DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

**Derbyshire commissioning guidance on biologic drugs for the treatment of Rheumatoid arthritis with methotrexate**

This algorithm is a tool to aid the implementation of NICE guidance on biologic drugs for the treatment of rheumatoid arthritis. It includes all of the biologic drugs approved by NICE for treatment and local variations for the commissioning algorithm.

- **Use standard DMARD treatment(s) for Rheumatoid arthritis**
  - **Is DAS28 score > 5.1?**
    - **Yes**
      - **Has the disease responded to intensive therapy with a combination of DMARDS?**
        - **Yes**
          - **If rituximab is not contra-indicated**
            - **Rituximab biosimilar + MTX (monoclonal antibody) [as per TA195] OR**
              - **Abatacept + MTX (selective modulator) [TA195] (local agreement) OR**
              - **Baricitinib \(^1\) (see drug table) + MTX (JAK1/2) [local agreement] OR**
              - **Tofacitinib + MTX (JAK1/3) [local agreement]**
          - **No**
            - **If rituximab is contra-indicated**
              - **Adalimumab biosimilar + MTX (TNFi) [TA375] or**
              - **Etanercept biosimilar + MTX (TNFi) [TA375] or**
              - **Infliximab biosimilar + MTX (TNFi) [TA375] or**
              - **Certolizumab pegol + MTX (TNFi) [TA375] or**
              - **Golimumab + MTX (TNFi) [TA225, TA375] or**
              - **Sarilumab + MTX (IL6) [TA485] or**
              - **Abatacept + MTX (selective modulator) [TA375] or**
              - **Tocilizumab + MTX (IL6) [TA247, TA375] (as SC)**
        - **No**
          - **Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?**
            - **Yes**
              - **Yes – maintain same treatment and monitor patient every 6 months**
              - **Rituximab biosimilar + MTX (monoclonal antibody) [local agreement]**
            - **No**
              - **Has the biologic drug been withdrawn because of an adverse event?**
                - **Yes**
                  - **Yes – maintain same treatment and monitor patient every 6 months**
                  - **Stop treatment**
                - **No**
                  - **Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?**
                    - **Yes**
                      - **Rituximab biosimilar + MTX (monoclonal antibody) [local agreement]**
                      - **Baricitinib \(^1\) (see drug table) + MTX (JAK1/2) [local agreement]**
                      - **Tofacitinib + MTX (JAK1/3) [local agreement]**
                    - **No**
                      - **Stop treatment**

- **If more than 1 treatment is suitable, the least expensive should be chosen. Choices are listed in most cost effective order.**
  - **First line biologic agent:**
    - **Adalimumab biosimilar + MTX (TNFi) [TA375]**
  - **Alternative biologic can be considered if first line biologic is clinically inappropriate:**
    - **Etanercept biosimilar + MTX (TNFi) [TA375] or**
    - **Tofacitinib + MTX (JAK1/3) [TA480] or**
    - **Infliximab biosimilar + MTX (TNFi) [TA375] or**
    - **Baricitinib \(^1\) (see drug table) + MTX (JAK1/2) [TA466] or**
    - **Sarilumab + MTX (IL6) [TA485] or**
    - **Golimumab + MTX (TNFi) [TA225, TA375] or**
    - **Certolizumab pegol + MTX (TNFi) [TA375] or**
    - **Abatacept + MTX (selective modulator) [TA375] or**
    - **Tocilizumab + MTX (IL6) [TA247, TA375] (as SC)**

The CCG’s will only commission 6 treatment options (5 switches) per patient - this includes 3 treatment failures and 2 intolerances. JAPC recognises the RMOC statement. Further sequential use outside of the commissioning algorithm should be undertaken after advice via MDT in-line with Trust processes but is limited by clinical appropriateness and safety.

Date reviewed: August 2020
Derbyshire commissioning guidance on biologic drugs for the treatment of Rheumatoid arthritis without methotrexate

This algorithm is a tool to aid the implementation of NICE guidance on biologic drugs for the treatment of rheumatoid arthritis. It includes all of the biologic drugs approved by NICE for treatment and local variations for the commissioning algorithm.

Date reviewed: August 2020

Use standard DMARD treatment(s) for Rheumatoid arthritis

Yes

Is DAS28 score > 5.1?

Yes

Has the disease responded to intensive therapy with a combination of DMARDs?

No

Use RA pathway with methotrexate

Yes

Yes – maintain same treatment and monitor patient every 6 months

No

Yes – consider an alternative biologic agent

If rituximab* as monotherapy is not contra-indicated

* Patients who have had a proven malignancy in the last 10 years or those with significant pulmonary fibrosis may be offered rituximab instead of TNF inhibitor

- Rituximab biosimilar (monoclonal antibody)(local agreement) or
- Baricitinib 1 (see drug table) (JAK1/2)(local agreement) or
- Tofacitinib (JAK1/3)(local agreement)

If rituximab is contra-indicated

- Adalimumab biosimilar (TNFi)(TA195) or
- Etanercept biosimilar (TNFi)(TA195) or
- Sarilumab (IL6)(TA645) or
- Certolizumab (TNFi)(TA415)

- Tocilizumab (IL6)(local agreement)(as SC)

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

Yes

- Rituximab biosimilar (monoclonal antibody)(local agreement)

- Tocilizumab (IL6)(local agreement)(as SC)

- Baricitinib 1 (see drug table) (JAK1/2)(local agreement) or
- Tofacitinib (JAK1/3)(local agreement)

Has the biologic drug been withdrawn because of an adverse event?

No

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

Yes

- Adalimumab biosimilar (TNFi)(TA375) or
- Etanercept biosimilar (TNFi)(TA375) or
- Sarilumab (IL6)(TA485) or
- Certolizumab (TNFi)(TA415)

Stop treatment

No

Has the biologic drug been withdrawn because of an adverse event?

Adequate response to treatment at 6 months (DAS28 score improved by ≥ 1.2)?

Yes

- Adalimumab biosimilar (TNFi)(TA375) or
- Etanercept biosimilar (TNFi)(TA375) or
- Sarilumab (IL6)(TA485) or
- Certolizumab (TNFi)(TA415)

- Rituximab biosimilar (monoclonal antibody)(local agreement) assuming no contra-indication

- Tocilizumab(IL6) (local agreement)(as SC) or
- Baricitinib 1 (see drug table) (JAK1/2)(local agreement) or
- Tofacitinib (JAK1/3)(local agreement)

The CCG’s will only commission 6 treatment options (5 switches) per patient - this includes 3 treatment failures and 2 intolerances. JAPC recognises the RMOC statement. Further sequential use outside of the commissioning algorithm should be undertaken after advice via MDT in-line with Trust processes but is limited by clinical appropriateness and safety.
<table>
<thead>
<tr>
<th>Drug &amp; Intravenous therapies</th>
<th>NICE TA</th>
<th>TA details</th>
<th>Route</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abatacept (+MTX)</td>
<td>Selective T-cell stimulation modulator</td>
<td>NICE TA195 NICE TA375</td>
<td>Disease has not responded to conventional DMARDs – 1st line and May also be used if disease has not responded to a previous TNF inhibitor.</td>
<td>SC or IV</td>
</tr>
<tr>
<td>Adalimumab (±MTX)</td>
<td>Monoclonal antibody that specifically binds to TNF</td>
<td>NICE TA195 NICE TA375</td>
<td>Disease has not responded to conventional DMARDs - 1st line and Inadequate response/ intolerance to TNF inhibitor and Cl/intolerance to rituximab therapy</td>
<td>SC</td>
</tr>
<tr>
<td>Certolizumab (±MTX)</td>
<td>Recombinant humanised antibody Fab’ fragment against TNF alpha</td>
<td>NICE TA415 NICE TA375</td>
<td>Disease has not responded to conventional DMARDs - 1st line and Inadequate response/ intolerance to TNF inhibitor and Cl/intolerance to rituximab therapy</td>
<td>SC</td>
</tr>
<tr>
<td>Etanercept Biosimilar (±MTX)</td>
<td>Recombinant human TNF receptor fusion protein.</td>
<td>NICE TA195 NICE TA375</td>
<td>Disease has not responded to conventional DMARDs - 1st line and Inadequate response/ intolerance to TNF inhibitor and Cl/intolerance to rituximab therapy</td>
<td>SC</td>
</tr>
<tr>
<td>Golimumab (+MTX)</td>
<td>Monoclonal antibody that prevents the binding of TNF to its receptors.</td>
<td>NICE TA225 NICE TA375</td>
<td>Disease has not responded to conventional DMARDs - 1st line and May also be used if disease has not responded to a previous TNF inhibitor.</td>
<td>SC</td>
</tr>
<tr>
<td>Infliximab biosimilar</td>
<td>Chimeric monoclonal antibody, with high</td>
<td>NICE TA195 NICE TA375</td>
<td>Disease has not responded to conventional DMARDs - 1st line</td>
<td>IV</td>
</tr>
<tr>
<td>Drug</td>
<td>Description</td>
<td>NICE TA</td>
<td>Indications</td>
<td>Dosing</td>
</tr>
<tr>
<td>------</td>
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<tr>
<td><strong>Rituximab Biosimilar (+MTX)</strong></td>
<td>Chimeric monoclonal antibody – depletes B-cell population.</td>
<td>NICE TA195</td>
<td>If pt has had an inadequate response or intolerant of DMARDS and at least one TNF inhibitor.</td>
<td>IV 2x 1000mg given 2 weeks apart, repeated no less than 16 weeks.</td>
</tr>
<tr>
<td><strong>Sarilumab (+MTX)</strong></td>
<td>Human monoclonal antibody selective for the IL-6 receptor</td>
<td>NICE TA485</td>
<td>Active RA for pts who have had an inadequate response to DMARDS and/or 1 biological DMARD, only if they cannot have rituximab and Disease responded inadequately to rituximab and at least 1 biological DMARD</td>
<td>SC 200mg once every 2 weeks. Reduce the dose to 150mg once every 2 weeks for patients with neutropenia, thrombocytopenia and increased LFTS.</td>
</tr>
<tr>
<td><strong>Tocilizumab (+MTX)</strong></td>
<td>Monoclonal antibody – inhibits interleukin-6 (IL-6) receptor</td>
<td>NICE TA375 NICE TA247</td>
<td>Disease has not responded to conventional DMARDS - 1\textsuperscript{st} line and May also be used if disease has not responded to a previous TNF inhibitor and the pt cannot receive rituximab because of CI or adverse event to rituximab</td>
<td>SC or IV</td>
</tr>
</tbody>
</table>

**Oral therapies**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
<th>NICE TA</th>
<th>Indications</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baricitinib (+MTX)</strong></td>
<td>Selective JAK1 and JAK2 inhibitor</td>
<td>NICE TA466</td>
<td>Active RA for pts who have had an inadequate response to DMARDS and/or 1 biological DMARD (only if they cannot have rituximab)</td>
<td>PO 4mg once daily. 2mg once daily is appropriate for pts ≥75 years and over \textsuperscript{1} MHRA Drug Safety Update August 2020 - Use baricitinib with caution in patients with diverticular disease and in those concomitantly treated with medications associated with an increased risk of diverticulitis</td>
</tr>
<tr>
<td><strong>Tofacitinib (+MTX)</strong></td>
<td>Inhibitor of JAK1 and JAK3.</td>
<td>NICE TA480</td>
<td>Active RA for pts who have had an inadequate response to DMARDS and/or 1 biological DMARD (if they cannot have rituximab)</td>
<td>PO 5mg taken twice daily</td>
</tr>
</tbody>
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