North Central London
Joint Formulary Committee

Crohn's Disease Prescribing Pathway

Document control

Date	Version	Amendments
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).
Nov 2025	5.0	Inclusion of NICE TA1080 (mirikizumab) and TA1095 (guselkumab) Inclusion of ustekinumab biosimilar as alternative first or second line treatment option Ustekinumab – standard dosing changed to 8 weekly dosing in line with clinical practice and 4 weekly dose escalation added Specific contraindications and cautions in relation to JAK inhibitor and vedolizumab use Specific patient cohort added for guselkumab/rizankizumab use before ustekinumab

Groups / Individuals who have overseen the development of this guidance:	NCL Specialist Clinicians, UCLH Formulary, NCL ICB High-Cost Drugs Team
Groups which were consulted and have given approval:	NCL wide consultation (NCL Specialist Clinicians, NCL ICB, NCL Formulary Pharmacists), NCL Joint Formulary Committee (Nov 2025)
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Disclaimer

This guideline is registered at North Central London (NCL) Joint Formulary Committee (JFC) and is intended solely for use by healthcare professionals to aid the treatment of patients within NCL. However, clinical guidelines are for guidance only, their interpretation and application remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Clinicians are advised to refer to the manufacturer's current prescribing information before treating individual patients.

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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

TNF inhibitors: **Adalimumab SC** biosimilar [Preferred for non-fistulising disease; TA187] OR **Infliximab SC/IV** biosimilar [Preferred for fistulising disease; TA187]	IL12 & IL23 inhibitor: **Ustekinumab** biosimilar [TA456]

2ND LINE TREATMENT OPTIONS

Alternative TNF inhibitor if secondary loss of response to 1st line TNF inhibitor – **Adalimumab SC** OR **Infliximab IV/SC** biosimilar [TA187]	IL12 & IL23 inhibitor: **Ustekinumab** biosimilar [TA456]

- **Vedolizumab SC/IV** (TA352) may be preferred 1st or 2nd line for certain patients (see footnotes)
- **Guselkumab** or **Risankizumab** (TA1095, TA888; not for fistulising disease[2]) may be considered ahead of ustekinumab in certain anti-TNF pre-treated or contraindicated patients†
- **Mirikizumab** also available but not preferred [TA828]
- **Upadacitinib**[4] [TA905] NB. MHRA update

3RD LINE ONWARDS TREATMENT OPTIONS

		Anti-TNF and ustekinumab pre-treated or contraindicated		
Alternative TNF inhibitor if secondary loss of response to 1st line TNF inhibitor – **Adalimumab SC** OR **Infliximab IV/SC** biosimilar [TA187]	IL12 & IL23 inhibitor: **Ustekinumab** biosimilar [TA456]	JAK inhibitor: **Upadacitinib**[4] [TA905] NB. MHRA update	IL23 inhibitor: **Guselkumab** or **Risankizumab**[5] [TA1095 / TA888; not for fistulising disease[2]] Mirikizumab also available but not preferred [TA828][6] † Consider guselkumab or risankizumab ahead of ustekinumab in anti-TNF pre-treated or contraindicated patients with: Peri-anal disease, penetrating disease, pan-enteric Crohn's, >1 resection surgeries, <16 years old at diagnosis.	**Vedolizumab IV loading, then SC (preferred)/IV**[7] [TA352]

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.

Commissioned treatments with RAG rating based on cost:

Drug	Price	Usual maintenance	Dose escalation
Adalimumab	£	40mg SC every 2 weeks	40mg every week (depending on drug levels, anti-drug antibodies, and response)
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)
Ustekinumab	£	90 mg SC every 8 weeks (off-label)[8]	90 mg SC every 4 weeks (off-label)[8]
Upadacitinib	££	15 to 30mg oral daily	Not available
Vedolizumab SC/IV	££	300mg IV every 8 weeks	300mg IV every 4 weeks; not included in TA352 economic assessment, clinically approved by NCL JFC provided Trusts have identified a mechanism of offset the budget impact).
Guselkumab	£££	100 mg every 8 weeks (££)	200 mg every 4 weeks (£££)
Risankizumab	£££	360 mg every 8 weeks	Not available
Mirikizumab	£££	300 mg every 4 weeks	Not available

Commissioning notes

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, consider that evidence to support this treatment approach is lacking; and there may be risk of interactions and additive adverse effects. 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.

Audit standards
Audit standards provide a framework for monitoring clinical effectiveness, financial accountability, and governance of NCL High Cost Drugs Pathways. These standards have been agreed across clinical teams in NCL Trusts and NCL ICB and are to be monitored on agreed timescales. Embedding audit standards into routine practice allows outcomes to be tracked, variations to be identified, and pathways to be continuously improved, ensuring both high-quality patient care and the sustainable use of NHS resources.

Footnotes/Clinical considerations

[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, guselkumab or mirikizumab for fistulising active Crohn's disease. [NCL JFC Nov 2023].

[3] In the first and second-line setting, vedolizumab may be preferred for patients who are: frail (Rockwood clinical frailty ≥6), elderly >70 years, comorbidities (heart failure/severe heart disease/COPD/bronchiectasis/recent sepsis), concurrent immunosuppression for other condition, chronic granulomatous disease, severe infections e.g. TB, active or recent cancer. Type 2 diabetes is NOT an exclusion criterion for anti-TNF or ustekinumab. [NCL JFC Nov 2025]

[4] JAK inhibitors are cautioned/contraindicated (MHRA warning) in patients with cardiovascular risk, > 60 years, previous VZV, previous VTE, concurrent oestrogen containing oral contraceptive tablet (COC) or hormone replacement therapy (HRT), childbearing age/plans/pregnant (BSG 2025). It is the consensus of local clinicians that other treatments may be used before JAK inhibitors in women of childbearing age in consultation with the patient and following appropriate patient counselling on risk vs benefit. [NCL JFC Nov 2025]

[5] The real-world price difference between guselkumab (combination of 100 mg q8w and 200mg q4w maintenance) and risankiuzmab is unclear at the time of pathway development; differences vary depending on the time horizon (induction costs of risankizumab are highest, but maintenance costs of guselkumab 200mg is highest) and the unknown ratio of gusekinumab 100mg:200mg. There is insufficient clinical evidence to prefer guselkumab to risankiuzmab. The SC induction dose of guselkumab is useful for Providers with limited infusion clinic capacity. Working group consensus was that at the time of writing, both drugs should be available. [NCL JFC Nov 2025]

[6] Mirankizumab has a slightly less convincing evidence-base in the anti-TNF pre-treated (non-inferiority vs. ustekinumab, whereas guselkumab and risankiuzmab demonstrated superiority for clinical remission and endoscopic response at week 48). Mirankizumab (IV induction) offers no practical advantage to risankizumab or guselkumab. Mirankizumab offers no cost-advantage over guselkumab 100mg. Working group consensus was to position mirankizumab as 'not preferred' to rationalise the number of drugs on the formulary. [NCL JFC Nov 2025]

[7] Whilst there are no comparative studies of vedolizumab to other agents, vedolizumab is not suggested for induction and maintenance of remission in patients with moderate to severe Crohn's disease [BSG 2025]. In contrast, real-world evidence demonstrated similarity between ustekinumab and vedolizumab in Crohn's following anti-TNF treatment (UK IBD BioResource) therefore vedolizumab remains a valid therapeutic option. [NCL JFC Nov 2025]

[8] Ustekinumab product license indicates initiation of SC dosing every 12 weeks. Based on trial evidence, initiation of 8 weekly dosing is approved in NCL. An escalated dose regimen of 90mg SC every 4 weeks may be used in patients who have shown partial response to 8 weekly dosing. [NCL JFC Nov 2025]

[9] Whilst there remains uncertainty about the benefit of therapeutic drug monitoring for anti-TNF therapies, strategies that lead to dose escalation, whether guided by TDM or not, tend to result in better clinical outcomes. Anti-TNF therapy dose escalation alone is less likely to be effective in the presence of anti-drug-antibodies and therefore testing for these, when loss of response occurs, may guide treatment decisions, favouring either dose escalation plus the addition of an immunomodulator or a switch to another [BSG 2025]. 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 guidelines on inflammatory bowel disease in adults: 2025

Biologic Therapy for Inflammatory Bowel Disease: Real-World Comparative Effectiveness and Impact of Drug Sequencing in 13 222 Patients within the UK IBD BioResource