North Central London
Joint Formulary Committee

Ankylosing spondylitis (AS) and Non-radiographic axial spondyloarthritis (nr-AxSpA) Prescribing Pathway

Document control

Date	Version	Amendments
Nov 2023	2.0	Pathway developed in accordance with NCL 'Principles for Commissioning High-Cost Drug Pathways for ICB Commissioned Indications' and includes relevant published NICE TAs.

Groups / Individuals who have overseen the development of this guidance:	UCLH Lead Pharmacist, Formulary & Clinical Trials, UCLH Specialised Commissioning Lead Pharmacist, NCL ICB Medicines Management Team, NCL Joint Formulary Principal Pharmacist, NCL Specialist Clinicians
Groups which were consulted and have given approval:	NCL wide consultation (NCL ICB, NCL Formulary Pharmacists, NCL Specialist Clinicians), NCL Joint Formulary Committee (Nov 2023), NCL Integrated Medicines Optimisation Board (Nov 2023)
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Ankylosing spondylitis (AS) and Non-radiographic axial spondyloarthritis (nr-AxSpA) Prescribing Pathway

Green: preferred best value **Amber**: not preferred (use where green not suitable) **Red**: not preferred (least cost-effective, use where green and amber not suitable)

Criteria to start treatment for Ankylosing spondylitis (AS) / Non-radiographic axial spondyloarthritis (nr-AxSpA):
AS: Severe active ankylosing spondylitis with confirmed X-ray changes showing sacroiliitis
nr-AxSpA: Severe non-radiographic axial spondyloarthritis with confirmed MRI changes or no MRI changes with a positive HLA-B27 test and ≥ 2 clinical features of axial SpA

- Inadequate response to ≥ 2 NSAIDs at the maximum tolerated dose for 2-4 weeks each (unless not tolerated due to contraindications/toxicity) **and;**
- Sustained active spinal disease demonstrated by a Bath Ankylosing Spondylitis Disease Activity (BASDAI) score ≥ 4 units and spinal pain visual analogue score (VAS) ≥ 4cm

1ST LINE TREATMENT OPTIONS

TNF inhibitor: **Adalimumab SC** (**Preferred**) OR Etanercept SC OR Infliximab SC/IV biosimilars [TA383; infliximab for AS only] Certolizumab (TA383) and golimumab (TA383/TA497) also available but not preferred.	Upadactinib (TA829/TA861), tofacitinib (TA920), secukinumab (TA407/TA719), ixekizumab (TA718), bimekizumab (TA918) and are available 1st line if TNF inhibitor not suitable[1] or contraindicated[2].

2ND LINE ONWARDS TREATMENT OPTIONS

Alternative TNF inhibitor: **Adalimumab SC** OR **Etanercept SC** OR **Infliximab IV/SC** biosimilars [TA383; infliximab for AS only] Certolizumab (TA383) and golimumab (TA383/TA497) also available but not preferred	JAK inhibitor: **Upadacitinib** [TA829/TA861] NB. MHRA update Tofacitinib (TA920) also available but not preferred[3].	IL17 inhibitor: **Secukinumab** [TA407/TA719] Ixekizumab (TA718) and bimekizumab (TA918) also available but not preferred[4].

Sequential treatments routinely commissioned: Up to one drug per mechanism of action, plus a second TNF inhibitor. If more than one treatment is suitable, the least expensive treatment should be used.

Drug	Price	Usual maintenance	Additional Information
Adalimumab	£	40mg SC every 2 weeks	
Etanercept	£	25mg SC twice weekly, or 50mg SC every weekly	Preferred TNF inhibitor for IGRA +ve patients
Infliximab	£	120mg SC once every 2 weeks 5mg/kg IV every 8 weeks	**For Ankylosing Spondylitis only**
Upadacitinib	££	15mg daily	
Tofacitinib	££	5mg twice daily	
Secukinumab	££	150mg monthly	**AS**: Temporary secukinumab dose escalation to 300mg monthly following primary or secondary failure. Where response is adequate and stable, consider returning to standard dosing. Discontinue treatment where response is inadequate. **nr-axSpA**: Secukinumab dose escalation is unlicensed and not recommended
Certolizumab	£££	200mg every 2 weeks	
Bimekizumab	£££	160mg every 4 weeks	
Ixekizumab	£££	80mg every 4 weeks	
Golimumab	££	50mg every 4 weeks	In patients weighing >100Kg who do not achieve adequate clinical response after 3-4 x 50mg doses, dose can be increase to 100mg/month taking into account the increased risk of serious adverse drug reactions. Continued therapy should be reconsidered if there is not therapeutic benefit after 3-4 additional doses of 100mg

Assessment of response - Assess initial induction response according to NICE TA timeframes (12-20 weeks). Treatment response is defined as:

- A reduction in the BASDAI score to 50% of pre-treatment value or by ≥ 2 **and**
- A reduction in the spinal pain VAS by ≥ 2 cm

Continuation of Biologic Treatment – Treat for 6 months or until treatment failure. Reassess at 6 monthly intervals to determine whether ongoing treatment is still clinically appropriate. Following 24 months of stable treatment, consider annual reviews.

Adverse drug reactions (ADRs) – For patients who experience an immediate ADR [within 1 month] or have responded to treatment but experience an ADR within 6 months of treatment initiation, another treatment option within the same mechanism of action (if available and appropriate) can be accessed. Where the ADR is likely to be a drug class effect, an alternative mechanism of action is preferable.

Dual biologic therapy for the same disease is not routinely commissioned; for individual cases, please consider RMOC advisory statement, discuss at MDT and contact Trust formulary teams for advice re IFR submission. **Concurrent biologic treatment for different co-morbidities,** is permissible provided NICE eligibility criteria for both treatments are met and there is MDT agreement across both specialities that dual therapy is appropriate and a single drug which is active against both co-morbidities is not available.

Treatment breaks & dose reductions – patients who reduce dose or hold biologic treatment can resume the standard biologic regimen (i.e. licensed dose), with an assessment of response made at 12-20 weeks.

Pregnancy – updated guidance from BSR

- Women with no/low disease activity established on a TNF inhibitor with known placental transfer (INF, ADA, GOL) do not need to be switched to an alternative TNF inhibitor with established minimal placental transfer (CZP) either before or during pregnancy (GRADE 1B, Strength of agreement 100%).
- CZP is compatible with all three trimesters of pregnancy, has no to minimal placental transfer compared with other TNF inhibitor, and does not require any alteration to the infant vaccination schedule (GRADE 1B, Strength of agreement 100%).
- Women considered to have low risk of disease flare on withdrawal of TNF inhibitor in pregnancy could stop INF at 20 weeks, ADA and GOL at 28 weeks, and ETA at 32 weeks so that a full-term infant can have a normal vaccination schedule, with rotavirus vaccination at 8 weeks as per the UK schedule (GRADE 1B, Strength of agreement 99.5%).
- INF, ADA, ETA or GOL may be continued throughout pregnancy to maintain maternal disease control; in these circumstances, live vaccines should be avoided in infants until they are 6 months of age (GRADE 1B, Strength of agreement 100%).
- If a TNF inhibitor is stopped in pregnancy, it can be restarted as soon as practical post-partum in the absence of infections or surgical complications, regardless of breastfeeding status, to ensure control of maternal disease (GRADE 1C, Strength of agreement 100%).

Footnotes

[1] Clinically patients with very severe concurrent psoriasis (unstable disease and rapid response required) may require treatment with IL-17 as a first line agent. Refer to NCL Psoriasis pathway.

[2] Relative contraindications to TNF inhibitors include: current malignancy, history of malignancy, recurrent infections, history of demyelinating disorders, interstitial lung disease, moderate to severe heart failure (NYHA class III/IV), systemic lupus erythematosus, and positive antinuclear antibodies (ANA).

[3] Upadacitinib is the preferred JAK inhibitor because it is the lowest-cost and there is no evidence that other JAKi have superior efficacy [doi: 10.1159/000525627].

[4] Secukinumab is the preferred IL-17 inhibitor it is the lowest-cost and there is no evidence that other IL-17 inhibitor have superior efficacy [NICE FAD for bimekizumab, see *Why these recommendations were made*].

References

British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids