Biologics Pathway for Adult Axial Spondyloarthritis and Non-Radiographic Axial Spondyloarthritis V3.0

Treatment criteria:

- Diagnosis of Axial Spondyloarthritis (AS)/Non-Radiographic Axial Spondyloarthritis (nr-axSpA) by modified New York or ASAS Criteria (see **Table 1**); **AND**
- Inadequate response to at least 2 NSAIDs administered individually and taken at the maximum tolerated dose for at least 2-4 weeks or NSAIDs contraindicated; **AND**
- BASDAI ≥4; **AND**
- Spinal VAS ≥ 4

1st line biologic

Anti-TNF (1st line = Adalimumab (Yuflyma® or Idacio®)

- ***If anti-TNF contraindicated,*** consider IL-17a (First line IL-17a= Secukinumab, Cosentyx®) **or** JAK inhibitor (First line JAK inhibitor=Upadacitinib, Rinvoq®)
  Consider co-morbidities and risk factors before choosing agent

Initial review period as per **Table 2**
Is there an adequate response to treatment?
Defined as:

- a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units; **AND**
- a reduction in the spinal pain visual analogue scale (VAS) score by 2cm or more.

Yes → **Continue & reassess 6-monthly**

No

Subsequent biologic options

Consider switching therapy to:

- Alternative anti-TNF from **Table 2** *(Nb Infliximab approved for use in AS only)*; **OR**
- Initiate IL-17A inhibitor (1st line IL-17A= Secukinumab, Cosentyx®) **or** JAK-inhibitor (First line JAK inhibitor =Upadacitinib, Rinvoq®)
  Consider co-morbidities and risk factors before choosing agent

Review period as per **Table 2**
Is there an adequate response to treatment?

Yes → **Continue & reassess 6-monthly**

No

Consider switching class/discuss with MDT

Table 1: NICE approved criteria for AS diagnosis

Modified New York Criteria for the classification of AS:
• Sacroiliitis on x-ray ≥ grade 2 bilaterally or ≥ grade 3 unilaterally; **AND**
• One or more of:
  ○ Low back pain present ≥ 3 months which is improved by exercise and not relieved by rest; **OR**
  ○ Limitation of lumbar spine motion in both the sagittal and frontal planes; **OR**
  ○ Limitation of chest expansion.
	ASAS Criteria for the classification of radiographic axSpA:
	• Back pain ≥ 3 months; **AND**
	• <45 years at age of onset; **AND**
	• One or more of:
	  ○ Sacroiliitis on MRI/ x-ray & ≥1 SpA feature; **OR**
	  ○ HLA-B27 positive & ≥2 SpA features.

Biologic choice considerations:

- Patient: comorbidities, dosing schedule
- Consider associated conditions such as extra-articular manifestations (enthesitis, dactylitis, uveitis, inflammatory bowel disease, psoriasis)
- Choose the least expensive

Table 2: NICE approved biologic medication for patients with AS and axSpA - in order of cost effectiveness for each mode of action

Drug (In order of cost)	Therapeutic class	Initial Review Period	Patient and clinical considerations	Administration and Dosage
Adalimumab (Hyrimoz®)	Anti- TNF	12 weeks	– **Contraindicated in moderate- severe heart failure** – Cautioned in demyelinating disorders – First line biologic in Inflammatory Bowel Disease (IBD) – Extensive data for use in pregnancy – Consider if extra articular features/ co-existent conditions e.g., uveitis, psoriasis, Crohn's Disease – Increased risk of infection when treating elderly over 65 years – Biosimilar Amgevita® contains latex in the cap	– **Subcutaneous injection** – 40mg every 2 weeks
Etanercept (Benepali®)	Anti- TNF	12 weeks	– **Contraindicated in active infection** – Latex allergy – Cautioned in heart failure – Cautioned in demyelinating disorders – Less effective in uveitis and may flare uveitis if past history – Monitor blood sugars in diabetic patient – Increased risk of infection in over 65-year-olds – Less effective in psoriasis – Not effective in inflammatory bowel disease	– **Subcutaneous injection** – 25mg twice weekly OR 50mg once weekly
Infliximab (Remsima®)	Anti- TNF	6 weeks	– **Licensed and approved by NICE for AS only and <u>not</u> for nr-axSpA** – **Murine protein allergy** – **Contraindicated in severe infection, moderate or severe heart failure** – Cautioned in demyelinating disorders, dermatomyositis, malignancy, mild heart failure, predisposition to infection. Risk of delayed hypersensitivity reaction. – Greater incidence of severe infections in patients aged over 65 years.	– **Intravenous infusion or SC injection** – For Iv infusion dose is 5mg/kg at week 0, 2 and 6, then maintenance dose, every 6-8 weeks – Discontinue if no response by 6 weeks of initial infusion (after 2 doses) – *IV infliximab loading is required prior to commencing SC doses. Give 5mg/kg at week 0 and Week 2 then 4 weeks after second loading dose, commence 120mg SC every two weeks.*
Golimumab (Simponi®)	Anti- TNF	12 weeks	– **Contraindicated in moderate-severe heart failure; severe active infection** – **Latex allergy** – Cautioned in demyelinating disorders; history or development of malignancy; mild heart failure; pre-disposition to infection; risk factors for dysplasia or carcinoma of the colon- screen for dysplasia regularly. – Homecare nursing service not currently available	– **Subcutaneous injection** – 50mg once a month – *For Adults >100kg, dosage may be increased after initial 3 months to 100mg once a month if inadequate response*
Certolizumab pegol (Cimzia®)	Anti- TNF	12 weeks	– **Contraindicated in moderate-severe heart failure; severe active infection** – **Latex allergy** – Cautioned in demyelinating disorders; do not initiate until active infections are controlled history or development of malignancy; mild heart failure; predisposition to infection – Biologic of choice in pregnant or lactating patients	– **Subcutaneous injection** Loading dose 400 mg every 2 weeks for 3 doses then maintenance 200 mg every 2 weeks or 400 mg every 4 weeks
Upadacitinib (Rinvoq®)	JAK-inhibitor	16 weeks	– **Contraindicated if** absolute lymphocyte count less than 0.5 x 10^9 cells/litre; absolute neutrophil count less than 1 x 10^9 cells/litre; haemoglobin less than 8 g/dL – active serious infection including localised infection; active tuberculosis. – Use with caution in patients with risk factors for VTE, discontinue if clinical features of VTE occur. – Avoid in patients aged 65 years and over, chronic or recurrent infection; diverticular disease including patients at increased risk of diverticular disease. Known malignancy. – Advise use of additional contraception	– **Oral** – 15mg once daily – Check BNF interactions prior to prescribing – Check for anti-epileptics, antivirals and antifungal use – Advise patient to avoid grape juice as can increase levels of Upadacitinib

			Janus kinase (JAK) inhibitors: measures to reduce the risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality: JAK inhibitors **(filgotinib, upadacitinib and tofacitinib)** should not be used in patients with the following risk factors unless there are no other suitable alternatives: - Age 65 or over - Current or past long-time smoking - Other risk factors for cardiovascular disease or malignancy Use caution when prescribing in patients with other risk factors for VTE and prescribe lower doses where possible Carry out periodic skin examinations on all patients to check for skin malignancy *(MHRA April 2023)*	
Tofacitinib (Xeljanz®)	JAK-inhibitor	16 weeks	– **Licensed and approved by NICE for AS only and <u>not</u> for nr-axSpA** – **Only recommended where a JAK inhibitor is indicated but upadacitinib is contraindicated** – **Contraindicated if** Absolute lymphocyte count less than 750 cells/mm3 (do not initiate); – absolute neutrophil count less than 1000 cells/mm3 (do not initiate); – active infection including localised infection; – active tuberculosis; – haemoglobin less than 9 g/dL (do not initiate); – risk factors for venous thromboembolism (high doses) **Janus kinase (JAK) inhibitors: measures to reduce the risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality:** JAK inhibitors **(filgotinib, upadacitinib and tofacitinib)** should not be used in patients with the following risk factors unless there are no other suitable alternatives: - Age 65 or over - Current or past long-time smoking - Other risk factors for cardiovascular disease or malignancy Use caution when prescribing in patients with other risk factors for VTE and prescribe lower doses where possible Carry out periodic skin examinations on all patients to check for skin malignancy *(MHRA April 2023)*	– **Oral** – 5mg BD – Check BNF interactions prior to prescribing – Check for anti-epileptics, antibiotics, antivirals and antifungal use
Secukinumab (Cosentyx®)	Anti-IL-17A	16 weeks	– **Contraindicated in severe active infection** – **Cautioned in inflammatory bowel disease** – Advise patient to contact the team if they develop signs and symptoms of IBD – Women of childbearing potential should be advised to use additional contraception during and after treatment, see SPC – Avoid in latex sensitive individuals. The removable needle cap contains a derivative of rubber	– **Subcutaneous injection** – **Radiographic** 150mg weekly for 5 doses, then maintenance 150mg monthly, dose may be increased to 300 mg SC according to clinical response – **Non-Radiographic** 150mg weekly for 5 doses, then maintenance 150mg monthly, review treatment if no response within 16 weeks of initial dose
Bimekizumab (Bimzelx®)	Anti-IL 17A,F		– **Contraindicated in active infections and inflammatory bowel disease** – Females of childbearing potential should use effective contraception during treatment and for at least 17 weeks after last treatment. – Cautioned in Chronic Infection; history of recurrent infection	– **Subcutaneous injection** – 160mg every 4 weeks **Drug Interactions** – Warfarin, may affect exposure to warfarin. Monitor INR
Ixekizumab (Taltz®)	Anti-IL-17A	16-20 weeks	– **Contraindicated in active infections and inflammatory bowel disease**	– **Subcutaneous injection** – Initially 160 mg for 1 dose, then maintenance 80 mg every 4 weeks

			– Women of childbearing potential should be advised to use additional contraception during and after treatment, see SPC	– Note additional loading doses if patient has concomitant psoriasis

NICE guidance:

- **NG65** Spondyloarthritis in over 16s: diagnosis and management. Jun 2017) https://www.nice.org.uk/guidance/ng65
- **TA383** TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis. Feb 2016 https://www.nice.org.uk/guidance/ta383
- **TA497** Golimumab for treating non-radiographic axial spondyloarthritis. Jan 2018 https://www.nice.org.uk/guidance/ta497
- **TA407** Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors. Sept 2016 https://www.nice.org.uk/guidance/ta407
- **TA719** Secukinumab for treating non-radiographic axial spondyloarthritis. Jul 2021 https://www.nice.org.uk/guidance/TA719
- **TA718** Ixekizumab for treating axial spondyloarthritis. Jul 2021 https://www.nice.org.uk/guidance/ta718
- **TA829** Upadacitinib for treating active ankylosing spondylitis. Sep 2022 1 Recommendations | Upadacitinib for treating active ankylosing spondylitis | Guidance | NICE
- **TA861** Upadacitinib for treating active non-radiographic axial spondyloarthritis Feb 2023 https://www.nice.org.uk/guidance/ta861
- **TA920** Tofacitinib for treating active ankylosing spondylitis. October 2023 Overview | Tofacitinib for treating active ankylosing spondylitis | Guidance | NICE
- **TA918** Bimekizumab for treating axial spondyloarthritis October 2023 Overview | Bimekizumab for treating axial spondyloarthritis | Guidance | NICE

Table 2: Record of changes. Version control

Date	Changes Made	Changes made by
18/11/2024	*Adalimumab brand names updated as Hyrimoz® withdrawn from UK market*	*FL*
19/11/1024	*Added Bimekizumab and Tofacitinib*	*FL*
19/11/2024	*Minor typos, colour scheme and outline of boxes*	*FL*