Gloucestershire Hospitals
NHS Foundation Trust

Biologics Pathway for MODERATE Rheumatoid Arthritis (RA) in adults

This pathway has been developed primarily for use by the specialist Rheumatology Team. It aims to standardise the management of moderate rheumatoid arthritis ensuring cost-effective evidence-based prescribing of biologics whilst reflecting the need for individual prescribing considerations.

In order to progress to this pathway, the patient must meet the following criteria:

- **Disease is MODERATE with a DAS28 of 3.2 - 5.1**
- **Patient must have tried intensive therapy with 2 or more conventional DMARDs**

NICE have not assigned any hierarchical ranking to these therapies but have stated that treatment ***should be started with the least expensive drug taking into account administration costs, dose needed and product price per dose.*** Therefore, the most cost-effective drug has been listed for each mode of action, in the algorithm. Others that may be considered are listed in Table 1, with pharmaceutical and clinical considerations that may be considered to support decision making.

Treatment should be continued only if there is an adequate/moderate response 6 months after treatment initiation (assessed using DAS28).

- After an initial response at 6 months, withdraw treatment if response is not maintained.
- *Adequate response is defined as an improvement in DAS28 of 0.6 – 1.2 achieved in 6 months*
- *If still active joint swelling and DAS28 ≥3.9 consider change in therapy*

If the first biological treatment fails and if the disease progresses to severe RA the Biologics Pathway for Severe RA should be followed

Table of abbreviations:	
cDMARD	Conventional Disease Modifying anti-rheumatic Drug
bDMARD	Biologic Disease Modifying anti-rheumatic Drug
tsDMARD	Targeted- Synthetic Disease Modifying anti-rheumatic Drug
MTX	Methotrexate

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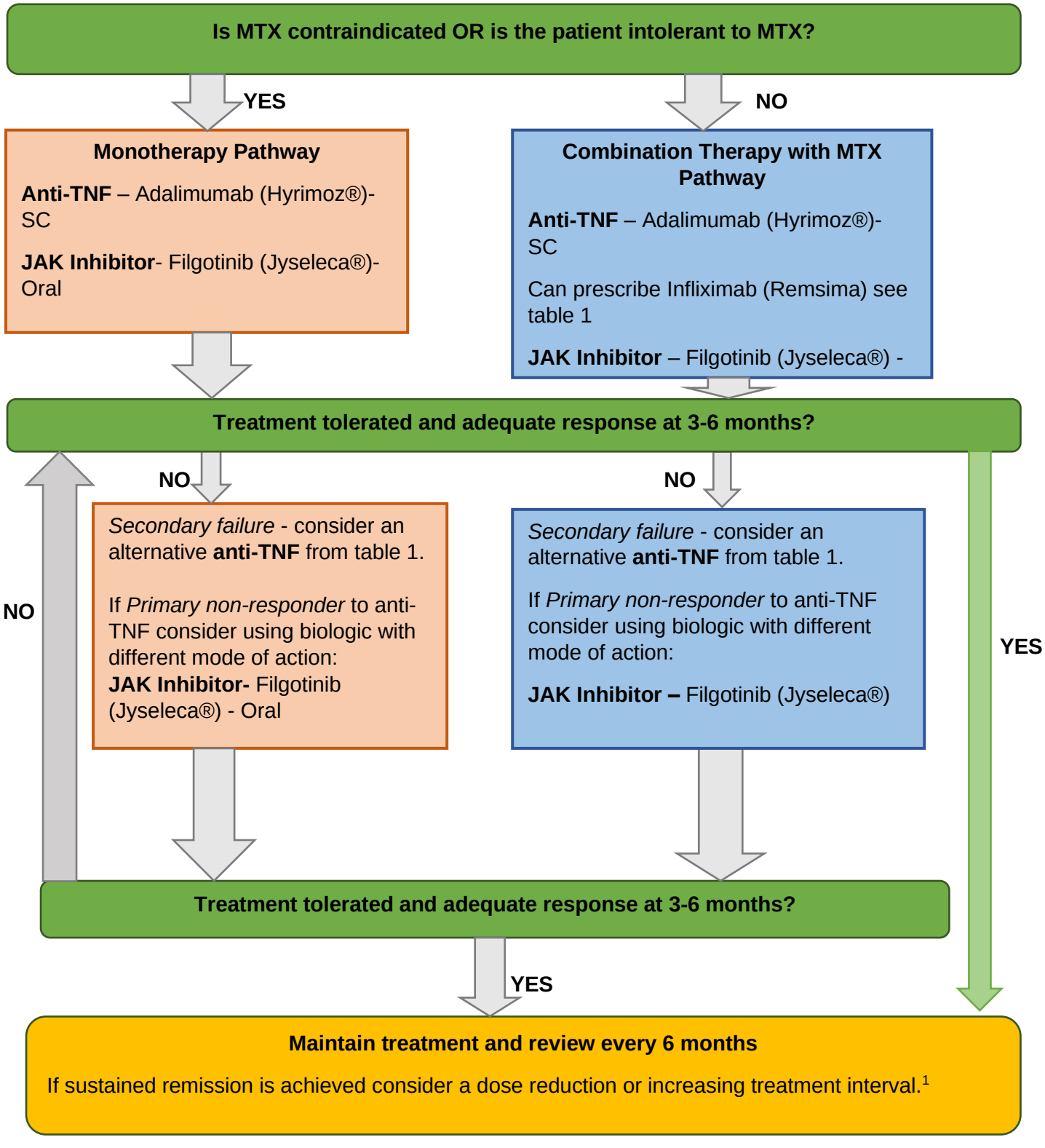

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Table 1: NICE Approved biologics, listed in order of cost-effectiveness for each therapeutic class

Drug (Brand &/or approved Biosimilar)	***Suitable for Monotherapy?***	***Pharmaceutical Considerations***	***Clinical Considerations***
Anti-TNFs			
Adalimumab *(Hyrimozi®)* **NICE TA715**	YES	SC injection only Store in Refrigerator Supplied via Homecare	***Allergies:*** Do not use if patient allergic to murine proteins and if patient has latex allergy ***Contraindicated*:** In active severe infections, moderate or severe heart failure, ***Cautions:*** Demyelinating disorders, malignancy or history of malignancy, infections; sepsis or risk of sepsis. First line biologic if patient has co-existent IBD Consider in patients with extra-articular co-existent conditions such as uveitis, psoriasis Extensive data for use in pregnancy Cautioned for use in over 65-year-olds **Interactions:** Immunosuppressive drugs and Live vaccinations
Etanercept *(Benepali®)* **NICE TA715**	YES	SC injection only Store in Refrigerator Supplied via Homecare	***Allergies:*** Care in patients with latex allergy; contains rubber needle cover and plunger ***Contraindicated****:* active infection ***Cautions*:** Malignancy, diabetes mellitis, heart failure, infections, blood disorders, demyelinating disorders, predisposition to septicaemia. May be suitable option for patients experiencing secondary failure Extensive data for use in pregnancy Monitor blood sugars if diabetic patient; antidiabetic doses may need reducing Increased risk of infections in over 65-year-olds **Interactions:** Immunosuppressive drugs and Live vaccinations
Infliximab *(Remsima®)* **NICE TA715**	NO	Intravenous injection NICE did not consider the SC preparation in their review of TA715	***Allergies:*** Do not use if patient allergic to murine proteins ***Contraindicated:*** Severe infection, moderate or severe heart failure

			Cautions: Demyelinating disorders, dermatomyositis, malignancy, mild heart failure, predisposition to infection; Risk of delayed hypersensitivity reactions. Explain risk of hypersensitivity reaction to patient Greater incidence of serious infections in patients aged 65-or over **Interactions:** Immunosuppressive drugs and Live vaccinations
JAK Inhibitors – Following recent MHRA update JAK-Inhibitors should not be used in patients with the following risk factors unless there are no suitable alternatives: - **Aged 65 years or over** - **patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers, diabetes, hypertension)** - **patients with malignancy risk factors (e.g., current malignancy or history of malignancy)** - **Use with caution when prescribing in patients with other risk factors for VTE and prescribe lower doses if possible.** - **Carry out periodic skin examination on all patients to check for skin malignancy.** **Inform patients and their carers of these risks, and the signs and symptoms that warrant urgent medical attention**			
Filgotinib *(Jyseleca®)* **NICE TA676**	YES	Oral formulation	***Allergies:*** Galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. ***Contraindications:*** Active serious infection. Absolute lymphocyte count less than 0.5 x 10^9 cells/litre; absolute neutrophil count less than 1 x 10^9 cells/litre; haemoglobin less than 80g/L. ***Cautions:*** Avoid in those aged 65 years and older. Serious or opportunistic infection Use with caution in patients with risk factors for DVT or PE; cardiovascular risk factors; Monitor renal function- Cautioned in moderate or severe impairment; avoid in end-stage renal disease. Avoid in severe hepatic impairment Interrupt treatment if absolute neutrophil count less than 1 x 10^9 cells/litre, absolute lymphocyte count less than 0.5 x 10^9 cells/litre, or haemoglobin less than 80g/L—treatment may be restarted when levels return above these values. • Monitor for signs and symptoms of infections • Monitor lipids; 12 weeks after treatment initiation and as needed thereafter.

			Hyperlipidaemia should be managed according to international clinical guidelines. • Monitor neutrophils, lymphocytes and haemoglobin • Periodic skin examination recommended. • Monitor hepatic transaminases. • Viral reactivation • Monitor renal function Females of childbearing potential should use effective contraception during and for at least 1 week after stopping treatment. **Interactions:** Other immunosuppressant drugs and live vaccines. See BNF **Also licensed for ulcerative colitis**
Upadacitinib (Rinvoq®) **NICE TA744**	YES	Oral formulation	***Contraindications:*** Active serious infection; absolute lymphocyte count less than 0.5 x 10^9 cells/litre; absolute neutrophil count less than 1 x 10^9 cells/litre; haemoglobin less than 80g/L; ***Cautions:*** Not recommended in over 65-year-olds. Avoid in patients with increased risk of cardiovascular events and malignancies. Risk of GI perforation (investigate new onset abdominal signs and symptoms promptly); malignancy risk factors; recurrent or history of serious infection; risk factors for VTE; risk of viral reactivation; risk of diverticulus. • Monitor for signs and symptoms of infection during and after treatment • Monitor neutrophils, lymphocytes and haemoglobin • Periodic skin examination recommended. • Monitor hepatic transaminases. • Viral hepatitis reactivation • Monitor renal function Risk of hypoglycaemia in patients receiving medication for diabetes; dose adjustment may be necessary

			Check interactions: Antivirals; anti-fungals; anti-epileptics; live vaccines, immunosuppressants. See BNF. **Also licensed for Ulcerative Colitis, Crohn's disease and Atopic Dermatitis**

Useful links:

Principles for COVID-19 Vaccination in Musculoskeletal and Rheumatology for Clinicians COVID-19 vaccination and MSK (arma.uk.net)

British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory and anti-rheumatic drugs and corticosteroids OP-BRHE220553 48..88 (silverchair.com)

The Handbook of Perioperative Medicines UKCPA The Handbook of Perioperative Medicines (ukcpa-periophandbook.co.uk)

References

1. Smolen JS. Landewé RBM. Bergstra SA. Kerschbaumer A. *et al*. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. Ann Rheum Disease 2022. [Accessed via EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update (bmj.com) 13/02/2024]

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