

Biologics pathway in RA (TA 375, TA195, TA 415, TA 466, TA 480) (Updated December 2019; Review December 2021)

TARGET
disease remission
DAS < 2.6 (or < 3.2 where lower not possible)

Combination therapy with 2 DMARDs (6 months per drug) including methotrexate (MTX) (unless contraindicated)

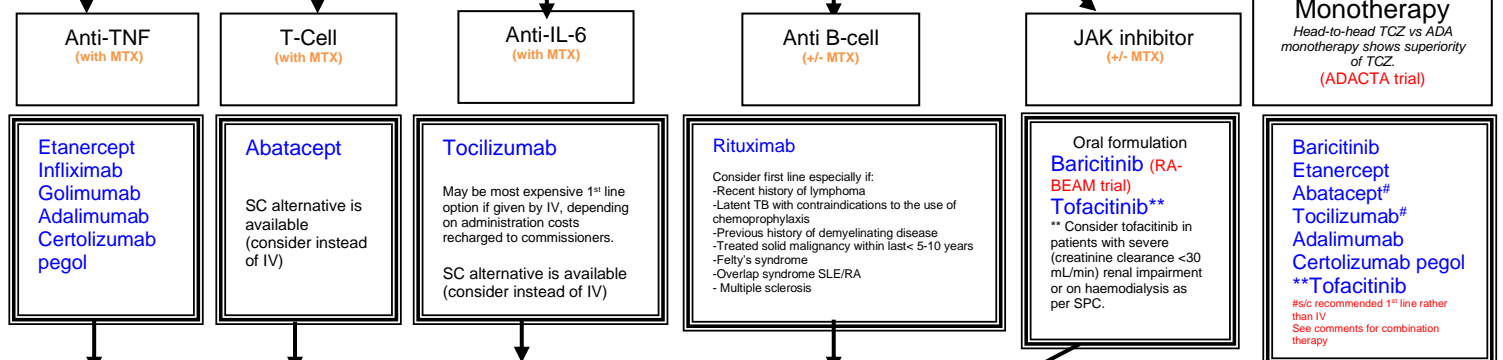
Subcutaneous (SC) MTX

Consider sc methotrexate **early** if oral not tolerated or effect is suboptimal¹

DAS28 score greater than 5.1 confirmed on at least 2 occasions 1 month apart?

Choose most appropriate agent and if no clear indication for a specific agent, then use the least expensive drug (please liaise with pharmacy)
Where both SC and intravenous (IV) formulations are available, **SC is recommended** 1st line. IV can be used if clinician feels this is most appropriate after evaluation of patient factors (page 2)

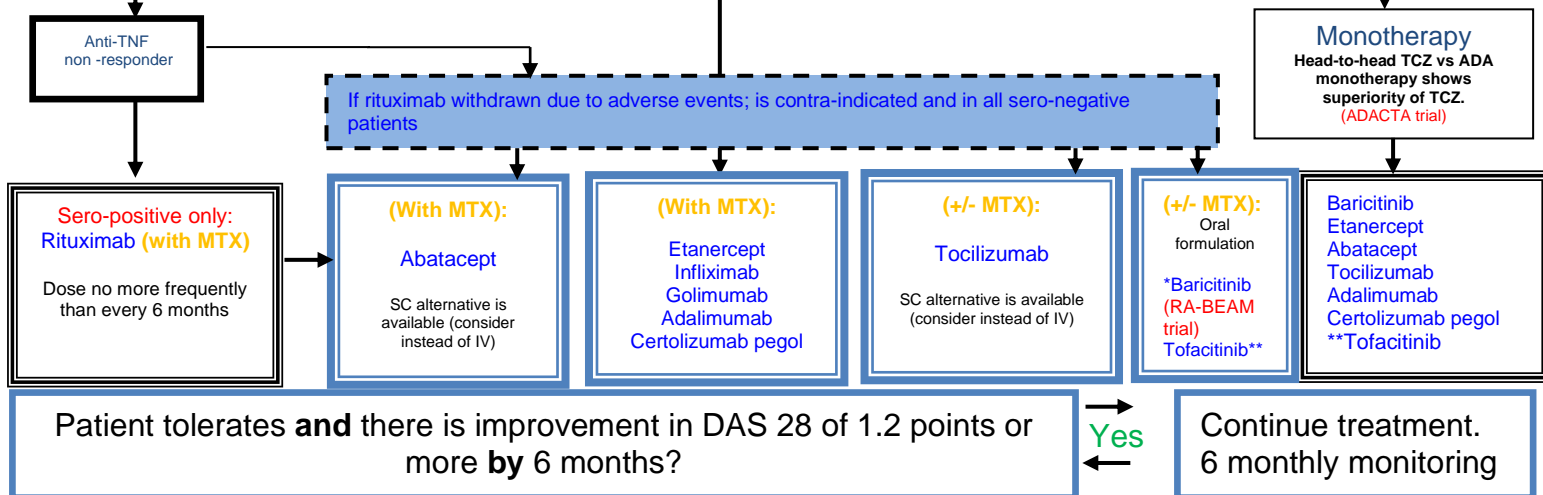
MTX not tolerated or contraindicated (including SC MTX)



Patient tolerates **and** improvement in DAS 28 of ≥ 1.2 points **by 6 months?**
An alternative TNF- α inhibitor may be considered for in case of adverse event before the initial 6-month assessment of efficacy, provided the risks and benefits have been fully discussed with the patient and documented.

Yes
Continue treatment.
6 monthly monitoring

Non responders to first biologic (evaluation of risks/benefits on individual basis)*



Patient tolerates **and** there is improvement in DAS 28 of 1.2 points or more **by 6 months?**

Yes
Continue treatment.
6 monthly monitoring

Evaluation of risks/benefits on individual basis *

*Evidence of safety/efficacy not currently available and therefore careful consideration of risks/benefits required on an individual basis for:

1. Anti-TNF or abatacept after tocilizumab
2. Anti-TNF or tocilizumab after abatacept
3. Rituximab after tocilizumab or abatacept
4. Abatacept after rituximab
5. Baricitinib before biologics/biosimilars

Certolizumab can be prescribed after anti-TNF failure (TA 415)

There is also limited evidence for use of tocilizumab after rituximab, but this has been recognised by NICE as appropriate (see TA 247)

Note: Up to 4 alternative biologics can be used per patient via the prior approval process. Subsequent biologics (from 5th line) require an application to relevant CCG IFR

Biologics pathway in Rheumatology Arthritis

SC methotrexate (MTX):

Prior to commencing a biologic/biosimilar/synthetic DMARD, consider subcutaneous methotrexate, this can be offered either via shared care or homecare, depending on local arrangements.

- SC MTX is significantly more effective²² than oral MTX at the same dosage with no increase in side effects.
- Routine use of SC MTX following oral MTX failure has the potential to provide considerable cost savings²³ through optimised use of MTX first line therapy.
- Option if patient experiences gastrointestinal side effects with oral methotrexate.

Contraindications and cautions for use of biologics, biosimilars and synthetic DMARDs:

- With all biologics, biosimilars and synthetic DMARDs there may be a generalised increased risk of infection, including reactivation of hepatitis B, herpes zoster and TB.
- Anti-TNF alpha drugs can be associated with an increased risk of melanoma and non-melanoma skin cancers. Education about sun protection and monitoring of skin lesions should be offered to every patient. Severe heart failure and demyelinating disease (including multiple sclerosis) are contraindications for the use of TNF inhibitors.
- Tocilizumab should be used with caution in patients with previous history of intestinal ulceration or diverticulitis, because of the risk of gastrointestinal perforation.
- In specific circumstances such as interstitial lung disease (ILD) careful assessment prior to treatment, systemic subsequent monitoring and respiratory opinion is advised regardless of treatment choice.

Specific circumstances that may suggest the use of a specific agent (in alphabetical order):

Biologic/Biosimilar	Advice
ABATACEPT:	Consider if injection site reactions to anti-TNFs ¹ (Level 1b evidence, Grade of recommendations B) Consider if previous hospitalised infection on anti-TNFs/potential serious infection risk ^{2,4} (Level III evidence, Grade of recommendation C) The efficacy is increased in patients with high levels of anti-CCP antibodies and high levels of pain ²⁵ . Consider if co-existent ILD (risk of developing ILD and risk of infection may be lower)
ADALIMUMAB:	Consider if patient has extra articular features/ co-existent conditions such as: <ul style="list-style-type: none"> Uveitis^{5,7} (Level IIb evidence, Grade of recommendations C) Psoriasis (TA 146) Crohn's disease (TA 187), Ulcerative colitis⁸⁻¹⁰ (Level Ia evidence, Grade of recommendation A)
BARICITINIB:	First line JAK1&2 inhibitor, consider in patients with severely impaired manual dexterity, needle phobia Fridge storage is not required Eliminates injection site reactions Consider in patients requiring frequent surgery (short half-life) RA –BEAM (JADV) trial adalimumab vs baricitinib, which showed superiority.
CERTOLIZUMAB PEGOL:	BSR recommends compatibility in pregnancy and breastfeeding after weighing potential risks versus benefits, and after discussion with the patient ²⁶ .
ETANERCEPT:	Consider if the patient has a potential risk of acquiring TB infection (Level III evidence, Grade of recommendation C) Consider in women planning a pregnancy in near future Consider if potential serious infection risk ² (Level III evidence, Grade of recommendation D) Can be considered in patients with pre-existing hepatitis C infection ^{11,12} (Only after hepatology consultation; Level III evidence, Grade of recommendation C) Consider in patients requiring frequent surgery Consider if the patient has latex allergy (etanercept biosimilar (Benepali)) is latex free ²⁴
GOLIMUMAB:	Consider if patient over 100kg (patient access scheme to double dose) Consider if patient has needle phobia/ compliance issues Potential patient convenience due to monthly dosing Consider in patients with co-existent ulcerative colitis ^{13,14} (Level Ia evidence, Grade of recommendations B)
INFLIXIMAB:	Consider if body weight <60kg (potential cost saving) Consider if compliance issues/ needle phobia/ severely impaired manual dexterity (IV infusion) Consider in patients with co-existing Crohn's disease (TA187), and ulcerative colitis (TA 163) Consider in patients with rheumatoid vasculitis ^{15,16} (Level IV evidence, Grade of recommendation B)
RITUXIMAB:	May be safest option in patients with a history of malignancy
TOCILIZUMAB:	Consider in patients who are intolerant of/have contraindications to MTX ^{17,18} (superior to Adalimumab monotherapy) (Level Ib evidence, Grade of recommendation B) Consider if there are features of IL-6 mediated diseases (High ESR/CRP, anaemia of chronic disease, high ferritin ¹⁹) Consider in patients with AA Amyloidosis ^{20,21} (Level IV evidence, Grade of recommendation D)

Prescribing points for biologics, biosimilars and synthetic DMARDs :

- Every intravenous biologic/biosimilar must be prescribed by brand.
- The brands prescribed for each biologic/biosimilar will be guided by the Trust formulary.
- Choice of biologic should continue to be guided by patient need, patient characteristics, clinician recommendation, and local service delivery as directed by this pathway.
- In the absence of a specific clinical need the 'most cost effective drug first' principle will apply with the pathways, but cost alone will not be the only principle to guide prescribing of biologic therapies.
- When a SC and IV version of medication is available (be mindful of capacity in infusion unit and consider IV only if clinician feels this is most appropriate)
- Consider patient factors such as latex allergies, device, and level of manual dexterity, frequency of administration, route, and adherence to drug.
- Selected Homecare schemes include enhanced nursing support; liaise with the homecare pharmacy team for more information.

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NB: This pathway is correct at the time of publication. Any NICE Technology Appraisals which are published after this date in relation to rheumatoid arthritis (adults) will be commissioned within 90 days from publication in line with the TA recommendations.