North Central London
Joint Formulary Committee

Crohn's Disease Prescribing Pathway

Document control

Date	Version	Amendments
Nov 2023	3.0	Pathway developed in accordance with NCL 'Principles for Commissioning High-Cost Drug Pathways for ICB Commissioned Indications' and includes relevant published NICE TAs.
Apr 2024	4.0	Minor typos corrected. Removal of requirement for vedolizumab dose escalation to be guided by drug levels based on JFC Nov 2020 decision and discussion with clinical teams. RAG rating definition amended to clarify that the rating is based on cost and not cost-effectiveness. Vedolizumab IV maintenance option added, noting a preference for SC maintenance (lower cost).

Groups / Individuals who have overseen the development of this guidance:	UCLH Lead Pharmacist, Formulary & Clinical Trials, UCLH Specialised Commissioning Lead Pharmacist, NCL ICB Medicines Management Team, NCL Joint Formulary Principal Pharmacist, NCL Specialist Clinicians
Groups which were consulted and have given approval:	NCL wide consultation (NCL ICB, NCL Formulary Pharmacists, NCL Specialist Clinicians), NCL Joint Formulary Committee (Nov 2023), NCL Integrated Medicines Optimisation Board (Nov 2023)
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Disclaimer

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The authors and NCL JFC accept no liability for use of this information beyond its intended use.

While we have tried to compile accurate information in this guideline, and to keep it updated in a timely manner, we cannot guarantee that it is fully complete and correct at all times. If you identify information within this guideline that is inaccurate, please report this to the admin.ncl-mon@nhs.net. If a patient is harmed as a consequence of following this guideline, please complete a local incident report and inform admin.ncl-mon@nhs.net.

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NCL JFC is funded by and provides advice to Acute Trusts and the Integrated Care Board in NCL.

Crohn's Disease (CD) Prescribing Pathway

Green: lowest cost **Amber**: moderate cost **Red**: highest cost.
If more than one treatment is suitable, the least expensive treatment should be used.

Criteria to start treatment for moderately to severely active disease, or active fistulising disease[1]:
Patients with moderate-to-severely active CD, with lack or loss of response, intolerance or contraindication to conventional therapy (steroids and/or immunosuppressant) are eligible for treatment. Moderate-to-severe disease corresponds with Harvey-Bradshaw (HBI) score of ≥ 6, or where HBI is not a relevant indicator of disease severity, alternative objective measures of severe disease may be used (e.g. colonoscopy, stoma output, CRP, faecal calprotectin).
Patients with active fistulising disease may be considered for early biologic therapy, and do not require prior treatment with conventional therapies.

1ST LINE TREATMENT OPTIONS

Adalimumab SC biosimilar [**Preferred for non-fistulising disease;** TA187]	**Infliximab SC/IV** biosimilar [**Preferred for fistulising disease;** TA187]	Ustekinumab (TA456), upadacitinib (TA905), vedolizumab (TA352), and risankizumab (TA888; not for fistulising disease2), also available but only if TNF inhibitors are contraindicated.

2ND LINE ONWARDS TREATMENT OPTIONS

Alternative TNF inhibitor if secondary loss of response to 1st line TNF inhibitor – **Adalimumab SC** OR **Infliximab IV/SC** biosimilar [TA187]	**Ustekinumab** (IL12 & IL23 inhibitor) [TA456]	**Upadacitinib** (JAK inhibitor) [TA905] NB. MHRA update	**Vedolizumab IV loading, then SC (preferred)/IV** [TA352]	**Risankizumab** (IL23 inhibitor) [TA888; not for fistulising disease[2]]

Sequential treatments routinely commissioned: Up to one drug per mechanism of action, plus a second biosimilar TNF inhibitor. If more than one treatment is suitable, the least expensive treatment should be used.

Drug	Price	Usual maintenance	Dose escalation
Adalimumab	£	40mg SC every 2 weeks	40mg every week (depending on drug levels, anti-drug antibodies, and response[3])
Infliximab	£	120mg SC once every 2 weeks 5mg/kg IV every 8 week	10mg/kg IV every 8 week or 5mg/kg IV every 4-6 weeks (depending on drug levels, anti-drug antibodies, and response[3])
Upadacitinib	££	15 to 30mg oral daily	Not available
Vedolizumab	££	108mg SC every 2 weeks 300mg IV every 8 weeks	300mg IV every 4 weeks[3]; not included in TA352 economic assessment, clinically approved by NCL JFC provided Trusts have identified a mechanism of offset the budget impact)
Ustekinumab	£££	90 mg SC every 12 weeks	90 mg SC every 8 weeks (depending on response, or can be used off-label post IV induction if patient has failed prior biologic)
Risankizumab	£££	360 mg every 8 weeks	Not available

Assessment of response - Assess initial induction and/or dose escalation response in 12- 16 weeks based on clinical symptoms and biological markers +/- endoscopy and imaging. Dose escalation should be guided by therapeutic drug monitoring. If partial response, consider dose escalation. If no response, stop biologic and consider initiating alternative drug, surgery, or a clinical trial.

Continuation of Biologic Treatment - Treat for 12 months or until treatment failure (including the need for surgery), whichever is shorter, then review and discuss the risks and benefits of continued treatment or continued dose escalation. Continue only if there is evidence of response as determined by clinical symptoms, biological markers and investigation, including endoscopy if necessary. Reassess at least every 12 months to determine whether ongoing treatment is still clinically appropriate. Consider a trial of withdrawal for patients who are in stable clinical remission. If disease relapses after treatment is stopped patients have the option to start treatment again. Dose escalation should be guided by therapeutic drug monitoring.

Use of Biologics Post Surgery All patients should be risk assessed after surgery. In patients at high risk of recurrence (e.g. more than one resection, or penetrating or fistulising disease, young age at diagnosis, multiple previous biologics, current smoker), prophylaxis with thiopurine or biologic should be considered where appropriate.
Adverse drug reactions (ADRs) – For patients who experience an immediate ADR [within 1 month] or have responded to treatment but experience an ADR within 6 months of treatment initiation, another treatment option within the same mechanism of action (if available and appropriate) can be accessed. Where the ADR is likely to be a drug class effect, an alternative mechanism of action is preferable.

Dual biologic therapy for the same disease is not routinely commissioned; for individual cases, please consider RMOC advisory statement, discuss at MDT and contact Trust formulary teams for advice re IFR submission. **Concurrent biologic treatment for different co-morbidities,** is permissible provided NICE eligibility criteria for both treatments are met and there is MDT agreement across both specialities that dual therapy is appropriate and a single drug which is active against both co-morbidities is not available.

Footnote

[1] Adalimumab, ustekinumab, vedolizumab and upadacitinib are not specifically licensed for fistulising active Crohn's disease (though all are licensed for moderate-to-severe Crohn's disease). The highest-quality evidence supports the use of infliximab as first choice for fistulising disease. In patients refractory or intolerant to infliximab, there is low-quality evidence to support the use of adalimumab [NCL JFC Oct 2017]. The current evidence is too limited to support the use of ustekinumab [NCL JFC Oct 2017], vedolizumab [NCL JFC Nov 2023] and upadacitinib [NCL JFC Nov 2023] in clinical practice. However, ustekinumab, vedolizumab or upadacitinib may be considered in patients where anti-TNFs are ineffective or contraindicated and there are no treatment options, especially when concomitant luminal disease is present.

[2] There is no peer-reviewed data available at the current time to support risankizumab for fistulising active Crohn's disease.

[3] Dose escalation of TNF inhibitors should be informed by therapeutic drug monitoring in line with British Society of Gastroenterology guidance [BSG 2019]. The approach to dose escalation applies equally to moderately to severely active disease, and active fistulising disease [NCL JFC Nov 2023].

References

British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults 2019

European Crohn´s and Colitis Organisation Guidelines on Therapeutics in Crohn's Disease: Medical Treatment 2019