NHS
North East London

High-Cost Drugs Treatment Pathway for Ankylosing Spondylitis and non-radiographic Axial Spondyloarthritis

NHS North East London

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Contents

Scope

This document outlines the treatment pathway for adult ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) patients with BASDAI score ≥ 4 units and spinal pain VAS ≥ 4cm in North East London.

It is to be used in conjunction with the National Institute for Health and Care Excellence (NICE) guidance and the published NICE Technology Appraisal (TA) guidance for each individual biologic therapy. The pathway is intended to be adopted by all acute provider Trusts within North East London.

NICE Guidance

At the time of publication, this treatment pathway considers the following NICE guidance:
NICE NG65 Spondyloarthritis in over 16s: diagnosis and management.

NICE Technology Appraisal Guidance

At the time of publication, this treatment pathway takes into account the following NICE TAs:

- TA383 TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis
- TA407 Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors
- TA497 Golimumab for treating non-radiographic axial spondyloarthritis
- TA718 Ixekizumab for treating axial spondyloarthritis after NSAIDs
- TA719 Secukinumab for treating non-radiographic axial spondyloarthritis
- TA829 Upadacitinib for treating active ankylosing spondylitis
- TA920 Tofacitinib for treating active ankylosing spondylitis
- TA918 Bimekizumab for treating active ankylosing spondylitis

Any NICE TAs published after the approval date of this pathway will be implemented in 90 days (30 days for fast-track TAs) of its publication date in line with the NICE TA recommendations.

Principles

This document is based on current NICE TAs and the British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) guideline for the management of axial spondyloarthritis (AS and nr-axSpA)[14]. The document also reflects local agreements which are based on clinical evidence considered by local drug and therapeutic and medicines optimisation (or equivalent) committees. This prescribing pathway has taken into consideration the Regional Medicines Optimisation Committee (RMOC) Advisory statement on the sequential use of biologic medicines (updated 07 May 2020) to formulate a position which meets the needs of patients in the region[1].

Local agreements outside of NICE recommendations aim to address an unmet clinical need for an established cohort of patients with AS or nr-axSpA. The use of medicines outside of NICE TAs will be monitored on a regular basis through Blueteq or clinical audit where Blueteq is not used.

The pathway is subject to change as new evidence, NICE TAs or local agreements are released or updated that will impact on the information outlined in this document. This includes changes in drug costs that may impact on cost-effectiveness and drug choice in the treatment pathway.

Where possible, it is expected drugs approved for use through a NICE TA are selected in preference to non-NICE approved options. It is also expected that drugs presenting best value are selected where clinically appropriate.

For further prescribing information including contraindications and cautions, please refer to **Appendix 2**, the relevant drug monograph in the latest version of the British National Formulary (BNF) or the respective drug's Summary of Product Characteristics (SPC).

Eligibility criteria

In line with NICE recommendations, AS and nr-axSpA patients are eligible for biological disease-modifying anti-rheumatic drugs (DMARDs) where the following criteria are met:

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

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 the responses to the questionnaires and make any adjustments as appropriate.

Assessing of response

Where possible, in line with NICE recommendations, the response to adalimumab, certolizumab pegol, etanercept, golimumab or infliximab treatment should be assessed 12 weeks after the start of treatment. The response to secukinumab, upadacitinib, tofacitinib and bimekizumab should be assessed 16 weeks after the start of treatment. The response to ixekizumab should be assessed 16 to 20 weeks after the start of treatment.

Treatment response

Treatment should only be continued if there is clear evidence of adequate response, defined as:

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

Where there is adequate response to treatment, disease activity and ongoing treatment response should be monitored and reviewed at 6-monthly intervals thereafter[14].

Lines of therapy

Only four lines of therapy for AS and nr-axSpA will be commissioned by the ICB under this pathway. Up to one drug per mechanism of action, plus a second TNF inhibitor. If more than one treatment is suitable, the least expensive medicine/biosimilar should be used.

Please note that primary or secondary failure of TNF-alpha inhibitors allows trial of another TNF-alpha inhibitor without it counting as a treatment line as there appears to be benefit even in primary failure.[16]

5th line treatment (and beyond) and sequential IL-17A inhibitor treatment is not routinely commissioned. Funding for such treatment will require the submission of an Individual Funding Request (IFR) where clinical exceptionality can be demonstrated.

	Mechanism of action			
	TNF-α inhibitor	**JAK inhibitor**	**Interleukin inhibitor (IL-17A)**	**Interleukin inhibitor (IL-17AF)**
Severe active ankylosing spondylitis (AS)	Adalimumab Etanercept Infliximab Golimumab Certolizumab	Upadacitinib Tofacitinib	Ixekizumab Secukinumab	Bimekizumab
Severe non-radiographic axial spondyloarthritis (nr-axSpA)	Adalimumab Etanercept Golimumab Certolizumab	Upadacitinib	Ixekizumab Secukinumab	Bimekizumab

Treatment choice

The choice of treatment should be made after discussion between the clinician and the patient about the advantages and disadvantages of the treatments available. This may include considering associated conditions such as extra-articular manifestations or other patient factors (e.g. pregnancy status, comorbidities, treatment history and administration route/frequency) (see **Appendix 2**).

The RAG (red, amber, green) system has been implemented as a means of communicating the differences in cost between treatment options. Administration costs have not been considered in the RAG system for treatments requiring intravenous infusion as these costs are derived from a separate budget. If more than one treatment is suitable, the least expensive should be chosen.

MHRA Alert for JAK inhibitors, Upadacitinib (Rinvoq▼) and Tofacitinib (Xeljanz):

On the 26th April 2023 The Medicines and Healthcare product and Regulatory Agency (MHRA)[22] issued updated safety advice to reduce risk of major adverse cardiovascular events, malignancy, venous thromboembolism (VTE), serious infections and increased mortality for all JAK inhibitors, in line with measures previously introduced for tofacitinib (Xeljanz®) in 2021, as follows:

Healthcare professionals are advised to:

- avoid use in patients aged 65 years or older, in patients who are current or past long-time smokers, and in patients with other cardiovascular disease or malignancy risk factors, unless there are no suitable alternatives;
- use with caution in patients with risk factors for VTE;
- use lower doses in patients with risk factors, where applicable;
- periodically examine all patients' skin for malignancy;
- inform patients and their carers of these risks, and the signs and symptoms that warrant urgent medical attention.

Treatment choice in pregnancy and breastfeeding

Certolizumab pegol is the drug of choice in women who are confirmed pregnant as it is compatible with all three trimesters of pregnancy[2,3,4]. If patients are required to be switched to certolizumab pegol due to confirmation of pregnancy, whether planned or unplanned, this will not count as a line of therapy if this drug is used for a limited duration with a planned exit strategy from its use. The drug should be reviewed post-parturition, reverting to the most clinically- and cost-effective agent where appropriate.

Certolizumab pegol prescribed pre-conception for patients planning for pregnancy will count as a line of therapy on the pathway.

Primary failure

The patient does not achieve an adequate response to treatment as outlined in the NICE TA.

Patients demonstrating primary failure are expected to progress to the next line of therapy on the pathway. A second line TNF-alpha inhibitor can be considered.

Secondary failure

The patient initially achieves an adequate response to treatment as outlined in the NICE TA which is subsequently not sustained, resulting in failure to maintain an adequate response.

Patients demonstrating secondary failure are expected to progress to the next line of therapy on the pathway. A second line TNF- alpha inhibitor can be considered.

Adverse drug reactions

An adverse drug reaction to a medicine will not count as a line of therapy. However, the patient must have shown a response to therapy for that biologic after the initial response assessment period for it not to count as a line of therapy.

- If the patient has the adverse event **before** this assessment period, it will not count as a line of therapy.
- If the adverse reaction occurs **after** the initial response assessment period and the patient has shown a response to therapy with that biologic, it will not count as a line of therapy.

Return to previous treatment

Patients may exhaust the 4 available lines of therapy and a return to a previous treatment which they previously had an adequate response to may be appropriate (e.g. developed a contraindication to therapy, perceived intolerance/hypersensitivity to a previous treatment, dose escalation of previous treatment was not available etc). Patients who have exhausted the different mechanisms of action, but who had a response to a previous treatment will be able to return to that drug provided they achieved an adequate response previously. Returning to a previous treatment is commissioned for one drug and must be documented

on the patients record and through the appropriate Blueteq form. If this treatment then fails the patient will need to exit the treatment pathway and return to standard care.

Dose escalation

Dose escalation of TNF-alpha inhibitors for treating AS and nr-axSpA is unlicensed and not commissioned.

For AS patients who have previously failed or have a contraindication/is intolerant to at least one TNF-alpha inhibitor, **temporary secukinumab dose escalation is commissioned following primary or secondary failure with secukinumab treatment**. The secukinumab dose can be escalated temporarily to 300 mg monthly as per SPC following primary or secondary failure[5,15]. Patients on the higher dose of 300mg secukinumab should be reviewed after 12 weeks. Where response is adequate and stable, consider returning to standard dosing. Discontinue treatment where response is inadequate.

For nr-axSpA patients, secukinumab dose escalation is unlicensed and not commissioned.

Funding

To support data-driven care, commissioners will be extracting outcomes data from Blueteq. In accordance with the pathway, Blueteq must be used for the management of all funding requests for biologic therapies. This includes recording treatment switches and cessation as a result of clinical review and/or remission, drug switching for patients who are confirmed/planning pregnancy and formulation switching.

Trusts are expected to obtain funding via Blueteq both prior to initiation and for continuation of biologic treatments for AS and nr-axSpA patients as described on the Blueteq forms.

Where Blueteq is not available, Trusts are expected to have a governance process in place to ensure compliance to this pathway. Commissioners may request evidence to demonstrate compliance if necessary.

Patients transferred from out of area or from overseas

For patients who have already commenced on their treatment for AS or nr-axSpA

• If the current treatment is covered by a NICE TA, then the patient can continue their treatment as per the TA.

• If the treatment is not covered by a NICE TA, or this pathway, then an application to IFR must be submitted to continue the funding for therapy.

It is the responsibility of the specialist Rheumatologist to ensure the patient's GP is informed that the patient is receiving treatment with a biologic. It will then be the responsibility of the GP to update a person's medical record with this biologic.

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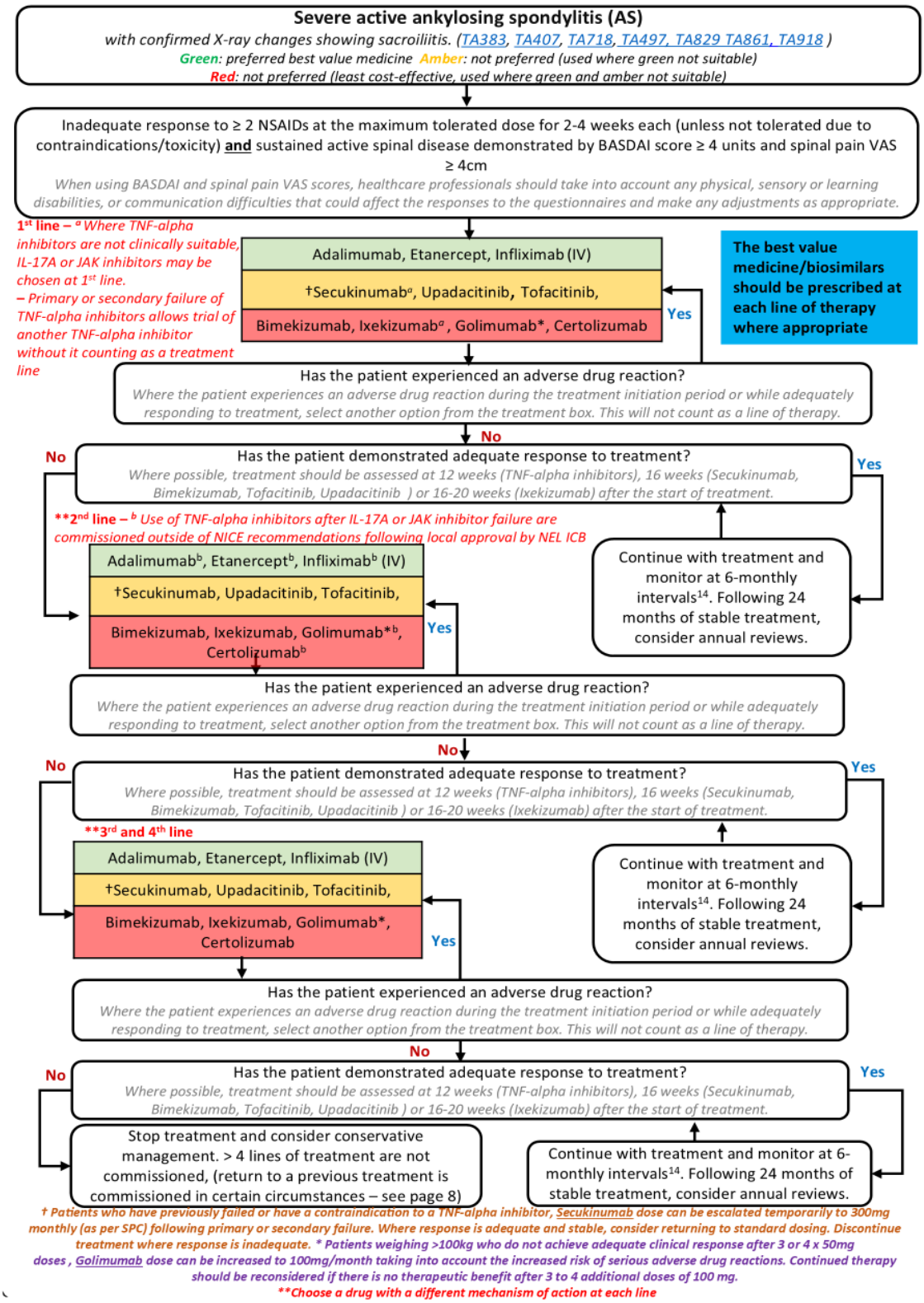
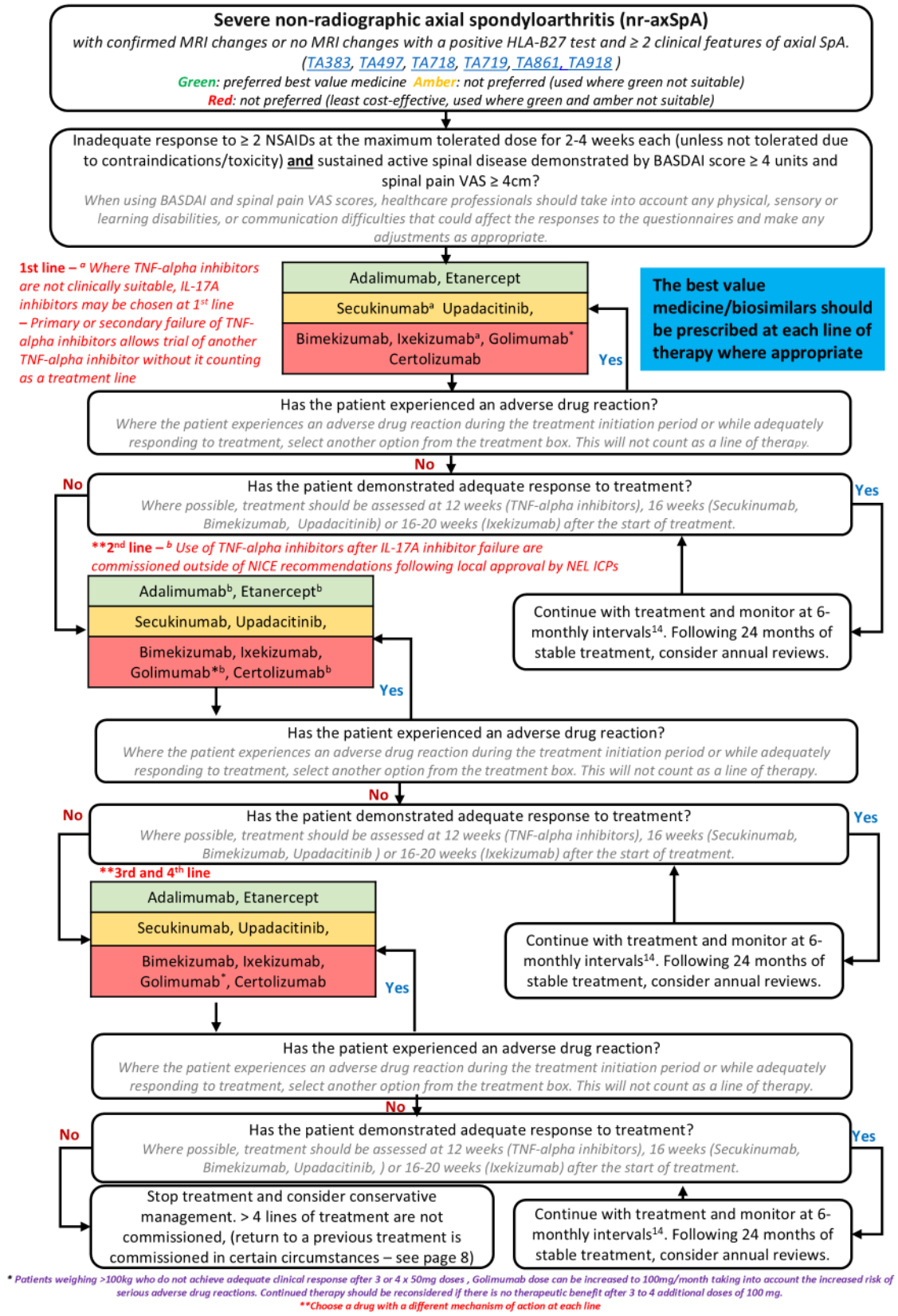
Appendix 1. Biologic treatment pathway: AS



Appendix 2. Biologic treatment pathway: nr-axSpA



Appendix 3. Specific circumstances which may suggest the use of specific agent

(This list is not exhaustive; please refer to summary of product characteristics (SPC) and the relevant technology appraisal for each drug for full information)

Drug	Alternative indications with published TA	Safety in pregnancy[2]	Compatible with breastfeeding[2]	*Cautions[7]	*Contraindications[7]
Adalimumab *TNF-α inhibitor* ***(Biosimilar available)***	TA146 - Psoriasis TA187 - Crohn's TA199 - Psoriatic arthritis TA195 - Rheumatoid arthritis TA329 - Ulcerative colitis TA373 - JIA TA392 - Hidradenitis suppurativa TA715 - Rheumatoid arthritis TA460 – Non-infectious uveitis	First and second trimester	✔	• Latent TB • Carrier of HBV • Pre-existing/recent onset central or peripheral nervous system demyelinating disorders • Mild heart failure (NYHA class I/II) • History of malignancy, haematologic abnormalities or pulmonary disease	• Active infections (e.g. TB, sepsis, opportunistic) • Moderate/severe heart failure (NYHA class III/IV)
Certolizumab *TNF-α inhibitor*	TA146 - Psoriasis TA375 - Rheumatoid arthritis TA415 – Rheumatoid arthritis TA445 – Psoriatic arthritis	Compatible with all trimesters	✔	• Latent TB • Carrier of HBV • Pre-existing/recent onset central or peripheral nervous system demyelinating disorders • Mild heart failure (NYHA class I/II) • History of malignancy, haematologic abnormalities or pulmonary disease	• Active infections (e.g. TB, sepsis, opportunistic) • Moderate/severe heart failure (NYHA class III/IV)

Drug	Alternative indications with published TA	Safety in pregnancy[2]	Compatible with breastfeeding[2]	*Cautions[7]	*Contraindications[7]
Etanercept *TNF-α inhibitor* *(Biosimilar available)*	TA195 - Rheumatoid arthritis TA199 – Psoriatic arthritis TA373 – JIA TA375 - Rheumatoid arthritis TA146 - Psoriasis	First and second trimester	✔	• Latent TB • Carrier of HBV • Pre-existing/recent onset central or peripheral nervous system demyelinating disorders • Congestive heart failure • Moderate to severe alcoholic hepatitis • History of malignancy, haematologic abnormalities, pulmonary disease, hepatitis C uveitis or inflammatory bowel disease	• Sepsis/risk of sepsis • Active infections (chronic/localised)
Golimumab *TNF-α inhibitor*	TA329 - Ulcerative colitis TA375 - Rheumatoid arthritis TA220 - Psoriatic arthritis	No data	No data	• Latent TB • Carrier of HBV • Pre-existing/recent onset central or peripheral nervous system demyelinating disorders • Mild heart failure (NYHA class I/II) • History of malignancy, haematologic abnormalities or pulmonary disease	• Active infections (e.g. TB, sepsis, opportunistic) • Moderate/severe heart failure (NYHA class III/IV)
Infliximab *TNF-α inhibitor* (Biosimilar available)	TA329 - Crohn's disease TA140,TA329 - Ulcerative colitis TA134 - Psoriasis TA375 - Rheumatoid arthritis TA199 - Psoriatic arthritis	Compatible until 16 weeks of pregnancy	✔	• Latent TB • Carrier of HBV • Pre-existing/recent onset central or peripheral nervous system demyelinating disorders	• Active infections (e.g. TB, sepsis, opportunistic) • Moderate/severe heart failure (NYHA class III/IV)

Drug	Alternative indications with published TA	Safety in pregnancy[2]	Compatible with breastfeeding[2]	*Cautions[7]	*Contraindications[7]
				• Mild heart failure (NYHA class I/II) • History of malignancy, haematologic abnormalities or pulmonary disease	
Secukinumab *IL-17A inhibitor*	TA350 - Psoriasis TA445 - Psoriatic arthritis	No data	No data	• Latent TB • Pre-existing inflammatory bowel disease	• Active infections (e.g. TB)
Ixekizumab *IL-17A inhibitor*	TA442 - Psoriasis TA537 - Psoriatic arthritis	No data	No data	• Latent TB • Pre-existing inflammatory bowel disease	• Active infections (e.g. TB)
Bimekizumab *IL-17A, IL-17F and IL-17AF inhibitor*	TA916 – active psoriatic arthritis TA723 - moderate to severe plaque psoriasis	No data	No data	• Latent TB • Chronic infection • History of recurrent infection	• Active infections (e.g. TB) • Inflammatory bowel disease
Upadacitinib *JAK inhibitor*	TA665 – Rheumatoid arthritis TA856 – Ulcerative colitis TA768 – Psoriatic arthritis TA814 – Atopic dermatitis	No data	No	• Latent TB • Cardiovascular disorders • History of malignancy, haematologic abnormalities or pulmonary disease Refer to MHRA Alert	• Active infections (e.g. TB, sepsis, opportunistic) • Severe hepatic impairment
Tofacitinib *JAK inhibitor*	TA547 – moderate to severe ulcerative colitis	No data	No data	• 65 years of age and older	• Active TB

Drug	Alternative indications with published TA	Safety in pregnancy[2]	Compatible with breastfeeding[2]	*Cautions[7]	*Contraindications[7]
	TA480 – moderate to severe rheumatoid arthritis TA735 – JIA TA543 – active psoriatic arthritis after inadequate response to DMARDs			• patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers) • patients with malignancy risk factors (e.g. current malignancy or history of malignancy) Refer to MHRA Alert	• Serious infections, such as sepsis or opportunistic infections • Severe hepatic impairment

* NB. List of cautions and contraindications not exhaustive. Please refer to the respective summary of product characteristics for further details[3,5,8,9,10,11,12,13,17, 18, 20, 21]