

Rheumatoid Arthritis 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.
Apr 2024	3.0	Infliximab IV changed to infliximab IV/SC (correction of omission). Link to BSR guidance reference added and abbreviations corrected to full drug names. RAG rating definition amended to clarify that the rating is based on cost and not cost-effectiveness.

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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Review date:	November 2026 (or sooner if updates required e.g. NICE TAs)

Disclaimer

This guideline is registered at North Central London (NCL) Joint Formulary Committee (JFC) and is intended solely for use by healthcare professionals to aid the treatment of patients within NCL. However, clinical guidelines are for guidance only, their interpretation and application remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Clinicians are advised to refer to the manufacturer's current prescribing information before treating individual patients.

The authors and NCL JFC accept no liability for use of this information beyond its intended use.

While we have tried to compile accurate information in this guideline, and to keep it updated in a timely manner, we cannot guarantee that it is fully complete and correct at all times. If you identify information within this guideline that is inaccurate, please report this to the admin.ncl-mon@nhs.net. If a patient is harmed as a consequence of following this guideline, please complete a local incident report and inform admin.ncl-mon@nhs.net.

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NCL JFC is funded by and provides advice to Acute Trusts and the Integrated Care Board in NCL.

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Green: lowest cost Amber: moderate cost Red: highest cost.

If more than one treatment is suitable, the least expensive treatment should be used.

Criteria to start treatment for DAS score 3.2 – 5.1:

- Inadequate response to 2 or more cDMARDs (unless limited by toxicity)
- DAS 28 score between 3.2 and 5.1

Criteria to start treatment for DAS score > 5.1

- Inadequate response to 2 or more cDMARDs (unless limited by toxicity)
- DAS 28 score > 5.1

1ST LINE TREATMENT OPTIONS

<p>TNF inhibitor: Adalimumab SC [Preferred; TA715] OR Etanercept SC OR Infliximab SC/IV with MTX biosimilars [TA715]</p>	<p>JAK inhibitor: Filgotinib [TA676] Upadacitinib (TA744) also available but not preferred¹.</p>
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1ST LINE TREATMENT OPTION

<p>TNF inhibitor: Adalimumab SC [Preferred; TA375] OR Etanercept SC OR Infliximab SC/IV with MTX (TNF inhibitor) biosimilar [TA375]</p>	<p>JAK inhibitor: Filgotinib [TA676] Tofacitinib (TA480), Baricitinib (TA466) and Upadacitinib (TA665) also available but not preferred¹.</p>	<p>Rituximab (off-label) can be used 1st line if anti-TNF is contraindicated/cautioned². Sarilumab (TA485), certolizumab, golimumab, tocilizumab and abatacept (TA375) also available but not preferred³.</p>
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2ND LINE TREATMENT OPTIONS

<p>TNF inhibitor: Adalimumab SC OR Etanercept SC OR Infliximab SC/IV with MTX biosimilar [TA715]^{4,5}</p>	<p>JAK inhibitor: Filgotinib [TA676]⁵ Upadacitinib (TA744) also available but not preferred¹.</p>
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2ND LINE TREATMENT OPTIONS

<p>Preferred if on MTX</p> <p>Rituximab [TA195]</p>	<p>Only if rituximab CI/intolerance or seronegative</p>			
<p>Alternative TNF inhibitor: Adalimumab SC OR Etanercept SC OR Infliximab SC/IV with MTX biosimilars [Preferred if not on MTX; TA375]</p> <p>Certolizumab (TA415) and golimumab (TA225) also available but not preferred⁴.</p>	<p>JAK inhibitor: Filgotinib [TA676] Tofacitinib (TA480), baricitinib (TA466) and upadacitinib (TA665) also available but not preferred⁴.</p>	<p>IL-6 inhibitor: Sarilumab OR Tocilizumab SC/IV [TA247/TA485]</p>	<p>Abatacept [TA195]</p>	

Only if DAS28 > 5.1

3RD LINE ONWARDS TREATMENT OPTIONS (IF MECHANISM OF ACTION NOT ALREADY USED 1ST/2ND LINE)

<p>Alternative TNF inhibitor: Adalimumab SC OR Etanercept SC OR Infliximab SC/IV with MTX biosimilars [TA375]</p> <p>Certolizumab (TA415) and golimumab (TA225) also available but not preferred⁴.</p>	<p>JAK inhibitor: Filgotinib [TA676] Tofacitinib (TA480), Baricitinib (TA466) and Upadacitinib (TA665) also available but not preferred.</p>	<p>Rituximab [TA195]</p>	<p>IL-6 inhibitor: Sarilumab OR Tocilizumab SC/IV [TA247/TA485]</p>	<p>Abatacept [TA195]</p>
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Sequential treatments routinely commissioned: Up to one drug per mechanism of action, plus a second biosimilar TNF inhibitor. If more than one treatment is suitable, the least expensive treatment should be used (see RAG rating below).

Drug	Price	Usual maintenance	Additional Information
Adalimumab	£	40mg SC every 2 weeks	
Etanercept	£	50mg SC every 2 weeks	Use in IGRA +ve patients
Infliximab	£	120mg SC every 2 weeks 3mg/kg IV every 8 weeks	
Filgotinib	£	200mg once daily	
Rituximab	£	1g repeated after 2 weeks	Minimum of 6 months between courses. Caution in patients at increased risk of covid i.e. absence of covid vaccination or low antibody titre in those previously vaccinated
Upadacitinib	££	15mg daily	
Baricitinib	££	4mg once daily	
Tofacitinib	££	5mg twice daily	
Sarilumab	££	200mg SC every 2 weeks	
Certolizumab	£££	200mg every 2 weeks	
Golimumab	£££	50mg every 4 weeks	
Tocilizumab	£££	162mg SC weekly 8mg/kg IV every 4 weeks	
Abatacept	£££	125mg SC once weekly 500mg (<60kg), 750mg (60-100kg), 1g (>100kg) IV every 4 weeks	

Concurrent MTX: Concurrent treatment with methotrexate (MTX) is preferred for all drugs, and required with infliximab. The following drugs are used off-label without MTX; Rituximab, Abatacept

Assessment of response: Assess initial induction response after 6 months of treatment:

For moderate RA (DAS28 3.2-5.1) adequate response is defined as a DAS28 improvement of > 0.6

For severe RA (DAS28 > 5.1) adequate response is defined as a DAS28 improvement of > 1.2

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 (infliximab, adalimumab, golimumab) do not need to be switched to an alternative TNF inhibitor with established minimal placental transfer (certolizumab) either before or during pregnancy (GRADE 1B, Strength of agreement 100%).
- Certolizumab 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 infliximab at 20 weeks, adalimumab and golimumab at 28 weeks, and etanercept 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%).
- Infliximab, adalimumab, etanercept or golimumab 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 Filgotinib is the preferred JAK inhibitor because it is the lowest-cost and there is no evidence that other JAKi have superior efficacy or improved tolerability [EULAR 2022].
- 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 TNF inhibitor and JAK inhibitors are preferred as they are lower-cost and there is no evidence that other classes have superior efficacy or improved tolerability [EULAR 2022].
- ⁴ Adalimumab, etanercept and infliximab are the preferred TNF inhibitor because they are lower-cost and there is no evidence that golimumab or certolizumab have superior efficacy or improved tolerability [EULAR 2022].
- ⁵ There is no TA which specifically recommends 2nd line treatment for moderate RA. The decision to include a 2nd line treatment is a pragmatic one and reflects:
- two mechanisms of actions with NICE TAs available in the 1st line setting (TA715 & TA676)
 - subsequent JAKi or TNF inhibitor would be available once the patient's disease has progressed (TA195)
 - lifetime cost for treatment is similar whether treatment is offered for moderate or severe disease

References

[Efficacy of synthetic and biological DMARDs: a systematic literature review informing the 2022 update of the EULAR recommendations for the management of rheumatoid arthritis](#)