Cannock Chase Clinical Commissioning Group
South East Staffordshire and Seisdon Peninsula Clinical Commissioning Group
Stafford and Surrounds Clinical Commissioning Group
East Staffordshire Clinical Commissioning Group
North Staffordshire Clinical Commissioning Group
Stoke on Trent Clinical Commissioning Group

Rheumatoid Arthritis Biologics and Targeted Therapies Pathway

NHS

Use standard DMARD treatment(s) for rheumatoid arthritis (CG79)

Has the disease responded to intensive therapy with a trial of at least two DMARDS?

YES → Continue to monitor

NO

Is the Das 28 score>5.1?

YES

Is the patient eligible and willing to enter a clinical trial?

YES → Enter trial #

NO

Can the patient tolerate methotrexate?

NO

Using the most cost effective preparation:

- **Etanercept TA375**
- **Adalimumab TA375**
- Certolizumab pegol TA375
- Tocilizumab TA375
- Baricitinib TA466
- Tofacitinib TA480
- Sarilumab TA485

YES

Using the most cost effective preparation:

- **Etanercept + MTX TA375**
- **Infliximab + MTX TA375**
- **Adalimumab + MTX TA375**
- Certolizumab pegol +MTX TA375
- Golimumab + MTX TA375
- Tocilizumab + MTX TA375
- Abatacept + MTX TA375
- Baricitinib + MTX TA466
- Tofacitinib +MTX TA480
- Sarilumab + MTX TA485

Has the biological been withdrawn because of an adverse event?

Yes – consider alternative biologic agent

NO

Has the biologic drug been withdrawn because of an adverse event?

Yes – consider alternative biologic agent

NO

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

Yes – maintain same treatment and monitor patient every 6 months

Response Lost

NO

Is patient seropositive? #

YES

Rituximab monotherapy
(Consider with alternative DMARD*)

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

Yes – maintain same treatment and monitor patient every 6 months

NO

Consider alternative biologic agent

YES

Has the biologic drug been withdrawn because of an adverse event?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

Use the most cost effective preparation that hasn't previously been tried:

- **Etanercept TA195**
- **Adalimumab TA195**
- Certolizumab pegol TA415
- Tocilizumab TA247 & TA375
- Baricitinib TA466
- Tofacitinib TA480
- Sarilumab TA485

Response Lost

Further treatment options are at the discretion of the clinician and agreement with the CCG. Funding decisions outside NICE guidance need to be approved with the CCG.

YES

Has the patient previously tried Rituximab?

NO

Response Lost

Yes – maintain same treatment and monitor patient every 6 months

Response Lost

NO

Use the most cost effective preparation that hasn't previously been tried:

- **Etanercept + MTX TA195**
- **Infliximab + MTX TA195**
- **Adalimumab +MTX TA195**
- Abatacept +MTX TA195
- Golimumab + MTX TA225
- Certolizumab pegol + MTX TA415
- Tocilizumab +MTX TA247 &375
- Baricitinib + MTX TA466
- Tofacitinib +MTX TA480
- Sarilumab + MTX TA485

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

YES → Consider alternative biologic agent

NO

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

NO → Response Lost

YES → **Yes** – maintain same treatment and monitor patient every 6 months

YES

Consider:
Rituximab + MTX TA195

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

NO → Consider alternative biologic agent → Response Lost

YES → **Yes** – maintain same treatment and monitor patient every 6 months

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Rheumatoid Arthritis Biologics and Targeted Therapies Pathway

Below are circumstances that may suggest the use of a specific agent (in alphabetical order):
With all biologics there may be a generalised increased risk of infection. In specific circumstances such as interstitial lung disease (ILD) careful assessment prior to treatment, systematic subsequent monitoring and respiratory opinion is advised regardless of chosen biologic. It is recommended that safety/alert cards are used where available at the point of initiation for all these medicines.

Abatacept (Antibody blocking T-cells)
Consider if injection site reactions to anti-TNFs or previous hospitalised infections on anti-TNFs/potential serious infection risk
SLE/Lupus like illness overlap
CHF stage 3 (not stage 4)
ILD

Adalimumab (TNF –alpha inhibitor)
Extra articular features/co-existent conditions such as Uveitis (NHSE), Psoriasis, Crohn's disease and Ulcerative colitis
Avoid in severe CCF

Baricitinib (Janus kinase (JAK) inhibitor)
Severely impaired manual dexterity and Needle phobia

Certolizumab (TNF –alpha inhibitor)
Pregnancy
Avoid in severe CCF

Etanercept (TNF –alpha inhibitor)
Potential risk of TB
Women planning a pregnancy in the near future
Consider if potential serious infection risk
Hepatitis C
Avoid in severe CCF

Golimumab (TNF –alpha inhibitor)
Consider if the patient is over 100kg
Needle phobia/compliance issues/patient convenience (monthly injection)
Ulcerative colitis
Avoid in severe CCF

Infliximab (TNF –alpha inhibitor)
Body weight <60kg (potential cost saving)
Compliance issues/Needle phobia
Severely impaired manual dexterity
Co-existent conditions such as Uveitis (NHSE), Crohn's disease, Ulcerative colitis and rheumatoid vasculitis
Avoid in severe CCF

Rituximab (B-cell depletion of lymphocytes -1 type of white blood cell)
Can be used first line if – Recent history of lymphoma
*Lefluomide is the preferred option instead of methotrexate
Latent TB with contraindications to the use of chemoprophylaxis
Previous history of demyelinating disease
Treated solid malignancy within the last 5 years (does not include non BCC/squamous cell skin cancer)
SLE/Lupus like illness overlap
CHF stage 3 (not stage 4)
Severely impaired manual dexterity
ILD
seronegative patients may also be trialled on Rituximab following agreement from the CCG.

Sarilumab (IL-6 (interleukin 6) receptor inhibitor)
As for Tocilizumab
UKMI have released a safety alert stating that patients receiving sarilumab should receive an alert card before the initiation of drug treatment. The alert card advises the patient on their treatment, but also the increased risk of serious infections, neutropenia, and gastrointestinal perforation, and when to seek immediate medical attention.

Tocilizumab (IL-6 (interleukin 6) receptor inhibitor)
Compliance issues/Needle phobia (IV Tocilizumab)
Severely impaired manual dexterity (IV Tocilizumab)
Features of IL-6 mediated disease (high ESR/CRP, anaemia of chronic disease, high ferritin, and systemic features)
AA Amyloidosis
SLE/Lupus like illness overlap
CHF stage 3 (not stage 4)
ILD
Use with caution in patients with colitis/diverticulitis

Tofacitinib (Janus kinase (JAK) inhibitor)
Severely impaired manual dexterity and Needle phobia

 # Clinical Trials:
In cases where treatment cannot be stopped at the end of the trial, exit arrangements and ongoing funding arrangements must be agreed with the Commissioner prior to commencement of the trial

NHS England Policy
https://www.england.nhs.uk/wp-content/uploads/2017/09/clinical-trials-comm-policy.pdf

Government Gateway- Good clinical practice for clinical trials
https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials

N.B Patients can enter trials at any point of the pathway or re-enter the pathway after trial as per the exit strategy.

+ If the patient has failed on two anti-TNFs then preferentially use an alternative treatment with a different mode of action.

Biosimilars
Biosimilar versions of biologics are becoming more accessible, usually with a lower cost than the originator product.
The prescribing of biosimilar preparations should be by brand name. The preparation with the lowest acquisition cost (taking into account administration costs, dosage and price per dose) should normally be used.

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