAIDs over no treatment with NSAIDs (PICO 2)</td>
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<td>² Conditionally recommend continuous treatment with NSAIDs over on-demand treatment with NSAIDs (PICO 1)</td>
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<td>² No recommendation of any particular NSAID as the preferred choice (PICO 3)</td>
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<td><strong>DMARDs</strong></td>
<td>² Patients with purely axial disease should normally not be treated with conventional synthetic DMARDs (Recommendation 8)</td>
<td>² Patients with axial disease should not receive long-term treatment with systemic glucocorticoids (Recommendation 7)</td>
<td>² In adults with active AS:</td>
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<td>² Consider sulfasalazine or pamidronate if TNF-alpha inhibitors are contraindicated or declined by patient (PICO 7)</td>
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<td>² In adults with active AS despite treatment with NSAIDs and who have contraindications to TNF-alpha inhibitor:</td>
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<td>² Conditionally recommend treatment with a SAARD over treatment with a non-TNF-alpha inhibitor biologic-agent (PICO 8)</td>
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<td><strong>Systemic glucocorticoids</strong></td>
<td>² Patients with axial disease should not receive long-term treatment with systemic glucocorticoids (Recommendation 7)</td>
<td>² In adults with active AS:</td>
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<td>² Strongly recommend against treatment with systemic glucocorticoids (PICO 4)</td>
<td>² In adults with AS and isolated active sacroiliitis despite NSAID treatment:</td>
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<td>² Conditionally recommend treatment with locally administered parenteral glucocorticoids over no treatment with local glucocorticoids (PICO 13)</td>
<td>² In adults with AS:</td>
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<td>² Conditionally recommend treatment with a SAARD over treatment with a non-TNF-alpha inhibitor biologic-agent over treatment with a non-TNF-alpha inhibitor biologic-agent (PICO 13)</td>
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<td><strong>Local glucocorticoids</strong></td>
<td>² Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered (Recommendation 7)</td>
<td>In adults with AS and isolated active sacroiliitis despite NSAID treatment:</td>
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¹ NICE (2016) TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis. Available from https://www.nice.org.uk/guidance/ta383 All rights reserved. Subject to Notice of rights.

² NICE guidance is prepared for the National Health Service in England. All NICE guidance is subject to regular review and may be updated or withdrawn. NICE accepts no responsibility for the use of its content in this product/publication.


ACR, American College of Rheumatology; AS, ankylosing spondylitis; ASAS, Assessment in SpondyloArthritis International Society; BSR, British Society for Rheumatology; CRP, C-reactive protein; DMARD, disease modifying antirheumatic drug; EAM, extra-articular manifestation; EULAR, European League Against Rheumatism; IBD, inflammatory bowel disease; IL, interleukin; MRI, magnetic resonance imaging; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; nr-axSpA, non-radiographic axial spondyloarthritis; NSAID, non-steroidal anti-inflammatory drug; PICO, patient, intervention, comparison, outcomes; SAARD, slow-acting antirheumatic drug; SpA, spondyloarthritis; TNF, tumour necrosis factor; VAS, visual analogue scale.

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Humira (Adalimumab)

For moderate to severe chronic plaque psoriasis with inadequate response to or if topical therapy is inappropriate. Reduces rate of progression of joint damage on X-ray and improves physical function, in combination with MTX.

Dosage: 80 mg initial loading dose one week prior to start of maintenance therapy. Evaluate on a yearly basis the need and benefit of continued long-term treatment. Humira should be available from an approved and monitored source depending on the individual treatment needs.

Contraindications: Hypersensitivity to the active substance or to any excipients (see SmPC). Active tuberculosis (TB) or other severe infections such as sepsis, or opportunistic infections (see precautions).

Moderate to severe heart failure (NYHA class II/III). Warnings and precautions: Clearly record the name and batch number of administered Humira. Patients should seek immediate medical follow-up as necessary. During treatment with Humira, other immunomodulatory agents (e.g., corticosteroids and/or immunomodulatory antibiotics) should be optimised. Rheumatoid arthritis (RA), adults: In combination with methotrexate (MTX) for moderate to severe, active RA with inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) or if intolerance to or when continued treatment with MTX is inappropriate. Reduces rate of progression of joint damage on X-ray and improves physical function, in combination with MTX.

Dosage: 40 mg single dose every other week (EOW). Concomitant MTX should be continued.

In re-treatment after 70 days or longer of discontinuation gave same results as in pre-/filled syringe; 40 mg and 80 mg solution for injection in pre-filled syringe. Each single dose 0.2 ml pre-filled syringe or 0.4 ml pre-filled pen contains 40 mg of adalimumab for subcutaneous injection. Each single dose 0.8 ml pre-filled syringe contains 80 mg of adalimumab for subcutaneous injection. Indications and Dosage: please see SmPC for full information.

Humira treatment should be initiated and supervised by a medical professional who is familiar with the disease and with appropriate treatment options.

Presentation and method of administration: Each single dose 0.2 ml pre-filled syringe or 0.4 ml pre-filled pen contains 40 mg of adalimumab for subcutaneous injection. Each single dose 0.8 ml pre-filled syringe contains 80 mg of adalimumab for subcutaneous injection. Each single dose 0.2 ml pre-filled syringe or 0.4 ml pre-filled pen contains 40 mg of adalimumab for subcutaneous injection. Each single dose 0.8 ml pre-filled syringe contains 80 mg of adalimumab for subcutaneous injection.

Psoriatic arthritis (PsA), adults: For active moderate to severe PsA with inadequate response to DMARDs. Reduces rate of progression of joint damage on X-ray and improves physical function, in combination with MTX.

Dosage: HS, adults: 180 mg dose initially at Day 1, followed by 80 mg two weeks later at Day 15. Two weeks later (Day 29) continue with a maintenance dose of 80 mg EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time. For patients with no response to treatment on Week 12 and 24, consider alternative anti-rheumatic therapy. Dosage: DSS, adults: 180 mg dose initially at Day 1, followed by 80 mg two weeks later at Day 15. Two weeks later (Day 29) continue with a maintenance dose of 80 mg EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

Psoriatic Arthritis without radiographic evidence of AS (paPsA), adults: For severe active AS with inadequate response to one or more DMARDs. Can be given as monotherapy if intolerance to or when continued treatment with MTX is inappropriate. Reduces rate of progression of joint damage on X-ray and improves physical function, in combination with MTX.

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