DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Derbyshire commissioning guidance on biologic drugs for the treatment of severe Rheumatoid arthritis with methotrexate

This algorithm is a tool to aid the implementation of NICE guidance on biologic drugs for the treatment of rheumatoid arthritis. It includes all of the biologic drugs approved by NICE for treatment and local variations for the commissioning algorithm.

Use standard DMARD treatment(s) for Rheumatoid arthritis

Is DAS28 score > 5.1?

- No → Use standard DMARD treatment(s) for Rheumatoid arthritis
- Yes →

Has the disease responded to intensive therapy with a combination of DMARDS?

- Yes → Use standard DMARD treatment(s) for Rheumatoid arthritis
- No →

If more than 1 treatment is suitable, the least expensive should be chosen.
Choices are listed in most cost effective order.
First line biologic agent:

- Adalimumab biosimilar + MTX (TNFi)(TA375)

Alternative biologic can be considered if first line biologic is clinically inappropriate:

- Filgotinib + MTX (JAK1)(TA676) or
- Infliximab biosimilar + MTX (TNFi)(TA375) or
- Etanercept biosimilar + MTX (TNFi)(TA375) or
- Upadacitinib + MTX (JAK1 or 1/3) (TA665) or
- Tofacitinib + MTX (JAK1 and 3)(TA480) or
- Baricitinib[1] (see drug table) + MTX (JAK1 and 2)(TA466) or
- Tocilizumab biosimilar + MTX (IL6)(TA247, TA375 (as SC) or
- Sarilumab + MTX (IL6)(TA485) or
- Abatacept +MTX (selective modulator)(TA375) or
- Tocilizumab + MTX (IL6)(TA247, TA375) (as SC) or
- Certolizumab pegol + MTX (TNFi)(TA375) or
- Golimumab + MTX (TNFi)(TA225, TA375)

- *Rituximab biosimilar + MTX (TA195) (monoclonal antibody)(local agreement)*

Has the biologic drug been withdrawn because of an adverse event?

- No →

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

- No →

If rituximab is **not** contra-indicated

- Rituximab biosimilar + MTX (Anti-lymphocyte monoclonal antibody)(as per TA195) or

- *Filgotinib +MTX (JAK1)(TA676) (local agreement) or*
- *Upadacitinib + MTX (JAK1 or 1/3) (TA665) (local agreement) or*
- *Tofacitinib + MTX (JAK1 and 3)(TA480)(local agreement) or*
- *Baricitinib[1] (see drug table) + MTX (JAK1 and 2)(TA466)(local agreement) or*
- *Abatacept + MTX (selective modulator)(TA195)(local agreement) or*

If rituximab is contra-indicated

- Adalimumab biosimilar + MTX (TNFi)(TA375) or
- Infliximab biosimilar + MTX (TNFi)(TA375) or
- Etanercept biosimilar + MTX (TNFi)(TA375) or
- Tocilizumab biosimilar +MTX (IL6)(TA247, TA375) (as SC) or
- Sarilumab + MTX (IL6)(TA485) or
- Tocilizumab + MTX (IL6)(TA247, TA375) (as SC) or
- Certolizumab pegol + MTX (TNFi)(TA375) or
- Golimumab + MTX (TNFi)(TA225, TA375)

Has the biologic drug been withdrawn because of an adverse event?

- Yes →
- No →

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

- No →

If rituximab is contra-indicated

- Adalimumab biosimilar + MTX (TNFi)(TA375) or
- Infliximab biosimilar + MTX (TNFi)(TA375) or
- Etanercept biosimilar + MTX (TNFi)(TA375) or
- Tocilizumab biosimilar +MTX (IL6)(TA247, TA375) (as SC) or
- Sarilumab + MTX (IL6)(TA485) or
- Abatacept +MTX (selective modulator)(TA375) or
- Tocilizumab + MTX (IL6)(TA247, TA375) (as SC) or
- Certolizumab pegol + MTX (TNFi)(TA375) or
- Golimumab + MTX (TNFi)(TA225, TA375)

- *Rituximab biosimilar + MTX (monoclonal antibody)(local agreement) assuming no contra-indication or*
- *Filgotinib +MTX (JAK1)(TA676) (local agreement) or*
- *Upadacitinib + MTX (JAK1 or 1/3) (TA665) (local agreement) or*
- *Tofacitinib + MTX (JAK1&3)(TA480)(local agreement) or*
- *Baricitinib[1] (see drug table) + MTX (JAK1&2)(TA466)(local agreement)*

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

- No → **Stop treatment**

Yes – maintain same treatment and monitor patient every 6 months

Yes – maintain same treatment and monitor patient every 6 months

Yes – consider alternative biologic agent

The ICB will only commission 6 treatment options (5 switches) per patient - this includes 3 treatment failures and 2 intolerances. JAPC recognises the RMOC statement. Further sequential use outside of the commissioning algorithm should be undertaken after advice via MDT in-line with Trust processes but is limited by clinical appropriateness and safety.

Local variation to NICE

NICE approved treatments

Date reviewed: April 2021

Derbyshire commissioning guidance on biologic drugs for the treatment of severe Rheumatoid arthritis without methotrexate

This algorithm is a tool to aid the implementation of NICE guidance on biologic drugs for the treatment of rheumatoid arthritis. It includes all of the biologic drugs approved by NICE for treatment and local variations for the commissioning algorithm.

* *Patients who have had a proven malignancy in the last 10 years or those with significant pulmonary fibrosis may be offered rituximab instead of TNF inhibitor therapy*

Use standard DMARD treatment(s) for Rheumatoid arthritis

Is DAS28 score > 5.1?

- No → Use standard DMARD treatment(s) for Rheumatoid arthritis
- Yes →

Has the disease responded to intensive therapy with a combination of DMARDS?

- Yes → Use standard DMARD treatment(s) for Rheumatoid arthritis
- No →

Is the patient intolerant to MTX, or is treatment with MTX considered to be inappropriate?

- No → Use RA pathway **with** methotrexate
- Yes →

If more than 1 treatment is suitable, the least expensive should be chosen.
Choices are listed in most cost effective order for monotherapy.
First line biologic agent:

- Adalimumab biosimilar (TNFi)(TA375)

Alternative biologic can be considered if first line biologic is clinically inappropriate:

- Filgotinib (JAK1)(TA676) or
- Etanercept biosimilar (TNFi)(TA375) or
- Upadacitinib (JAK1 or 1/3) (TA665) or
- Tofacitinib (JAK1 and 3)(TA480) or
- Baricitinib[1] (see drug table) (JAK1 and 2)(TA466) or
- Tocilizumab biosimilar (IL6) (TA247, TA375) (as SC) or
- Sarilumab (IL6)(TA485) or
- Tocilizumab (IL6)(TA247, TA375) (as SC) or
- Certolizumab pegol (TNFi)(TA375)

- *Rituximab biosimilar (monoclonal antibody)(local agreement)*
- *Abatacept monotherapy (selective modulator) – by local agreement***

Has the biologic drug been withdrawn because of an adverse event?

- No →
- Yes – consider an alternative biologic agent → Use standard DMARD treatment(s) for Rheumatoid arthritis

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

- No →
- Yes – maintain same treatment and monitor patient every 6 → Has the biologic drug been withdrawn because of an adverse event?

If rituximab* as monotherapy is **not contra-indicated**

- *Rituximab biosimilar (monoclonal antibody)(local agreement) or*
- *Filgotinib (JAK1)(TA676) (local agreement) or*
- *Upadacitinib (JAK1 or 1/3) (TA665) (local agreement) or*
- *Tofacitinib (JAK1&3)(TA480)(local agreement) or*
- *Baricitinib[1] (see drug table) (JAK1&2)(TA466)(local agreement)*
- *Abatacept monotherapy (selective modulator) – by local agreement***

If rituximab **is contra-indicated**

- Adalimumab biosimilar (TNFi)(TA195) or
- Etanercept biosimilar (TNFi)(TA195) or
- Sarilumab (IL6)(TA485) or
- Certolizumab (TNFi)(TA415)

- *Tocilizumab + biosimilar (IL6)(TA247,TA375)(local agreement)(as SC)*

Has the biologic drug been withdrawn because of an adverse event?

- Yes →
- No →

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

- No →
- Yes - maintain same treatment and monitor patient every 6 months → Has the biologic drug been withdrawn because of an adverse event?

Monotherapy options:

- Adalimumab biosimilar (TNFi)(TA375) or
- Etanercept biosimilar (TNFi)(TA375) or
- Sarilumab (IL6)(TA485) or
- Certolizumab (TNFi)(TA415)

- *Rituximab biosimilar (monoclonal antibody)(local agreement) assuming no contra-indication or*
- *Filgotinib (JAK1)(TA676) (local agreement) or*
- *Upadacitinib (JAK1 or 1/3) (TA665) (local agreement) or*
- *Tofacitinib (JAK1&3)(TA480)(local agreement) or*
- *Baricitinib[1] (see drug table) (JAK1&2)(TA466)(local agreement) or*
- *Tocilizumab + biosimilar (IL6)(TA247,TA375) (local agreement)(as SC)*
- *Abatacept monotherapy (selective modulator) – by local agreement***

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

- Yes - maintain same treatment and monitor patient every 6 months → Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?
- Yes → **Stop treatment**

The ICB will only commission 6 treatment options (5 switches) per patient - this includes 3 treatment failures and 2 intolerances. JAPC recognises the RMOC statement. Further sequential use outside of the commissioning algorithm should be undertaken after advice via MDT in-line with Trust processes but is limited by clinical appropriateness and safety.

Date reviewed: April 2021

Drug		NICE TA	TA details	Route	Dose
Intravenous therapies					
Abatacept (+MTX)	Selective T-cell stimulation modulator	NICE TA195 NICE TA375	Disease has not responded to conventional DMARDS – 1st line **and** May also be used if disease has not responded to a previous TNF inhibitor.	SC or IV	**SC** – 125mg once weekly **IV for pts:** <60kg – 500mg dose 60-100kg - 750mg dose >100kg - 1000mg dose Given initially at week 0, 2, and 4 and then every 4 weeks thereafter.
****Abatacept monotherapy**	abatacept monotherapy for patients with RA and interstitial lung disease – outside of NICE guidance – by local agreement				
Adalimumab (±MTX)	Monoclonal antibody that specifically binds to TNF	NICE TA195 NICE TA375	Disease has not responded to conventional DMARDS - 1st line **and** Inadequate response/ intolerance to TNF inhibitor and CI/intolerance to rituximab therapy	SC	40mg every other week For monotherapy – dose may increase to 40mg per week, if patient experiences a decrease in response.
Certolizumab (±MTX)	Recombinant humanised antibody Fab' fragment against TNF alpha	NICE TA415 NICE TA375	Disease has not responded to conventional DMARDS - 1st line **and** Inadequate response/ intolerance to TNF inhibitor and CI/intolerance to rituximab therapy	SC	Initially 400mg given at Week 0, 2 and 4 and then 200mg every 2 weeks thereafter Or 400mg every 4 weeks, once clinical response confirmed.
Etanercept Biosimilar (±MTX)	Recombinant human TNF receptor fusion protein.	NICE TA195 NICE TA375	Disease has not responded to conventional DMARDS - 1st line **and** Inadequate response/ intolerance to TNF inhibitor and CI/intolerance to rituximab therapy	SC	50mg every week Or 25mg twice weekly
Golimumab (+MTX)	Monoclonal antibody that prevents the binding of TNF to its receptors.	NICE TA225 NICE TA375	Disease has not responded to conventional DMARDS - 1st line **and** May also be used if disease has not responded to a previous TNF inhibitor.	SC	For pts < 100kg - 50mg every month For pts >100kg - 100mg every month, if inadequate clinical response after 3-4 doses.)
Infliximab	Chimeric monoclonal	NICE TA195	Disease has not responded to conventional	IV	3mg/kg IV dose, given at week 0, 2, 6 and then every 8 weeks

biosimilar (±MTX)	antibody, with high affinity to TNF.	NICE TA375	DMARDS - 1st line **and** Inadequate response/ intolerance to TNF inhibitor and CI/intolerance to rituximab therapy		thereafter. If there is an inadequate response or loss of response after 12 weeks of treatment, consider increasing dose step-wise by approximately 1.5mg/kg up to a maximum of 7.5mg/kg every 8 weeks or 3mg/kg every 4 weeks
Rituximab Biosimilar (+MTX)	Chimeric monoclonal antibody – depletes B-cell population.	NICE TA195	If pt has had an inadequate response or intolerant of DMARDS and at least one TNF inhibitor.	IV	2x 1000mg given 2 weeks apart, repeated no less than 16 weeks.
Sarilumab (±MTX)	Human monoclonal antibody selective for the IL-6 receptor	NICE TA485	Active RA for pts who have had an inadequate response to DMARDs and/or 1 biological DMARD , only if they cannot have rituximab **and** Disease responded inadequately to rituximab and at least 1 biological DMARD	SC	200mg once every 2 weeks. Reduce the dose to 150mg once every 2 weeks for patients with neutropenia, thrombocytopenia and increased LFTS.
Tocilizumab Biosimilar (±MTX)	Monoclonal antibody – inhibits interleukin-6 (IL-6) receptor	NICE TA375 NICE TA247	Disease has not responded to conventional DMARDS - 1st line **and** May also be used if disease has not responded to a previous TNF inhibitor and the pt cannot receive rituximab because of CI or adverse event to rituximab	SC or IV	**SC** - 162mg once weekly (as per SPC) or **IV** - 8mg/kg every 4 weeks For patients >100kg, doses exceeding 800mg are not recommended
Oral therapies					
Baricitinib (±MTX)	Selective JAK1 and JAK2 inhibitor	NICE TA466	Active RA for pts who have had an inadequate response to DMARDs and/or 1 biological DMARD (only if they cannot have rituximab)	PO	4mg once daily. 2mg once daily is appropriate for pts ≥75 years and over [1]MHRA Drug Safety Update August 2020 - Use baricitinib with caution in patients with diverticular disease and in those concomitantly treated with medications associated with an increased risk of diverticulitis
Filgotinib (±MTX)	Selective JAK1 inhibitor	NICE TA676	Active RA for pts who have had an inadequate response to DMARDs and/or 1 biological DMARD (only if they cannot have rituximab)	PO	200mg once daily for adult 18-74 yrs 100mg once daily increasing to 200mg daily if necessary for adult 75 years and over

Tofacitinib (±MTX)	Inhibitor of JAK1 and JAK3.	NICE TA480	Active RA for pts who have had an inadequate response to DMARDs and/or 1 biological DMARD (if they cannot have rituximab) MHRA Oct 2021 - Tofacitinib should not be used in patients older than 65 years of age, people who are current or past smokers, or individuals with other cardiovascular (such as diabetes or coronary artery disease) or malignancy risk factors unless there are no suitable treatment alternatives	PO	5mg taken twice daily
Upadacitinib	selective and reversible inhibitor of the Janus-associated tyrosine kinase JAK1 or JAK 1/3	NICE TA665	For treating severe rheumatoid arthritis	PO	15mg taken once daily