BLMK Integrated Care System

NHS

BEDFORDSHIRE, LUTON AND MILTON KEYNES AREA PRESCRIBING COMMITTEE (APC)

Rheumatoid Arthritis Treatment Pathway for Moderate and Severe Disease (Algorithm A)

(NB Use **Algorithm B** for patients who are not suitable for treatment with a TNF inhibitor due to having certain co-morbidities **i.e.** • Patient has had a proven malignancy in the last 10 years • pulmonary fibrosis • malignant melanoma at any point • multiple sclerosis • bronchiectasis • SLE

(updated Dec 2021)

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Clinical Commissioning Group; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

CO-PRODUCTION COMMUNITY COMPASSION COLLABORATION COMMITMENT

Drug Treatment Options for the Management of Moderate and Severe Rheumatoid Arthritis (i.e., DAS 28 ≥ 3.2 and >5.1 respectively)
Preferred Treatment Pathway (in line with NICE TAs and locally agreed JPC guidance) Algorithm A (Approved by BLMK APC Dec 2021)

General Prescribing notes:

- **Where possible, prescribe the least expensive agent (taking into account individual patient factors)**
- **Biosimilars are the preferred cost-effective choice over the originator.**
- **Always prescribe by brand name**
- **NB. If using infliximab for moderate disease , NICE only supports the use of a biosimilar version.**
- **Switching from originator brand to a biosimilar should be carried out as per locally agreed switching protocols.**
- **Clinicians should refer to the individual SPmCs for full prescribing information, noting ▼black triangle status where applicable. – click here**
- **mtx = methotrexate**
- **Refer to Algorithm B for different treatment choices if a patient has any of the following comorbidities :- Proven malignancy in last 10 years; malignant melanoma at any point ; MS ; Bronchiectasis ;Pulmonary Fibrosis ; SLE**

Moderate Disease (DAS 28 ≥ 3.2) Treatment Pathway

1st line :- intensive therapy with a combination of 2 or more conventional disease-modifying anti rheumatic drugs (DMARDs)

2nd line:- if 1st line therapy has resulted in an inadequate response , consider using either one of the specific TNF inhibitors or JAK inhibitors listed below :-
Ie. either adalimumab (biosimilar)+/- mtx or etanercept(biosimilar) +/- mtx or infliximab (biosimilar) (IV) plus mtx) or filgotinib ▼ +/- mtx (in particular noting effect of filgotinib on male fertility) or Upadacitinib ▼ +/- mtx

Review process

- **Review after 6 months, continue if a moderate response achieved (improvement in DAS28 score of 0.6 or more (based on EULAR guidelines).**
- Discontinue if adequate response is not achieved - If the first biological treatment fails, and if the disease progresses to severe, - **follow the severe disease pathway if disease severity has increased to DAS 28 > 5.1**

NB: If using a TNF inhibitor: An alternative TNF inhibitor may be used if treatment stopped due to an adverse event within the first 6 months, unless it's deemed to be a class effect reaction (as per local agreement).

Following an inadequate response to DMARDs, NICE supports the use of one agent at the moderate treatment stage.(see above). If the patient does not respond or loses response, clinicians should then progress down through the severe disease stage pathway. Regardless at what stage of the pathway, treatment is started, it has been agreed locally that a maximum of 4 drugs with different mode of action (MOA) can be used. Any request for a fifth agent will require an IFR application.

Severe Disease (DAS 28 > 5.1) Treatment Pathway

Consider **either** a **Biological DMARD OR a JAK inhibitor** (NB: Choice depends if any agent has previously been used to treat moderate disease)

Biologic DMARD Treatment Pathway options

prescribed in combination with methotrexate unless methotrexate is contraindicated/not tolerated.

For patients who are able to receive methotrexate:

Choice of TNF inhibitors in combination with mtx:

- **Adalimumab (biosimilar) s/c (locally preferred first line)**

If not appropriate; alternative options are:

- etanercept(biosimilar) s/c
- certolizumab pegol s/c
- golimumab s/c
- infliximab (biosimilar) IV

Alternatives to a TNF inhibitor plus MTX (if more clinically appropriate)

- abatacept s/c
- sarilumab s/c
- tocilizumab s/c

NB: Alternatives if s/c route is not suitable:

- Abatacept IV or tocilizumab IV or infliximab IV

For patients who are unable to have methotrexate

Choice of TNF inhibitors as monotherapy:

- **Adalimumab (biosimilar) s/c (preferred first line)**

If not appropriate; alternative options are:

- Etanercept (biosimilar) s/c or certolizumab pegol s/c

Alternatives to a TNF inhibitor monotherapy (if more clinically appropriate)

- sarilumab s/c
- tocilizumab s/c

NB: Alternatives if s/c route is not suitable:

- Tocilizumab IV

NB: If using a TNF inhibitor : An alternative TNF inhibitor may be used if treatment stopped due to an adverse event within the first 6 months, unless its deemed to be a class effect reaction (as per local agreement).

JAK Inhibitors Options: Prescribe in combination with mtx unless mtx is contraindicated/ not tolerated.

Choice of JAK inhibitor: (NB All JAKI'S have ▼ triangle status)

- Baricitinib po +/- mtx **or**
- Filgotinib po +/- mtx **or**
- Tofacitinib po +/- mtx **or**
- Upadacitinib po +/- mtx

NB: The current pathway does not support switching to a different JAK inhibitor in the event of treatment failure / loss of response. This also applies to situations where a JAK inhibitor may have been started for moderate disease – patients should be switched to a biologic agent in such circumstances (choice depends on what previously has been tried)

Assess response after 6 months:

- If a moderate response*, **continue** treatment and monitor every 6 -12 months. **Withdraw** treatment and consider a second line agent if moderate response not achieved or if not maintained. If intolerance develops, **withdraw** treatment and consider the next line treatment options.

***moderate response (in severe disease)**: as measured using the European League against Rheumatism (EULAR) i.e., an improvement in DAS28 of 1.2 points

NEXT LINE TREATMENT OPTIONS (SEVERE DISEASE PATHWAY) (as per NICE ; local agreement {with regards choice following 1ST line use of a JAK inhibitor)

Preferred next line choice:

- **Rituximab (biosimilar) IV in combination with methotrexate**
- Rituximab should be given no more frequently than every 6 months

Alternative to rituximab if rituximab is contraindicated or not tolerated (NB: Choice will depend on which agent has previously been used).

Consider using either:

- one of the biologic options plus methotrexate (for choices see yellow box above)

or

- a JAK inhibitor plus methotrexate NB only suitable if no JAK inhibitor has previously been tried see red box above)

Alternative to rituximab If methotrexate is contraindicated or not tolerated: (NB: Choice will depend on which agent was used first line)

Consider using either:

- one of the monotherapy biologic options (for choices see green box above

or

- a JAK inhibitor (monotherapy) (NB only suitable if no JAK inhibitor has previously been tried see red

Assess response after 6 months; if no response/loss of response: **consider third line option**

FURTHER TREATMENT OPTIONS (SEVERE DISEASE PATHWAY)

If Rituximab used above : available options if not already used earlier in the pathway include:
sarilumab s/c +/- mtx or tocilizumab s/c* +/- mtx or Upadacitinib po +/- mtx or filgotinib po +/- mtx

NB switching between sarilumab and tocilizumab, and ,between filgotinib and upadicitinib is not supported in this pathway.

If alternative biologic or a JAK inhibitor used above: available options if not already used earlier in the pathway include sarilumab s/c +/- mtx or tocilizumab s/c* *NB: Tocilizumab IV is an alternative option if s/c route not suitable

IF PREVIOUSLY TRIED 3 DIFFERENT MOA treatments, (regardless if started at moderate or severe stage of the pathway):-

If no response / loss of response after 6 months; clinicians can consider switching agent. The new option **must have a different mode of action** to any of the previously tried agents. (Local agreement). **Further requests beyond a TOTAL OF 4 AGENTS will require an IFR application to be submitted**