NHS
Greater Glasgow and Clyde

# CLINICAL GUIDELINE

# Rheumatoid Arthritis bDMARD and ts DMARD

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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| **Approval Group:** | Medicines Utilisation Subcommittee of ADTC |

**Important Note**:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

# GREATER GLASGOW AND CLYDE Biologics (bDMARD) and targeted synthetic DMARD (tsDMARD) GUIDELINE:

# RHEUMATOID ARTHRITIS

## 1. Eligibility

Eligibility criteria for bDMARD/tsDMARD in rheumatoid arthritis (RA) are defined by NICE MTA 375 technology appraisal endorsed by HIS (Healthcare Improvement Scotland) and subsequent SMC (Scottish Medicines Consortium) advice as summarised below:

## 2. Severe Disease: (DAS28>5.1)

Biologic agents included in Table 1, all in combination with methotrexate, are options for treating rheumatoid arthritis, only if disease has not responded to intensive therapy with a combination of conventional disease-modifying anti-rheumatic drugs (csDMARDs): i.e., at least two csDMARDs including methotrexate (unless contraindicated)

a) Adalimumab, etanercept, certolizumab pegol, tocilizumab & tsDMARDS can be used as monotherapy for people who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria above are met. Off- label monotherapy for other biologics may be appropriate in some clinical circumstances.

b) Rituximab has not been included as a first line treatment by NICE and is 'off label'. However, given clinical trial data, cost effectiveness and current clinical practice it is suitable as a first line biologic drug in specific clinical scenarios provided the above criteria are met.

c) tsDMARD (JAK inhibitors) can be used based on the above criteria as an alternative to first line biologic treatment or as second line treatment where patients are ineligible for rituximab (SMC) or where the clinician anticipates better clinical response over other Mechanism of Action (MOA's)

## 3. Summary of drug class and most cost-effective option

**Table 1**

| | TNF Blockade | Anti- CD 20 (B cell) | Costimulatory Blockade | IL-6 Blockade | JAK Inhibitors |
|---|---|---|---|---|---|
| **Most cost effective drug in class** | Amgevita - Adalimumab* | Rixathon - Rituximab* | Abatacept | Sarilumab | Filgotinib |
| **Alternatives** | Infliximab IV* | | | Tocilizumab | Baricitinib |
| | Certolizumab | | | | Upadicitinib |
| | Etanercept* | | | | Tofacitinib |
| | Golimumab | | | | |
| | Infliximab s/c | | | | |

*Biosimilar drugs of the originator product are available for these agents. *The table above should guide treatment selection. Where there are no clear clinical reasons for selecting a particular MOA then the lowest cost option taking account of route of administration and dosing schedule should be selected. A medicine annotated as 'most cost effective' should generally be selected initially.*

Currently adalimumab is the most cost effective TNFi and should be used in preference to other biologic agents unless specific clinical considerations require a specific TNFi or medicine with a different mechanism of action.

Medicine costs, inclusive of impact of any patient access schemes or discounts, are made available to the service in strict confidence to assist in identifying preferred treatment options.

## 4. Moderate Disease (DAS 28 3.2-5.1)

HIS has endorsed the NICE TA 715 which approved adalimumab, etanercept and infliximab with methotrexate for moderate RA only if disease has not responded to intensive therapy with a combination of conventional disease-modifying anti-rheumatic drugs (csDMARDs): i.e. at least two csDMARDs including methotrexate (unless contraindicated)

- Adalimumab and etanercept can be used as monotherapy when methotrexate is contraindicated or not tolerated.

- Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. If this initial response is not maintained, stop treatment.
- Rituximab is not licenced for moderate disease. However, the clinical evidence suggests that both rituximab and filgotinib would be effective in the moderate space. Given that these agents fall within the financial bracket of the TNFi biosimilars, they are included as a cost-effective option, thus opening the opportunity for patients to whom TNFi may be contraindicated or likely to be less effective.

**Summary of drug class and most effective option in moderate disease**

**Table 2**

| | **TNF Blockade** | **Anti- CD 20 (B cell)** | **JAK Inhibitor** |
|---|---|---|---|
| **Most cost effective drug in class** | Amgevita - Adalimumab | Rixathon - Rituximab* | Filgotinib |
| **Alternatives** | Infliximab IV & S/C<br>Benepalli<br>Etanercept | | |

*Off label

## 5. Withdrawal/Continuation for moderate and severe RA

- Continue treatment only if there is at least a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy or DAS reduction of >1.2.
- After initial response within 6 months, withdraw treatment if a moderate EULAR response is not maintained, or DAS reduction of >1.2

## 6. Cost Effectiveness

- The most cost-effective drug in class should be used unless clinical need requires a specific agent.

## 7. Off-label dosing and drug monitoring for moderate and severe RA

- A decision to prescribe a biologic drug for an approved condition but using doses that are 'off label' e.g. tapering, is a decision for the rheumatologist and patient.
- Increasing the interval of dosing or dose reduction at same frequency could be considered when:
    1. Patients have maintained remission/LDA for a sustained period
    2. Infection concerns have developed
    3. Tolerability/patient request
- All bDMARDS and smDMARDS are not included in near patient testing arrangements.
  Responsibility for any blood monitoring remains with the prescriber.
- Use of biologic drug level monitoring (for infliximab and adalimumab) could be considered when adjusting dose, or where secondary failure has occurred to inform choice of subsequent therapy.

  Advice can be found at https://www.nhsggc.org.uk/about-us/professional-support-sites/laboratorymedicine/laboratory-disciplines/biochemistry/biological-therapy-monitoring/