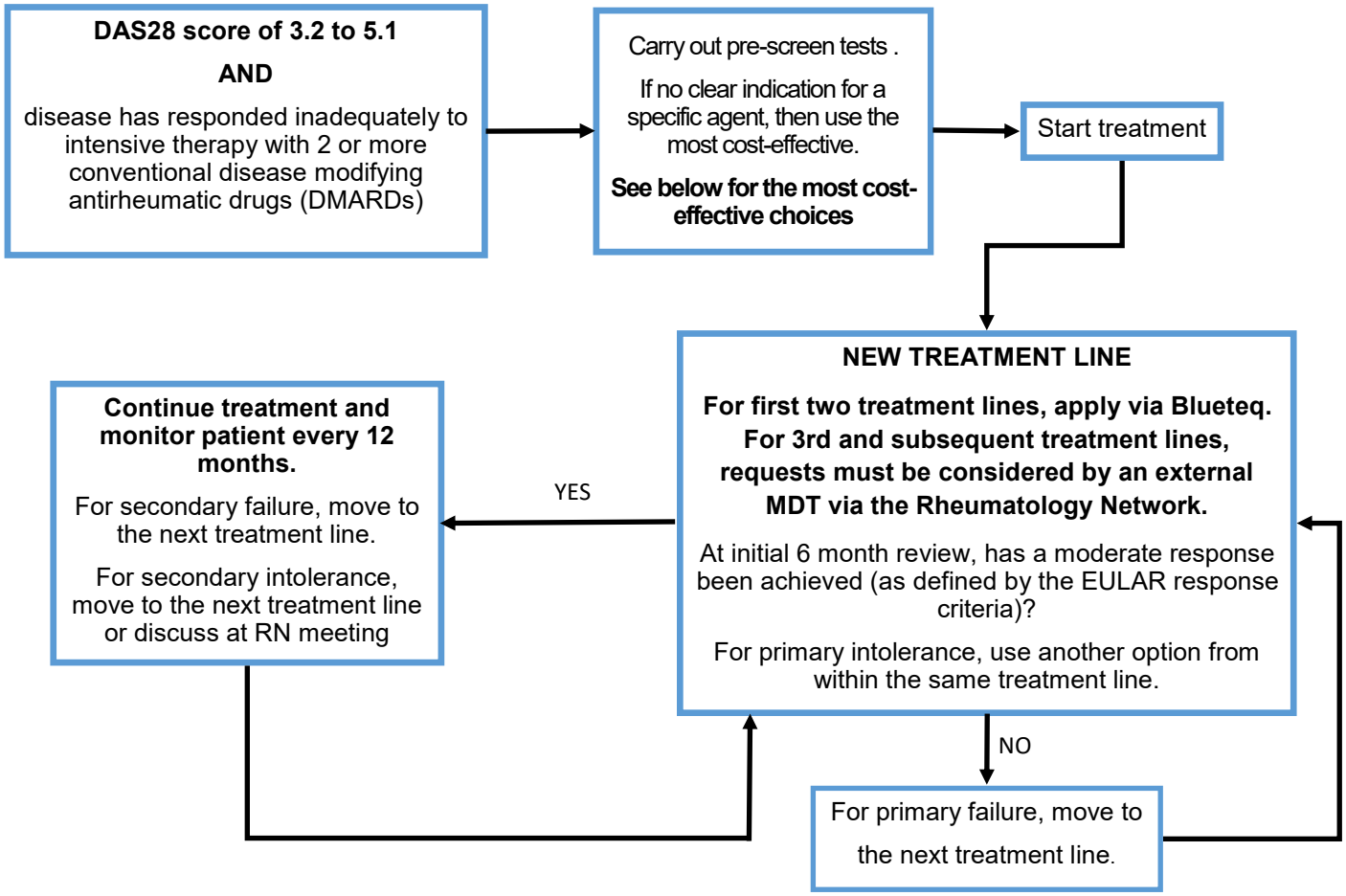
RHEUMATOID ARTHRITIS IMMUNOMODULATOR TREATMENT PATHWAY (ADULTS)

1. MODERATE RHEUMATOID ARTHRITIS WITH DAS28 3.2 to 5.1

Approved by NHS Surrey Heartlands CCG Area Prescribing Committee - April 2024



Drug choices:

Mode of action		Drug
TNF alpha inhibitor		**Adalimumab***
		Etanercept
		Infliximab
Janus-associated tyrosine kinase (JAK) - oral	JAK 1 and JAK 3	Upadacitinib
	JAK 1	**Filgotinib***

*the most cost-effective choices. Biosimilar adalimumab is more cost-effective than filgotinib.

Notes:

- Two lines of treatment are commissioned for moderate use—one from each mode of action.
- A request for a **third** line of treatment must be considered by an external MDT via the Rheumatology Network.
- People moving from the moderate stream to the severe would not be required to strictly fulfil the criteria of the severe RA NICE TAs with regard to combination cDMARD use, as they indirectly fulfil this by moving through the moderate stream first.

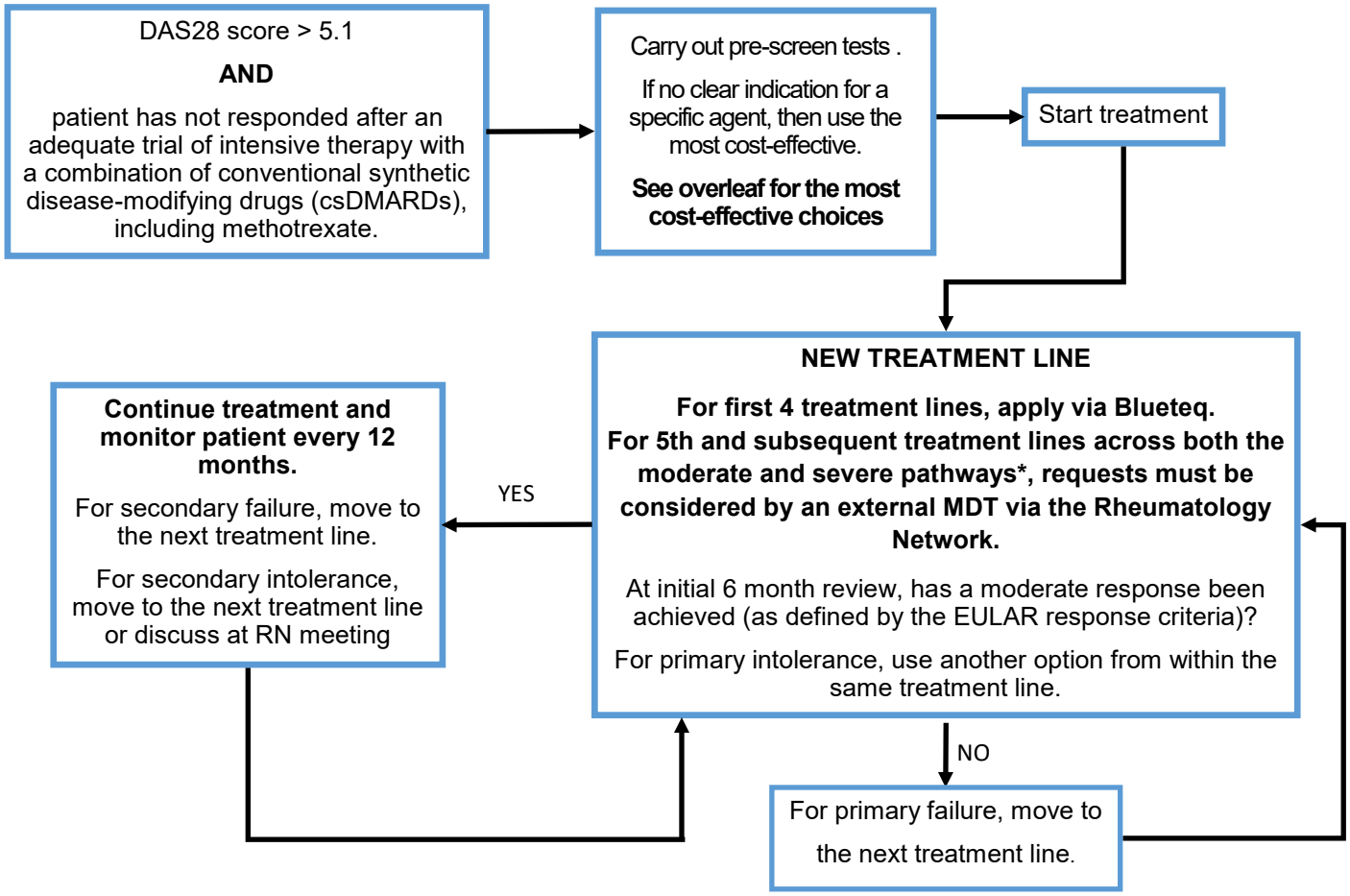
EULAR response criteria

			DAS28 improvement		
			> 1.2	> 0.6 and ≤ 1.2	≤ 0.6
Present DAS28	Low	≤ 3.2	good response	moderate response	no response
	Moderate	> 3.2 and ≤ 5.1	moderate response	moderate response	no response
	High	> 5.1	moderate response	no response	no response

RHEUMATOID ARTHRITIS IMMUNOMODULATOR TREATMENT PATHWAY (ADULTS)

2. SEVERE RHEUMATOID ARTHRITIS WITH DAS28 > 5.1

Approved by NHS Surrey Heartlands CCG Area Prescribing Committee April 2024



*this includes any that are used under moderate use e.g., if two immunomodulators are used in the moderate pathway, an MDT is required for the second request under the severe pathway i.e., the fourth immunomodulator.

Requests for additional lines of treatment to external network MDT

- Request the 'Additional lines of treatment application form' from the Surrey PAD at https://surreyccg.res-systems.net/PAD/
- Each consultation will last for seven days.
- Agreement requires **3 positive** endorsements (from clinicians of **at least 3 trusts other** than from the requesting clinician) **+ no negative/severe concerns.**
- If there are negative/severe concerns then decision should be postponed until the next face-to-face Rheumatology Network meeting. The requesting clinician should attend this meeting, or be prepared to dial into the meeting, with access to the patient's notes (in case of further questions).

EULAR response criteria

			DAS28 improvement		
			> 1.2	> 0.6 and ≤ 1.2	≤ 0.6
Present DAS28	Low	≤ 3.2	good response	moderate response	no response
	Moderate	> 3.2 and ≤ 5.1	moderate response	moderate response	no response
	High	> 5.1	moderate response	no response	no response

Pathway definitions:

	Definition	Action
Primary Failure	Occurs when the response criteria (as defined within the NICE TA) is **not fully met** when response to treatment is assessed at the time interval defined within the NICE TA	Move to the NEXT treatment line/mode of action (if one is available)
Secondary Failure	Occurs when the response to treatment (as defined within the NICE TA) is **no longer met**	Move to the NEXT treatment line/mode of action (if one is available)
Primary intolerance/adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side-effects of that treatment that occurs **during the initial time period defined by the NICE TA**	Use another option from the SAME treatment line
Secondary intolerance/adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side effects of that treatment that occurs **after the initial time period defined by the NICE TA**	Move to the NEXT treatment line OR discuss at RN meeting
Conception	If conception plans or pregnancy indicate a change of drug is advisable, it is agreed that this **does not constitute a change in line of treatment**	Please update Blueteq accordingly

Drug choices:

Mode of action		Drug	Moderate RA with DAS > 3.2	NICE TA	Severe RA with DAS > 5.1	NICE TA
T-cell co-stimulation inhibitor		Abatacept			✓	TA195
TNF alpha inhibitor		Adalimumab	✓	TA715	✓	TA195
		Certolizumab			✓	TA415
		Etanercept	✓	TA715	✓	TA195
		Golimumab			✓	TA225
		Infliximab	✓	TA715	✓	TA195
B-cell inhibitor		Rituximab			✓	TA195
IL-6 inhibitor		Tocilizumab			✓	TA247
		Sarilumab			✓	TA485
JAK inhibitor (oral)	JAK 1 and JAK 2	Baricitinib			✓	TA466
	JAK 1 and JAK 3	Tofacitinib			✓	TA480
	JAK 1	Upadacitinib	✓	TA744	✓	TA665
	JAK 1	Filgotinib	✓	TA676	✓	TA676

The most cost-effective drugs are:

TNFα inhibitor: Biosimilar adalimumab

IL-6 inhibitor: Sarilumab

JAK inhibitor: Filgotinib

Notes:

- **JAK inhibitors**
  If patients on JAK inhibitors need to change therapy due to the MHRA alert[5] issued 26th April 2023, then this would be considered a change within the same treatment line.
- **Rituximab**
  BSR/BHPR guidelines - if methotrexate is contraindicated then rituximab can be used alone, or with leflunomide(off-label).
- As of November 2023, the Rheumatology Network agreed the following wording for its pathways "n*o differentiation between medicines targeting a specific part of the same pathway is applied e.g., the different JAK inhibitors and the different IL inhibitors. Until evidence is available that targeting a specific part of the same pathway gives different and additional gains in health-related outcomes and cost-effectiveness, these medicines will be considered to be within the same treatment line*".

References:
1. NICE Technical Appraisals. Available at: www.nice.org.uk
2. NICE Commissioning Guide – Implementing NICE guidance. Biologic drugs for the treatment of inflammatory disease in rheumatology, dermatology and gastroenterology. 6th December 2010. Available from: http://www.nice.org.uk/media/BB8/C9/biological_therapies_PDF.pdf. Accessed 16.12.10.
3. Deighton, C et al. British Society for Rheumatology and British Health Professionals in Rheumatology rheumatoid arthritis guidelines on safety of anti-TNF therapies. Sept 2010. Available from: http://www.rheumatology.org.uk/includes/documents/cm_docs/2010/r/ra_guidelines_on_safety_of_antitnf_therapies_sept_2010.pdf. Accessed 21.9.10.
4. Lloyd S, Bujkiewicz S, et al. The effectiveness of anti-TNF-a therapies when used sequentially in rheumatoid arthritis patients: a systematic review and meta-analysis. Rheumatology 2010;49:2313–2321.
5. Drug Safety Update. Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality. Available at: Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality

Reviewed: NHS Surrey Heartlands CCG Pharmaceutical Commissioning Team **Input from:** Rheumatology Network - November 2023

Agreed date: Area Prescribing Committee April 2024 **Review date:** March 2027 or as needed