Clinical Guideline

Rheumatoid Arthritis
Drug Treatment Pathway

Guideline Summary
This clinical guideline outlines the biologic treatment pathway for adult patients with rheumatoid arthritis.
### Document Detail

<table>
<thead>
<tr>
<th>Document Type</th>
<th>Clinical Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document name</td>
<td>Rheumatoid Arthritis Biologic Drug Treatment Pathway</td>
</tr>
<tr>
<td>Document location</td>
<td>Intranet of Individual Trusts</td>
</tr>
<tr>
<td>Version</td>
<td>Approved version 7.0</td>
</tr>
<tr>
<td>Effective from</td>
<td>September 2019</td>
</tr>
<tr>
<td>Review due date</td>
<td>September 2020 (1 year)</td>
</tr>
<tr>
<td>Owner</td>
<td>South East London Rheumatology Steering Group</td>
</tr>
<tr>
<td>Author</td>
<td>South East London Rheumatology Steering Group</td>
</tr>
<tr>
<td></td>
<td>Acute Trusts:</td>
</tr>
<tr>
<td></td>
<td>Guys and St Thomas’ NHS Foundation Trust</td>
</tr>
<tr>
<td></td>
<td>Principal Pharmacist Immunotherapy (Rheumatology, Dermatology, Allergy) and Clinical Commissioning</td>
</tr>
<tr>
<td></td>
<td>Highly Specialist Pharmacist Rheumatology</td>
</tr>
<tr>
<td></td>
<td>Consultant Pharmacist and Clinical Lead Rheumatology</td>
</tr>
<tr>
<td></td>
<td>Consultant Rheumatologist</td>
</tr>
<tr>
<td></td>
<td>Consultant Rheumatologist</td>
</tr>
<tr>
<td></td>
<td>Advanced Nurse Specialist, Rheumatology</td>
</tr>
<tr>
<td></td>
<td>Kings College Hospital NHS Foundation Trust</td>
</tr>
<tr>
<td></td>
<td>Consultant Rheumatologist (Chair)</td>
</tr>
<tr>
<td></td>
<td>Clinical pharmacy team leader – Post-acute and Planned Medicine</td>
</tr>
<tr>
<td></td>
<td>Consultant Pharmacist and Clinical Lead Rheumatology</td>
</tr>
<tr>
<td></td>
<td>Lewisham and Greenwich NHS Trust</td>
</tr>
<tr>
<td></td>
<td>Consultant Pharmacist</td>
</tr>
<tr>
<td></td>
<td>Clinical Nurse Specialist, Rheumatology</td>
</tr>
<tr>
<td></td>
<td>Lead Pharmacist Long term Conditions</td>
</tr>
<tr>
<td>Clinical Commissioning Groups:</td>
<td>NHS Lambeth CCG (Lead CCG), NHS Southwark CCG, NHS Bexley CCG, NHS Bromley CCG</td>
</tr>
<tr>
<td></td>
<td>NHS Greenwich CCG, NHS Lewisham CCG</td>
</tr>
</tbody>
</table>

### Approved by, date

Medicines and Pathways Review Group August 2019 Area Prescribing Committee Chair’s ratification: 02.09.19

### Superseded documents

Nil

### Keywords

Rheumatoid, arthritis, biologic, adalimumab, certolizumab, etanercept, golimumab, infliximab, abatacept, rituximab, tocilizumab, baricitinib, tofacitinib, sarilumab, biosimilar

### Change History

<table>
<thead>
<tr>
<th>Date</th>
<th>Change details, since approval</th>
<th>Approved by</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.11.16</td>
<td>3.1 Update of pre-biologic therapy definition</td>
<td></td>
</tr>
<tr>
<td>3.11.16</td>
<td>7. Update of vaccination requirement</td>
<td></td>
</tr>
<tr>
<td>3.11.16</td>
<td>9. Addition of free of charge schemes</td>
<td></td>
</tr>
<tr>
<td>3.11.16</td>
<td>13. Addition of biologic choice in women planning therapy</td>
<td></td>
</tr>
<tr>
<td>3.11.16</td>
<td>14-16 Revision of pathways</td>
<td></td>
</tr>
<tr>
<td>3.11.16</td>
<td>17.0 Addition of treatment options following multiple biologic failures</td>
<td></td>
</tr>
<tr>
<td>3.11.16</td>
<td>18.0 Update of key performance indicators for annual audit</td>
<td></td>
</tr>
<tr>
<td>09.12.16</td>
<td>14 Golimumab 50mg twice monthly dosing statement added to notes box</td>
<td></td>
</tr>
<tr>
<td>27.01.17</td>
<td>7 – added info on administration of vaccinations by early outpatient biologic initiation service</td>
<td></td>
</tr>
<tr>
<td>27.01.17</td>
<td>11 – added info on administration of first dose biologic via OP clinic and VAT charge to commissioners</td>
<td></td>
</tr>
<tr>
<td>08.03.17</td>
<td>5 &amp; 8 – detail added re: STRAP trial</td>
<td></td>
</tr>
<tr>
<td>October 2017</td>
<td>Addition of baricitinib and tofacitinib following positive NICE approval</td>
<td>MPRG</td>
</tr>
<tr>
<td>March 2018</td>
<td>Addition of subcutaneous methotrexate billing information, pre-biologic infection screen addition of quantiferon</td>
<td>MPRG</td>
</tr>
<tr>
<td>March 2018</td>
<td>Addition of sarilumab following positive NICE approval and update of NICE guidelines in references</td>
<td>MPRG</td>
</tr>
</tbody>
</table>

### Review History

<table>
<thead>
<tr>
<th>Date</th>
<th>Review details</th>
<th>Approved by</th>
</tr>
</thead>
<tbody>
<tr>
<td>May - July 2019</td>
<td>Updated in line with pathway discussions at January 2019 and May 2019 meetings. Added Appendix 1 Best Value Biologic</td>
<td>MPRG, Aug 19</td>
</tr>
</tbody>
</table>
1 Scope
This treatment pathway applies to adult patients with a diagnosis of highly active rheumatoid arthritis (DAS 28>5.1) who are approaching treatment with biologic therapy.

2 Rationale
This treatment pathway provides an evidence based approach for the treatment of rheumatoid arthritis whilst maximising cost effectiveness and clinical outcome.
3. **Principles**

This treatment guideline is based on current available national guidance (National Institute for Health and Care Excellence, NICE), locally approved guidance and is subject to frequent change as guidance is updated and costs change.

This pathway is correct at the time of publication. NICE Technology Appraisals (TAs) relating to Rheumatoid Arthritis in adults which are published after the approval date of this guideline will be commissioned 90 days (30 days for fast track TAs) from publication in line with the TA recommendations.

4. **Definitions**

EULAR Response Criteria:

<table>
<thead>
<tr>
<th>DAS28 Improvement →</th>
<th>&gt; 1.2</th>
<th>&gt; 0.6 and ≤ 1.2</th>
<th>≤ 0.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present DAS 28 ↓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 3.2</td>
<td>good response</td>
<td>moderate response</td>
<td>no response</td>
</tr>
<tr>
<td>&gt; 3.2 and ≤ 5.1</td>
<td>moderate response</td>
<td>moderate response</td>
<td>no response</td>
</tr>
<tr>
<td>&gt; 5.1</td>
<td>moderate response</td>
<td>no response</td>
<td>no response</td>
</tr>
</tbody>
</table>

**Primary failure** – patient does not respond after 6 months treatment (3 months for certolizumab pegol) – refer to section 14

**Secondary failure** – patient initially achieves a good or moderate response after 6 months but this is not sustained resulting in failure to maintain a reduction of 1.2 points or more – refer to section 16

5. **Pre-biologic therapy [disease modifying anti-rheumatic drugs (DMARDs)]**

5.1. **Pre-biologic therapy**

Persistent Active Rheumatoid Arthritis (DAS 28>5.1) + Failure of intensive therapy with a combination of conventional DMARD therapy

**Strategies for maximising the use of DMARDs prior to biologic therapy:**

- Adjusting folic acid dose/frequency/formulation to improve tolerance to oral methotrexate (e.g. folic acid liquid 1mg daily except day of methotrexate)
- Subcutaneous methotrexate where clinically appropriate (e.g. gastrointestinal adverse effects with oral methotrexate or poor compliance) When used in this situation, billable to CCGs for approved indications in line with the CCG high cost drugs policy and CCG commissioned drug list. Whilst the majority of dispensing will be via homecare, commissioners have agreed that there may be exceptional circumstances where homecare may not be possible (e.g. due to patient circumstances or to cover initiation doses) and these can be billed.
- Maximum intensification of combination therapy, for example:
  - Has maximum tolerable dosage been achieved?
  - Has triple DMARD therapy been considered (unless contraindicated)?
5.2. In combination with biologics

Where patients are intolerant of methotrexate or methotrexate is considered inappropriate, other DMARDs may be used in combination with biologics although this combination may be considered ‘off-label’.

If subcutaneous methotrexate has been initiated to enhance efficacy and patients are then started on a biologic medication, the route of methotrexate should be reviewed and de-escalated where possible to oral therapy.

6. Pre-biologic Infection screen

- TB (T spot or quantiferon and chest x-ray)
- Viral serology: hepatitis B, C and HIV as clinically appropriate

7. Vaccinations (click for Department of Health and Social Care Green Book)

Patients should be counselled on the need to avoid live vaccines and the implication that may have for travelling.

Eligible patients may be offered vaccination against shingles with Zostavax™ (herpes zoster vaccine) in line with Department of Health and Social Care guidelines. Refer to the Department of Health and Social Care website for the eligibility criteria for receiving the vaccination and the Green book for clinical information. **This is a live vaccination and patients should not be given the vaccine if they are receiving biologic treatments. To avoid inadvertent administration of this live vaccine, on receipt of clinic letters, GPs should update practice records to indicate which patients are currently receiving biologic treatment.**

Patients should receive annual influenza vaccine and pandemic influenza vaccine when recommended and pneumococcal vaccination prior to biologic therapy. This can be prescribed and administered in the community or by the hospital as part of an outpatient biologic initiation service. **GPs must be informed if the hospital administer to outpatients.**

Patients initiated on Janus kinase (JAK) inhibitors should be counselled on the risk of shingles. Patients should be advised to contact their GP urgently if infection is suspected for initiation of aciclovir treatment. The Rheumatology team should inform the GP in writing of the initiation of a JAK inhibitor and advise them of the need for urgent aciclovir treatment in the event of shingles. Current management of patients due to start JAK inhibitors does not include the routine administration of the varicella zoster virus vaccination. Patients who are eligible for the vaccine should be counselled that they should have the vaccine prior to initiation of biologic therapy, if not already done so. This should be documented in communication to the GP and patient.

8. Recruitment into clinical trials

Where possible, patients should be invited to participate in clinical trials being undertaken within rheumatology departments. Where a clinical trial does not meet the requirements of the pathway approval should be obtained from commissioners prior to initiation.

STRAP (Stratification of Biologic Therapies for RA by Pathobiology) is a Medical Research Council funded multi centre phase III randomised, open-label, biopsy-driven stratification trial in DMARD inadequate responders, fulfilling NICE criteria to commence biological therapy. It aims to identify treatment response predictors which will allow the stratification of patients to the biological therapy they are most likely to respond to.
9. **Free of Charge Schemes**

New biologic and non-biologic DMARDs are often licensed and made commercially available many months before NICE are due to issue their NICE Technology Appraisal Guidance. Where this situation exists, individual rheumatology departments may enter discussions with the pharmaceutical company to determine if a ‘free of charge’ (FOC) early access scheme is feasible.

When a FOC is proposed it must satisfy the following criteria:

- The scheme must not replace or override the agreed pathway and the FOC drug should only be considered if pathway options are exhausted or not clinically appropriate.
- Fund the treatment at zero cost to the commissioners or negligible cost to the NHS trust up to and for 90 days after the positive NICE Technology Appraisal Guidance is issued and formally commissioned.
- Continue to fund treatment in the event of a negative NICE Technology Appraisal Guidance until:
  - 90 days after a future positive NICE Technology Appraisal Guidance.
  - Until the rheumatologist considers it no longer clinically appropriate to continue the drug.
- All schemes require sign off in each NHS Trust and this usually requires the Chief Pharmacist, the Pharmacy Procurement Lead and Director of Finance to authorise the scheme.

10. **Extended interval dosing (‘off-label’ indication) and biologic withdrawal in remission**

After discussion with the patient a Consultant may decide to extend the dosage interval or withdraw biologic therapy completely as appropriate for the clinical situation. This may require the use of ultrasound to confirm if patient is in remission. If patients flare following extension in dose interval or withdrawal; re-initiation of the previous biologic at the same dosage regimen is acceptable but consider using an alternative agent due to immunogenicity. Whilst a patient maintains remission or low disease activity on an extended dose interval, the Trust can recover a share of the savings from the commissioner. This is subject to local discussion and contractual agreement.

11. **Method of medication supply**

Subject to local arrangements patients may be offered a choice of method of supply. This may include a traditional homecare service or enhanced outpatient pharmacy service via outsourced outpatient pharmacies on main hospital sites. Where there is agreement with pharmaceutical companies, unbundling of homecare and direct procurement via outsourced pharmacies may result in a reduction in the drug acquisition cost. This may further influence the biologic choice at local trust level.

In order to reduce the time to biologic initiation, the first biologic doses (2 – 4 weeks supply) may be given in clinic as part of an outpatient biologic initiation service. This provides sufficient supply, improved patient training and assessment in clinic prior to initiation on homecare. As the first dose(s) are administered in the outpatient clinic, the cost will incur VAT and this will be passed onto commissioners.

12. **Biologic choice in patients unable to take methotrexate (MTX, oral and subcutaneous)**

The majority of patients commencing biologics are on concurrent methotrexate. However, for the minority who are not, the chances of a meaningful response to therapy are lower. Between 10 – 37% of patients discontinue methotrexate due to adverse effects13 and data from the British Society of Rheumatology Biologics Register indicate that approximately a third of patients take biological disease modifying antirheumatic drugs as monotherapy14.
13. **Biologic choice in women planning pregnancy**

Certolizumab pegol is compatible with all three trimesters of pregnancy and has reduced placental transfer when compared with other TNF inhibitors. For these reasons it is often the biologic of choice before, during and after pregnancy (whilst breast feeding). Patients may require to be switched from their current biologic to certolizumab pegol in advance of conception. This should not count as a routine biologic switch and is subject to clinical judgement. Certolizumab should be stopped approximately 2 weeks before the expected delivery date of the baby and restarted once fully healed from any pregnancy trauma or surgical intervention.

Adalimumab and Etanercept are compatible with the first and second trimesters of pregnancy. Female patients of child bearing potential or pregnant and stable on either of these TNF inhibitors will have their biologic therapy reviewed with their clinician regularly as it may be clinically more appropriate to remain on their current regimen rather than switch therapy. Treatment can then be stopped temporarily in the third trimester.

For further recommendations on biologic or conventional DMARD choice in pregnancy or breast feeding, refer to the British Society for Rheumatology (BSR)/British Health Professionals in Rheumatology (BHPR) guideline:
http://www.rheumatology.org.uk/resources/guidelines/default.aspx
14. Initiation of first biologic

Cautions or contraindication to anti-TNF drugs?
E.g. recent solid tumour (< 5 years), history of melanoma, multiple sclerosis, autoimmune rheumatic lung disease, ILD, septic arthritis < 12 months, heart failure NYHA III/IV

Yes Go to 15

No

Consideration of patient factors
Is a shorter half-life required? For example (but not limited to) history of TB, infections requiring hospitalisation, co-morbidities or other patient factors (e.g. diabetes, COPD, concurrent corticosteroid use). See notes below Is STRAP information available? If so see STRAP protocol

Yes

No

Does patient requires intravenous therapy due to risk of non-compliance?

Yes

No

FIRST CHOICE Bio相似 etanercept
SECOND CHOICE Subcutaneous Abatacept
If patient requires intravenous route – Abatacept intravenous

FIRST CHOICE Bio相似 Infliximab Intravenous
SECOND CHOICE Tocilizumab or Abatacept Intravenous

FIRST CHOICE Choice of best value subcutaneous anti-TNF OR Oral Janus Kinase inhibitor (see Appendix 1 for best value tool)
SECOND CHOICE Choice of subcutaneous anti IL-6 inhibitor OR abatacept

NOTES
1. If unable to administer subcutaneous injection or history of poor compliance use intravenous formulation.
2. Certolizumab pegol first line in pregnancy or pregnancy planning (monotherapy), see section 13
3. Avoid sarilumab or tocilizumab (IL-6 inhibitor) if history of diverticulitis or intestinal ulceration
4. Baricitinib and tofacitinib (oral JAK inhibitor) are options when an oral agent is preferred to improve compliance and concordance
5. It is preferable where there is no contra-indication or intolerance to use methotrexate alongside the biologic, if this is not possible a licensed monotherapy agent should be used.
6. The second choice agent should be used if there are patient contra-indications or specific clinical factors that make it more preferable than first choice options
7. See best value biologics table in appendix 1 for further information on drug selection.

Assess response at 6 months

EULAR Response Criteria

Moderate: DAS 28 3.2 – 5.1
Good: DAS28 ≤ 3.2

If moderate or good EULAR response not achieved at 6 months go to section 15 or trial of second anti-TNF.

Continue to reassess response every 6 – 12 months if moderate or good response achieved and consider dose optimisation /withdrawal (see section 10)

If minor adverse effects (e.g. injection site reactions) develop at any time or initial response is not sustained (secondary failure) go to section 16. Wherever possible use biologic in combination with methotrexate (including subcutaneous if necessary) to maximise efficacy.
15. Initiation of first biologic (anti-TNF contraindicated) OR primary failure* with first anti-TNF\(^5,7,19,20,21\)

(*defined as no patient response after 6 months treatment [3 months for certolizumab pegol] see section 4)

Contraindication to or intolerance to MTX?

- **YES**
  - Co-morbidity of Interstitial Lung Disease (ILD)
    - **YES**
      - FIRST CHOICE: Biosimilar rituximab monotherapy
      - SECOND CHOICE: Abatacept subcutaneous (IV therapy if required for compliance reasons)
    - **NO**
      - FIRST CHOICE: Subcutaneous IL-6 inhibitor or JAK inhibitor
      - SECOND CHOICE: Biosimilar Rituximab

- **NO**
  - Is patient at high risk of infection?
    - **YES**
      - Oral JAK inhibitor or subcutaneous abatacept
    - **NO**
      - Subcutaneous IL-6 Inhibitor

Adequate response

- Continue treatment and assess response every 6 – 12 months
  - For rituximab – option to retreat after six months to maintain response

Inadequate response or adverse effect

- Go to section 16

NOTES

1. Intravenous route ONLY if unable to administer subcutaneous injection or history of poor compliance with oral or subcutaneous medication
2. Avoid sarilumab or tocilizumab (IL-6 inhibitor) if history of diverticulitis or intestinal ulceration
3. It is preferable where there is no contra-indication or intolerance to use methotrexate alongside the biologic
4. Baricitinib and tofacitinib (oral JAK inhibitor) are options when an oral agent is preferred to improve compliance and concordance
5. The second choice agent should be used if there are patient contra-indications or specific clinical factors that make it more preferable than first choice options
6. See best value biologics table in appendix 1 for further information on drug selection
16. Secondary Failure or minor adverse effects (e.g. injection site reactions) with first anti-TNF

Patients may be eligible for a number of treatments following section 14 and 15. Drug choice is based on clinician judgement. All treatment switches should be discussed via a Rheumatology MDT discussion. Where clinically appropriate the best value biologic should be used. In addition, patient factors that may influence drug choice may include infection risk, preference for oral treatment, frequency of hospital visits and administration device.

Following failure of a second line option the patient may receive a further number of drug switches as per options A-D below.

If all therapeutic options (A – D) are exhausted patients should proceed to section 17 of the pathway.

Treatment options:

- **A**
  - Trial of ONE alternative best value anti-TNF if patient achieved sustained response to first anti-TNF
  - Patients should not receive a third anti-TNF (unless switch is to certolizumab due to pregnancy)
  - Switch to alternative mode of action drug

- **B**
  - Seropositive:
    - Biosimilar rituximab

- **C**
  - Seronegative:
    - Choice of:
      - Subcutaneous IL-6 inhibitor
      - Subcutaneous abatacept

DAS 28 measured at 12 - 24 weeks. Continue if adequate response and reassess every 24 - 52 weeks. If possible use biologic in combination with methotrexate (oral or subcutaneous) to maximise efficacy. Where methotrexate cannot be used, alternative DMARD(s) should be used.

17. Treatment options following multiple biologic treatment failures including where biologics are contraindicated, not tolerated or in cases of hypersensitivity.

For a small number of patients all pathway therapeutic options may be exhausted. The following is recommended for this patient cohort:

- Consultant rheumatologist to determine if active synovitis present (if in any doubt ultrasound should be considered)
- Consider novel agents if accessible via clinical trials or free of charge patient access schemes
- Revert back to biologic that delivered best clinical outcomes or use alternative biologic in same mode of action class with lowest acquisition costs (see best value biologic table Appendix 1)
  - Decision should be made in a Multidisciplinary Team (MDT) discussion in the local rheumatology department
  - Clinical outcomes and baseline scores must be reported to the CCG using a Category B* form
  - Include current corticosteroid dose or use of methylprednisolone in previous 6 – 12 months
  - Measure disease scores e.g HAQ, DAS

---

Approved: September 2019  
Review date: September 2020  
Not to be used for commercial or marketing purposes. Strictly for use within the NHS
18. Monitoring adherence with the guideline

Adherence to this pathway will be reviewed using the SEL Rheumatology Pathways, Outcomes and Monitoring Framework which includes Key Performance Indicators agreed by South East London Area Prescribing Committee. See http://www.lambethccg.nhs.uk for further details. The Rheumatology and Pharmacy Departments may undertake separate clinical audits as part of their annual clinical audit plan.

19. Supporting documents (see relevant local guidelines)

- Protocol for administration and reducing infusion times of infliximab in adult rheumatology patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis.
- Protocol for the use of self-administered sub-cutaneous methotrexate injection (Metoject) in adult patients with rheumatoid arthritis.
- Protocol for the use of rituximab for the treatment of autoimmune rheumatic diseases (including rheumatoid arthritis) in adults.

Consultation Process for current version:
SEL Medicines and Pathways Review Group (MPRG): August 2019
References


12. NICE Technology appraisal guidance TA 280 Abatacept for treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs (rapid review of technology appraisal guidance 234).


17. NICE technology appraisal guidance TA 375 Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed. January 2016.


19. NICE Technology appraisal guidance TA 485 Sarilumab for moderate to severe rheumatoid arthritis. November 2017

20. NICE Technology appraisal guidance TA 466 Baricitinib for moderate to severe rheumatoid arthritis. August 2017

21. NICE Technology appraisal guidance TA 480 Tofacitinib for moderate to severe rheumatoid arthritis. October 2017
### Appendix 1: Best value biologics cost tool - Rheumatoid arthritis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mode of action</th>
<th>Route of administration</th>
<th>Licensing</th>
<th>NICE monotherapy in RA recommendation (i.e. without methotrexate)</th>
<th>Intravenous (requiring day case admission)</th>
<th>Cost tier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pricing tier one section 14 RA pathway best value anti-TNF (subcut) or oral JAK inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab best value product</td>
<td>TNF inhibitor</td>
<td>Subcutaneous</td>
<td>x</td>
<td>£</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etanercept best value product</td>
<td>TNF inhibitor</td>
<td>Subcutaneous</td>
<td>x</td>
<td>£</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baricitinib</td>
<td>Janus kinase inhibitor</td>
<td>Oral</td>
<td>x</td>
<td>£</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>Janus kinase inhibitor</td>
<td>Oral</td>
<td>x</td>
<td>£</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pricing tier two section 14 RA pathway IL-6 inhibitor, abatacept (subcut) and alternative anti-TNFs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>IL-6 inhibitor</td>
<td>Subcutaneous</td>
<td>see below</td>
<td>££</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarilumab</td>
<td>IL-6 inhibitor</td>
<td>Subcutaneous</td>
<td>see below</td>
<td>££</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abatacept</td>
<td>Fusion protein</td>
<td>Subcutaneous</td>
<td>see below</td>
<td>££</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Golimumab</td>
<td>TNF inhibitor</td>
<td>Subcutaneous</td>
<td>see below</td>
<td>££</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Certolizumab</td>
<td>TNF inhibitor</td>
<td>Subcutaneous</td>
<td>see below</td>
<td>££</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pricing tier three additional medications not listed above (intravenous options)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rituximab biosimilar</td>
<td>CD20 inhibitor</td>
<td>Intravenous</td>
<td>x</td>
<td>££</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infliximab biosimilar</td>
<td>TNF inhibitor</td>
<td>Intravenous</td>
<td>££</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infliximab originator</td>
<td>TNF inhibitor</td>
<td>Intravenous</td>
<td>££</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abatacept</td>
<td>Fusion protein</td>
<td>Intravenous</td>
<td>x</td>
<td>££</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>IL-6 inhibitor</td>
<td>Intravenous</td>
<td>x</td>
<td>££</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Notes:

1. Choice of best value biologic will be dependent upon a number of factors (for example, contraindications to therapy, co-morbidities and other patient factors). Where more than one agent is suitable for the patient, the agent with the lowest acquisition cost (taking into account method of administration) will be chosen.

2. Excluding Rituximab it is always preferable to use the subcutaneous options above over intravenous due to the charge of infusion related tariffs (costing of rituximab is based on maximum dose of 1000mg given as four doses per year).

3. £ rating is a banded price range of £ (low) to £££ (high).

4. Price banding is based on average drug cost per patient per year (average for first 3 years on therapy).