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

Rheumatoid Arthritis Treatment Pathway for Severe Disease

(This pathway is designed to follow on from the moderate disease pathway)

(updated September 2023, previous March 2022)

General Prescribing notes

- Patients may already have received either a TNFi or a JAKi as part of the Moderate disease treatment pathway. Usage at the moderate stage must be taken into account when considering further treatment options within the Severe disease pathway.
- Regardless of whether treatment is started at the moderate stage or at the severe disease stage, it has been agreed locally that a maximum of 5 drugs, each with a different mode of action (MOA) can be used in total.
- In cases where clinical exceptionality can be demonstrated, a request for a sixth line agent can be considered via the Individual Funding Request (IFR) route
- Clinicians should refer to the SmPCs for each individual drug for full prescribing information, noting ▼black triangle status where applicable. – click here
- **TNF inhibitors should be avoided in patients with any of the following co-morbidities:- (Δ Specific patient population):** Proven malignancy in last 10 years; malignant melanoma at any point; MS; Bronchiectasis; Pulmonary Fibrosis; SLE; Congestive heart failure (NYHA Class III / IV)
- **JAK inhibitors** –The MHRA have issued a drug safety update (DSU) bulletin (April 2023) detailing new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality with JAK inhibitors. See **MHRA advice** on measures to consider before considering prescribing a JAK inhibitor.
- Always prescribe by brand name
- Biosimilar biologics are preferred over the originator brand (cost effective)
- Switching from originator brand to a biosimilar should be carried out as per locally agreed switching protocols.

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Clinical Integrated Care Board (ICB); 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

Management of Severe Rheumatoid Arthritis (i.e. DAS 28 > 5.1)

Preferred Treatment Pathway (in line with NICE TAs and locally agreed APC guidance) (Updated Sept 2023)

STEP ONE:-Take individual patient factors and co-morbidities into account when making initial choice of therapy. Always prescribe in combination with methotrexate (mtx) unless contra-indicated / not tolerated.

Choice of TNF inhibitors

-Adalimumab* s/c +/- mtx (preferred option)
-Etanercept* s/c +/- mtx
-Certolizumab pegol s/c +/- mtx
-Golimumab s/c **plus** mtx
-Infliximab* s/c or IV **plus** mtx

*Biosimilar brand available

An alternative TNFi may be used if treatment stopped due to an adverse event within the first 6 months unless deemed to be a class effect reaction (local agreement).

NB: Avoid TNFi s in patients with the following comorbidities:- (Δ **specific patient subgroup:-** Proven malignancy in last 10 years; malignant melanoma at any point ; MS ;Bronchiectasis ;Pulmonary Fibrosis ; SLE ; congestive heart failure (class III / IV)

Choice of JAK Inhibitors*

(**note all JAKi have a ▼**status – See individual SmPCs)
-Baricitinib po +/- mtx
-Filgotinib po +/- mtx
-Tofacitinib po +/- mtx
-Upadacitinib po +/- mtx

***See MHRA advice on measures to consider before prescribing a JAK inhibitor**.

Choice of IL-6 Inhibitors

-Sarilumab s/c +/- mtx
-Tocilizumab s/c +/- mtx

(tocilizumab IV +/- mtx is an option if s/c not suitable)

Selective co-stimulation modulator

Abatacept plus mtx

NB: In a small, specific patient subgroup Δ who cannot have a TNFi and where the use of rituximab is preferable to any of the 3 remaining step one agents (listed above) :-
-rituximab plus mtx may be considered as a **STEP ONE** option. If the patient cannot have mtx, then rituximab may be given with another DMARD **or** as monotherapy (local agreement). A switch to subsequent agents with different mode of action each time may then be tried. The subsequent choice of agents is dependent on exact nature of comorbidities.

Assess response after 6 months:

- If a moderate response*, c**ontinue** treatment and monitor every 6 -12 months.
- **Withdraw** treatment if moderate response not achieved / not maintained/ if intolerance develops and consider a STEP TWO agent. ***Moderate response (in severe disease)**: (as defined by EULAR) i.e., an improvement in DAS28 of 1.2 points

STEP TWO:-
Rituximab plus mtx is the preferred treatment to try in step 2. Alternative options can be used if rituximab or methotrexate is contra-indicated / not tolerated. Take individual patient factors and co-morbidities into account.

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

Alternative if rituximab contraindicated or not tolerated (choice dependent on previous agents tried)

- An alternate biologic options from step one +/- mtx (use a biologic with different mode of action than initial drug) **OR**
- a JAK inhibitor +/- mtx (NB not suitable if a JAKi has been tried previously)

Alternative if mtx is contraindicated or not tolerated (choice dependent on what agents have previously been tried)

- TNFi (monotherapy) i.e. adalimumab; etanercept; certolizumab **or**
- a JAK inhibitor (monotherapy) (NB this is not suitable if a JAKi has been tried previously at earlier stage) **or**
- IL-6 inhibitor (monotherapy) i.e. sarilumab; tocilizumab

Assess response after 6 months (as per grey box above); if no response / loss of response: consider STEP THREE option

STEP THREE:-

If Rituximab plus mtx used in step 2: options if not already used earlier in the pathway include:
Upadacitinib **po +/- mtx or** filgotinib **po +/- mtx or** sarilumab **s/c +/- mtx or** tocilizumab **s/c +/- mtx**
(NB switching between filgotinib & upadicitinib or sarilumab & tocilizumab, is not supported in this pathway.)

If alternative biologic or a JAK inhibitor was used in step 2: available options if not already used earlier in the pathway include:- sarilumab **s/c +/- mtx or** tocilizumab **s/c +/- mtx** NB: Tocilizumab IV is an alternative option if s/c route not suitable.

Assess response after 6 months (as per grey box above) ; if no response / loss of response: consider STEP FOUR option

STEP FOUR / FIVE (local agreement)

Clinicians can consider switching to a 4th agent with a different mode of action that has not yet been tried previously.
Assess response after 6 months (as per grey box above); if no response / loss of response.
A 5th agent (with a different mode of action) may be considered.

A total of 5 different modes of action will be routinely commissioned. **Any request for a sixth line agent, where clinical exceptionality can be demonstrated, can be considered via the Individual Funding Request (IFR) route**".