Use of excluded high cost drugs (HCD) with methotrexate in the treatment of Severe Rheumatoid Arthritis in Adults
Treatment pathway in line with NICE TAs 195, 225, 247, 375, 415, 466, 480, 485, 665, 676 & local agreement

Adequate trial of ≥2 conventional DMARDs in combination, including MTX (unless contra-indicated/not tolerated), with at least 2 months at standard dose, unless significant toxicity limits dose or duration?

No → Does not qualify for HCD treatment

Yes

Established severe disease with a DAS-28 score >5.1

No → Does not qualify for treatment via the severe pathway. If DAS-28 score between 3.2 to 5.1 refer to the moderate pathway.

Yes

Box 1 - Treatment options + MTX: TA 375, 466, 480, 485, 665, 676 and local agreement
Usually start treatment with least expensive appropriate treatment#
(options listed by mechanism of action and overall cost [including admin costs]):

TNF inhibitors
1. **adalimumab (biosimilar) is usual 1st line choice**
2. etanercept (biosimilar)
3. infliximab (biosimilar)
4. certolizumab
5. golimumab

JAK inhibitors (targeted synthetic DMARDs)
1. filgotinib
2. upadacitinib
3. tofacitinib
4. baricitinib

IL-6 inhibitors
1. sarilumab
2. tocilizumab s/c (higher cost than abatacept s/c)
3. tocilizumab IV (high cost – s/c preferred)

T-cell activation modulator
1. abatacept s/c (lower cost than tocilizumab s/c)
2. abatacept IV (high cost – s/c preferred)

Local agreement -
Patients with severe disease previously treated under the **moderate** RA pathway should join the **severe** pathway at **Box 2**. **Note**: a **total of 5 lines** of treatment will be commissioned across both the moderate & severe pathways.

Local Agreement –
Consider alternative TNFi biosimilar if intolerance within 1st 6 months of initial TNFi

***Adequate response:**
DAS28 improvement ≥1.2.

Local Agreement:
- **# Adalimumab (biosimilar) is usual 1st line choice** but it is acknowledged that there are clinical circumstances when particular treatments may be preferred. These may relate to specific warnings or contraindications or to BSR guidance on treatment choice with co-morbidities.
- Pregnancy: Women within 3 months of trying to conceive – certolizumab (women of child bearing age to be initiated on adalimumab (biosimilar). At 3 months before trying to conceive consider option to switch to certolizumab). Following birth (Note BSR guidelines caution all TNFis in breast feeding) if planning for future pregnancies option to remain on certolizumab, if not switch back to adalimumab (biosimilar).

Assess response by 6 months.
Adequate response achieved* and treatment tolerated?

Yes → Continue treatment with 6-12 monthly monitoring.
Stop treatment if adequate response (DAS28 improvement ≥1.2) not maintained / intolerance and consider next pathway step

No

Box 2 - TA 195 # rituximab (biosimilar) + MTX (see below if contraindicated) [+]
Treatment should be given no more frequently than every 6 months.

Contraindications to rituximab that are not contraindications for all recommended treatments[+]

Assess response by 6 months.
Adequate response achieved* and treatment tolerated?

Yes → Continue treatment with 6-12 monthly monitoring.
Stop treatment if adequate response (DAS28 improvement ≥1.2) not maintained / intolerance and consider next pathway step

No

[+] Interim local agreement to bypass rituximab during COVID19-pandemic
- Where next step is rituximab, clinician can offer alternative biologic or JAK inhibitor.
- Established rituximab patients starting to flare due next course – consider switch to alternative biologic or JAK inhibitor.

Box 3 – Biologic options +MTX: TAs 195, 225, 247, 415, 466, 480, 485, 665, 676 & local agreement
Consider changing to an alternative biologic drug from a different class (alternative TNF inhibitor can be considered if rituximab contraindicated) (see box 1).
- Preference is for least expensive appropriate biologic (see box 1 for cost order).

Assess response by 6 months.
Adequate response achieved* and treatment tolerated?

Yes → Continue treatment with 6-12 monthly monitoring.
Stop treatment if adequate response (DAS28 improvement ≥1.2) not maintained / intolerance and consider next pathway step

No

Box 4 – Biologic options +MTX: local agreement
Consider changing to an alternative biologic drug from a different class (see box 1).
- Preference is for least expensive appropriate biologic (see box 1 for cost order).

Assess response by 6 months.
Adequate response achieved* and treatment tolerated?

Yes → Continue treatment with 6-12 monthly monitoring.
Stop treatment if adequate response (DAS28 improvement ≥1.2) not maintained / intolerance and consider next pathway step

No

Box 5 – Biologic options +MTX: local agreement
Consider changing to an alternative biologic drug from a different class (see box 1).
- Preference is for least expensive appropriate biologic (see box 1 for cost order).

Assess response by 6 months.

If adequate response achieved* and treatment tolerated:
- Continue treatment with 6-12 monthly monitoring.

Stop treatment if adequate response not achieved / maintained or intolerance

Treatment requests beyond the end of the algorithm are not routinely commissioned

Conventional DMARDS include: Methotrexate (MTX) (oral and s/c), sulfasalazine, hydroxychloroquine, penicillamine, azathioprine, leflunomide

Refer to individual SPC's for full prescribing information including dose restrictions, adverse drug reactions, contraindications and cautions; and to Drug Safety Updates for latest drug safety notices.

Use of excluded high cost drugs (HCD) Monotherapy in the treatment of Severe Rheumatoid Arthritis in Adults
Treatment pathway in line with NICE TAs 195, 375, 415, 466, 480, 485, 665, 676 and local agreement

Adequate trial of ≥2 conventional DMARDs in combination, including MTX (unless contra-indicated/not tolerated), with at least 2 months at standard dose, unless significant toxicity limits dose or duration?

No → Does not qualify for HCD treatment

Yes ↓

Established severe disease with a DAS-28 score >5.1

No → Does not qualify for treatment via the severe pathway. If DAS-28 score between 3.2 to 5.1 refer to the moderate pathway.

Yes ↓

Is patient unable to take methotrexate?

No → Refer to pathway on Page 1

Yes ↓

Box 1 -Treatment options (monotherapy): TA 375, 466, 480, 485, 665, 676 and local agreement
Usually start treatment with least expensive appropriate treatment (see #with MTX pathway for clinical circumstances when particular treatments may be preferred)
(options listed by mechanism of action and overall cost [including admin costs]):

TNF inhibitors
1. **adalimumab (biosimilar) is usual 1st line choice**
2. etanercept (biosimilar)
3. certolizumab

Anti-CD20 (B cell)
1. rituximab (biosimilar) – 1st and subsequent line option if multiple sclerosis, SLE, previous malignancy, ILD/pulmonary fibrosis

JAK inhibitors (targeted synthetic DMARDs)
1. filgotinib
2. upadacitinib
3. tofacitinib
4. baricitinib

IL-6 inhibitors
1. sarilumab
2. tocilizumab s/c
3. tocilizumab IV (high cost – s/c preferred)

↓

Assess response by 6 months.
Adequate response achieved* and treatment tolerated?

Yes → Continue treatment with 6-12 monthly monitoring.

Stop treatment if adequate response (DAS28 improvement ≥1.2) not maintained / intolerance and consider next pathway step

No ↓

Box 2 - Biologic options (monotherapy): TA 195, 415, 466, 480, 485, 665, 676 & local agreement
Consider changing to an alternative biologic drug from a different class (alternative TNF inhibitor can also be considered)[Δ #] (see box 1)
- Preference is for least expensive appropriate biologic (see box 1 for cost order).

↓

Assess response by 6 months.
Adequate response achieved* and treatment tolerated?

Yes → Continue treatment with 6-12 monthly monitoring.

Stop treatment if adequate response (DAS28 improvement ≥1.2) not maintained / intolerance and consider next pathway step

No ↓

Box 3 – Biologic options (monotherapy): local agreement
Consider changing to an alternative biologic drug from a different class (see box 1).
- Preference is for least expensive appropriate biologic (see box 1 for cost order).

↓

Assess response by 6 months.
Adequate response achieved* and treatment tolerated?

Yes → Continue treatment with 6-12 monthly monitoring.

Stop treatment if adequate response (DAS28 improvement ≥1.2) not maintained / intolerance and consider next pathway step

No ↓

Box 4 – Biologic options (monotherapy): local agreement
Consider changing to an alternative biologic drug from a different class (see box 1).
- Preference is for least expensive appropriate biologic (see box 1 for cost order).

↓

Assess response by 6 months.

If adequate response achieved* and treatment tolerated:
- Continue treatment with 6-12 monthly monitoring.

Stop treatment if adequate response not achieved / maintained or intolerance

Local agreement -
Patients with severe disease previously treated under the **moderate** RA pathway should join the **severe** pathway at **Box 2 or 3** depending on number of treatments trialled.
Note: a **total of 4 lines** of treatment will be commissioned across both the moderate & severe pathways.

[Δ]Local Agreement – Consider alternative TNFi biosimilar if intolerance within 1st 6 months of initial TNFi

[#]Local Agreement – For those on adalimumab monotherapy and experiencing a loss of response, dose escalation can be considered i.e. 40mg every week or 80mg every other week. This should be reviewed within 12 weeks and a trial of de-escalation back to standard dose considered.

***Adequate response:**
DAS28 improvement ≥1.2.

Treatment requests beyond the end of the algorithm are not routinely commissioned

Refer to individual SPC's for full prescribing information including dose restrictions, adverse drug reactions, contraindications and cautions; and to Drug Safety Updates for latest drug safety notices.

Conventional DMARDS include: Methotrexate (MTX) (oral and s/c), sulfasalazine, hydroxychloroquine, penicillamine, azathioprine, leflunomide

Version	1.0
Developed by	Pharmacy and medicines optimisation team Hertfordshire and West Essex (HWE) ICB with relevant HWE ICS stakeholders.
Approved by	Hertfordshire & West Essex Area Prescribing Committee
Date approved / updated	December 2022
Review Date	This HWE APC recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available
Superseded version	Pathway for use of biologics with Methotrexate for Rheumatoid Arthritis. WEMOPB, August 2021 Pathway for use of biologic monotherapy for Rheumatoid Arthritis. WEMOPB, May 2021 Use of excluded HCDs with methotrexate in the treatment of severe Rheumatoid Arthritis in Adults Treatment pathway in line with NICE TAs 195, 225, 247, 375, 415, 466, 480, 485, 665, 676 & local agreement Use of excluded HCD Monotherapy in the treatment of severe Rheumatoid Arthritis in Adults Treatment pathway in line with NICE TAs 195, 375, 415, 466, 480, 485, 665, 676 and local agreement Both HMMC, November 2021