BEDFORDSHIRE, LUTON AND MILTON KEYNES AREA PRESCRIBING COMMITTEE (APC)

Treatment of Moderately to Severely active Crohn's Disease after failure of conventional therapy

(Main update Sept 2023, minor update Sept 2024),

This treatment pathway is applicable for use in patients whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments), or who are intolerant of or have contraindications to conventional therapy as per NICE NG 129)

Contents

NB Clinicians should refer to the SmPCs for each individual drug for full prescribing information, noting ▼black triangle status where applicable. – click here

Treatment requests beyond the end of the pathway, where clinical exceptionality can be demonstrated, can be considered via the Individual Funding Request (IFR) route.

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

Approved Sept 2023 Review Sept 2026

Bedfordshire, Luton and Milton Keynes Health and Care Partnership

NHS

Treatment of Moderately to Severely Active Crohn's disease in Adults (18 years and older) AFTER failure of conventional therapy (in line with NICE TAs and local guidance)

There are currently 6 NICE approved drug options for treating moderately to severely active Crohn's disease ; Adalimumab and infliximab (both TNFi s), ustekinumab , risankizumab, vedolizumab and upadacitinib (JAKi) . The approved drug options all have a unique mode of action and are each NICE approved at varying stages in the pathway. At each stage, choice of treatment should be made on an individual basis, taking into account individual patient factors such as therapeutic need, co-morbidities and adherence. **NB If more than 1 treatment is suitable, the most appropriate, least expensive should be chosen (taking into account administration costs, dosage and price per dose).**
(**Biosimilar options#** are now available for adalimumab , infliximab and ustekinumab.)

Moderately to severely active Crohn's Disease

(For treatment option for patients with active fistulating disease – see opposite box)

First line treatment biologic options (NICE approved)	**Initial review**
• Adalimumab# s/c *(TNF inhibitor)* +/- immunosuppressant	at 12 weeks
• Infliximab# (s/c or IV) *(TNF inhibitor)* +/- immunosuppressant	at 6 weeks
• Ustekinumab # *(IL12 & IL23 inhibitor)*	at 8 weeks

(NB TNFi s are the preferred first line choice (local agreement) ; biosimilars# are cost-effective options.)

IF TNFi s contraindicated / not suitable due to other comorbidities *, possible alternative treatment options include:

• Ustekinumab # s/c *(IL12 & IL23 inhibitor)*	at 8 weeks
• Risankizumab *(IL23 inhibitor)*	*at 12 weeks*
• Vedolizumab s/c or IV (α4β7 integrin inhibitor)	at 10 – 14weeks
• *Upadacitinib po (JAK inhibitor)***	at 12 weeks

***avoid TNFi s** in Δspecific patient population; Proven malignancy (see ECCO Guidelines), malignant melanoma at any point, bronchiectasis, pulmonary fibrosis, MS , SLE, congestive heart failure (NYHA Class III/IV)
****see MHRA drug safety update on use of a JAKi before initiating upadacitinib (see note 2)**

Severe Active Fistulating Crohn's disease (that has not responded to conventional therapy (including antibiotics, drainage and immunosuppressive treatments)

NICE approved treatment option

- Infliximab# –Review after the 3rd dose
- Continue if adequate response
- If adequate response not achieved , review patient and consider alternative treatment options if applicable

Assess patient's initial response (see note 1) :- Has an adequate response been achieved ?

If adequate clinical response* achieved after the initial review period

- Continue treatment and **review after a total of 12 month period of treatment has been given** (unless treatment failure occurs or surgery is required during this time)
- Continue treatment beyond 12 months **only if** there is clear evidence of response as determined by clinical symptoms, biological markers and investigation, including endoscopy if necessary.
- Continue to review every 12 months thereafter to assess if adequate response is being maintained
- Consider option of stopping treatment in patients who have achieved stable clinical remission if applicable (see note 4)

If no clinical response or loss of response or adverse effects occur, move to second line treatment options:- choice is dependent on first line option used

If used either adalimumab# or infliximab # first line ,

- Consider if dose escalation / interval shortening is an option (clinical assessment and monitoring of serum blood levels can be measured to inform possible decision options (eg dose escalation/ interval shortening – see note 3)
- Consider switching to the alternate TNFi if loss of response due to development of drug antibodies
- If switching to the other TNFi is not appropriate , consider switching to a drug with a different mode of action (MOA) eg ustekinumab or risankizumab or vedolizumab or upadacitinib

If ustekinumab # was used first line,

- consider switching to TNFi option, **if** the use of a TNFi is feasible

If used ustekinumab # or vedolizumab or Risankizumab or upadacitininb first line due to unsuitability of a TNFi ,

- consider a switch to any of the other agents (As all have different mode of action)

Assess patient's response after initial trial period of an alternative treatment option

If adequate response - follow guidance above

If no clinical response or loss of response or development of adverse effects

- **consider switching to an alternative drug with a different mode of action (choice will vary depending on which agents have been previously tried)**

A total of 6 different agents can be used as part of routine commissioning. Any treatment requests beyond this, where clinical exceptionality can be demonstrated, can be considered via the Individual Funding Request (IFR) route.

Supporting notes

Note 1

Definition of response

- **Remission** HBI score ≤4, correlates with CDAI < 150 or 50% fistula drainage
- **Partial response** fall of HBI ≥3, correlates with CDAI > 150 but no remission
- **No symptomatic response** – no clinical improvement, fall of HBI ≤ 2, no reduction in fistulae drainage

Note 2

Upadacitinib

Special warnings and precautions (as per SmPC)

Upadacitinib should only be used if no suitable treatment alternatives are available in patients:-

- Who are 65 years of age and older;
- patients with history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers);
- patients with malignancy risk factors (e.g. current malignancy or history of malignancy)

See MHRA advice on measures to consider before considering prescribing upadacitinib (JAK inhibitor) - April 2023

Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality - GOV.UK (www.gov.uk)

Note 3

DOSE ESCALATION / DOSE INTERVAL SHORTENING REGIMENS (applicable to adalimumab / infliximab / ustekinumab)

A dose escalation / dose interval shortening regimen can be considered to recapture response in the following scenarios:

- in patients who have responded initially and subsequently lost response
- in patients receiving either adalimumab **or** infliximab who have **sub-optimal therapeutic drug levels and who are still clinically symptomatic**

Dose escalation regimens are funded for an initial period of 6 months, at which time the patient should be reviewed with a view to de-escalating dose or frequency back to the standard treatment regimen.

- If clinically indicated, patients may be maintained on escalated dosing and monitored for effectiveness at least 6 monthly.

  NB Longer term requirement for a dose escalation regimen can be considered on an individual case basis

Adalimumub

- 40mg weekly

Infliximab IV – options

- infliximab 10mg/kg infusions every eight weeks
- infliximab 5mg/kg infusions every month

(NB s/c infliximab is not licensed for dose escalation / dose interval shortening regimens)

Ustekinumab

- Ustekinumab every eight weeks (review at week 16

  (NB: Dose interval shortening for ustekinumab to every 4 weeks or every 6 weeks is not routinely commissioned at the current time – In situations where a case for clinical exceptionality can be demonstrated, requests can be considered via the Individual Funding Request (IFR) route.)

Note 4

Patients in stable clinical remission

- Patients who are deemed to be in a stable clinical remission should be reviewed and the option of stopping treatment should be considered and discussed, noting that if a treatment is stopped then it can be restarted if a relapse occurs. (NICE recommendation)
- Monitoring of faecal calprotectin may be helpful in this context as levels may rise before clinical relapse occurs