DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Guideline for the treatment of Crohn's Disease - July 2023

Adult with active Crohn's disease

Does the adult have **severe** active Crohn's disease?

No

Yes

Has the patient's disease failed to respond to **or** is the patient intolerant of **or** does the patient have contraindications to conventional therapy, including:

- immunosuppressant's **and/or**
- Corticosteroid treatments?

Yes

First line treatment option:

- **Adalimumab biosimilar** (TNFi) (TA187)

Yes

Alternate first line treatment option if first line biologic is clinically inappropriate:

- **Infliximab biosimilar SC/IV** (TNFi)

Has treatment with a TNF Inhibitor failed or not tolerated?

- **Adalimumab** biosimilar (TNFi) (TA187) *(local decision)*

Has treatment with a TNF Inhibitor failed or is a TNF inhibitor CI or not tolerated? Treatment should be started with the least expensive drug:

- **Upadacitinib** (JAK1) (TA905) **or**
- **Ustekinumab biosimilar** (IL12/23) 12 weekly is the cost-effective choice (TA456) (See dosing schedule) **or**
- **Vedolizumab** SC/IV (Anti-integrin) (TA352) **or**
- **Risankizumab** IV/SC (IL23) (TA888)

Please Note: Initiate a thiopurine alongside a biologic unless contraindicated Evidence shows early use of thiopurine reduces the likelihood of anti-TNF failure.

No

Does the adult have active **fistulising** Crohn's disease?

Yes

Has the patient's disease failed to respond **or** is the patient intolerant of **or** does the patient have contraindications to conventional therapy, including:

- antibiotics **and**
- drainage **and**
- immunosuppressive treatments?

Yes

First line treatment option:

- **Infliximab biosimilar SC/IV** (TNFi) (TA187) as a planned course of treatment

Has treatment with a TNF Inhibitor failed or is a TNF inhibitor CI or not tolerated?

- **Adalimumab** (TNFi) (TA187) *(Local decision)*

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery)?

No

At 12 months after the start of treatment, reassess the disease. Is there evidence of active disease?

No

Is the patient in stable clinical remission?

Yes

Discuss the risks and benefits of continued treatment. Is a trial withdrawal considered appropriate?

Yes

Trial withdrawal from biologic drug used. Restart treatment if patient relapses after treatment is stopped.

Yes

Maintain treatment and reassess patient at least every 12 months.

No

No

For some centres TDM may be used for infliximab and Adalimumab to check response to the anti-TNF inhibitor
See appendix 1.

Yes

Cease treatment with the biologic drug used.

NICE approved treatment

Local variation to NICE

The ICB will only commission 4 treatment options (3 switches) per patient - this includes 2 treatment failure and 1 intolerance. 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

Appendix 1 - Dosing schedule for Crohn's disease

<table>
<tr><th>Biologic</th><th>Induction dose</th><th>Maintenance dose</th><th>Dose escalation</th><th>Adequate response</th><th>Further information</th></tr>
<tr><td>Adalimumab (SC)</td><td>Week 0 – 80mg SC
Week 2 – 40mg SC
Or
Rapid response:
Week 0 – 160mg SC
Week 2 – 80mg SC</td><td>40mg SC every other week thereafter</td><td>Maintenance dose can be increased to 40 mg every week in people whose disease shows a decrease in response to treatment.</td><td>Week 12</td><td>Adalimumab is a recombinant human monoclonal antibody that binds specifically to tumour necrosis factor alpha (TNF-α)</td></tr>
<tr><td>Infliximab (SC)</td><td>Week 0, 2 – 5mg/kg IV
Week 6 – 120mg SC</td><td>120mg SC every 2 weeks</td><td rowspan="2">Dose escalation is an option for people whose disease has stopped responding on the basis on drug and antibody levels.</td><td>Week 6</td><td rowspan="2">Infliximab is a chimeric human-murine IgG1 monoclonal antibody</td></tr>
<tr><td>Infliximab (IV)</td><td>Week 0, 2, 6 – 5mg/kg IV</td><td>5mg/kg IV every 8 weeks thereafter</td><td>Week 6</td></tr>
<tr><td>Risankizumab (IV and SC)</td><td>Week 0, 4, 8 - 600 mg IV
Week 12 - 360mg SC</td><td>360mg SC every 8 weeks thereafter</td><td>No</td><td>Currently unknown</td><td>Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody selective to the interleukin (IL)-23 protein</td></tr>
<tr><td>Upadacitinib (oral)</td><td>45mg OD for 12 weeks</td><td>15mg or 30mg OD</td><td>15mg is recommended for patients at higher risk of VTE, MACE and malignancy, and for ≥65years.

30mg may be appropriate for patients with high disease burden who are not at higher risk of VTE, MACE and malignancy or who do not show adequate therapeutic benefit to 15 mg once daily.</td><td>30mg od may be appropriate for patients who have not achieved adequate therapeutic benefit after the initial 12-week induction.

Upadacitinib should be discontinued if there is no evidence of therapeutic benefit after 24 weeks of treatment.</td><td>Upadacitinib is a selective and reversible inhibitor of the Janus associated tyrosine kinase JAK1.</td></tr>
<tr><td>Ustekinumab (IV & SC)</td><td>Week 0 – 6mg/kg IV
Initial intravenous dosing of ustekinumab
<table><tr><th>Body weight of patient</th><th>Dose</th><th>No. of vials</th></tr><tr><td>≤55kg</td><td>260mg</td><td>2</td></tr><tr><td>>55kg - ≤85kg</td><td>390mg</td><td>3</td></tr><tr><td>>85kg</td><td>520mg</td><td>4</td></tr></table></td><td>Week 8 - 90mg SC
Then 90mg SC every 12 weeks thereafter.</td><td>Dose escalation can be increased to 8 weekly dosing for people whose disease has stopped responding.
(Prescribers are reminded that 8 weekly dosing is the most expensive dosing schedule)</td><td>Week 16</td><td>Ustekinumab is a fully human monoclonal antibody that targets interleukin-12 (IL-12) and IL-23.</td></tr>
<tr><td>Vedolizumab (SC)</td><td>Week 0, 2, 6* - 300mg IV</td><td>108mg SC every 2 weeks thereafter</td><td>No</td><td>Week 14</td><td>Vedolizumab is a humanised IgG1 monoclonal antibody that binds to the human α4β7 integrin.

*The recommended dose regimen of subcutaneous vedolizumab as a maintenance treatment, following at least 2 intravenous infusions, is 108 mg administered by subcutaneous injection once every 2 weeks.</td></tr>
<tr><td>Vedolizumab (IV)</td><td>Week 0, 2, 6 – 300mg IV</td><td>300mg IV every 8 weeks thereafter</td><td>People who have not shown a response by week 6 may benefit from an additional dose at week 10.</td><td>Week 14</td><td>Vedolizumab is a humanised IgG1 monoclonal antibody that binds to the human α4β7 integrin.</td></tr>
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