DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Guideline for the treatment of Crohn's Disease - August 2020

Adult with active Crohn's disease

Does the adult have **severe** active Crohn's disease? — No

Does the adult have active **fistulising** 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** (TNFi) (TA187)

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:
- **Ustekinumab** (IL12/23) 12 weekly is the cost effective choice (TA456) (See dosing schedule) **or**
- **Vedolizumab** SC/IV (Anti-integrin) (TA352)

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** (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)*

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

No

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

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

Yes

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

Yes — Maintain treatment and reassess patient at least every 12 months.

No — Trial withdrawal from biologic drug used. Restart treatment if patient relapses after treatment is stopped.

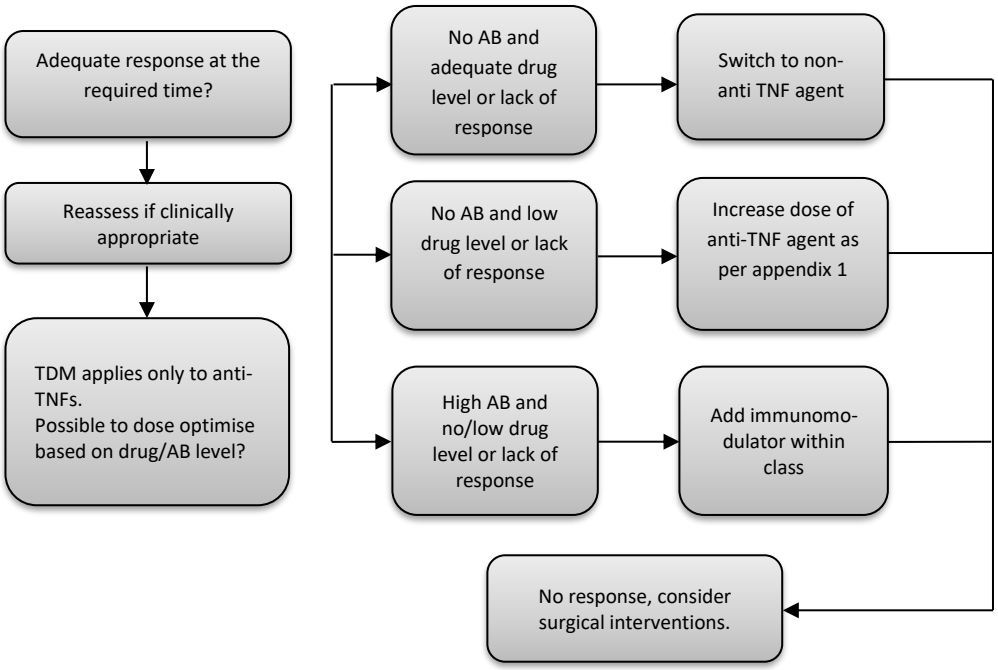
No — Cease treatment with the biologic drug used.

NICE approved treatment

Local variation to NICE

The CCG's 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- Therapeutic drug monitoring (TDM)



Clinical response includes clinical symptoms, biological markers and investigation, including endoscopy.

The CDAI is frequently used to assess disease severity. It is a composite of overall activity of Crohn's disease as assessed by clinicians, and has eight variables weighted according to their ability to predict disease activity. It gives a score ranging from 0 to over 600, based on a diary of symptoms kept by the patient for 1–7 days, and other measurements such as the patient's weight and haematocrit.

- CDAI score < 150 is considered to be remission,
- CDAI score > 220 is considered to define moderate to severe disease,
- CDAI score > 300 is considered to be severe disease.

Appendix 2 - Dosing schedule for Crohn's disease

Biologic	Induction dose	Maintenance dose	Dose escalation	Adequate response	Further information
Adalimumab (SC)	Week 0 – 80mg SC Week 2 – 40mg SC Or Rapid response: Week 0 – 160mg SC Week 2 – 80mg SC	40mg SC every other week thereafter.	Maintenance dose can be increased to 40 mg every week in people whose disease shows a decrease in response to treatment.	Week 12	Adalimumab is a recombinant human monoclonal antibody that binds specifically to tumour necrosis factor alpha (TNF-α)
Infliximab (IV) (Biosimilar or originator)	Week 0, 2, 6 – 5mg/kg IV	5mg/kg IV every 8 weeks thereafter.	Dose escalation is an option for people whose disease has stopped responding on the basis on drug and antibody levels	Week 6	Infliximab is a chimeric human-murine IgG1 monoclonal antibody
Vedolizumab (SC)	Week 0, 2, 6* - 300mg IV	108mg SC every 2 weeks thereafter	No	Week 14	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

<table>
<tr><td></td><td></td><td></td><td></td><td></td><td>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>
<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>
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