Inflammatory Bowel Disease Biologic Pathway Immunosuppressant to Biologic Gloucestershire Hospitals Patient requiring escalation of IBD therapy **NHS Foundation Trust Hospitalised patient** Start azathioprine (AZA) based on TPMT result (corticosteroids will also likely be required) and EBV if male and <30 years "Acute severe" ulcerative colitis Refer to Pathway A Note 1: High risk/Complex IBD - Young patients (<40 years) Pathway A or B High risk IBD¹? - Fulminant disease - Previous surgery for Crohn's disease / early recurrence - Fistulising / penetrating Crohn's disease - Unable to use steroids as a bridge to AZA monotherapy immunosuppression - Previous admission for ulcerative colitis (see after 6 weeks in nurse-led clinic) Consider 6-mercaptopurine or AZA & allopurinol if standard dose AZA is not tolerated. Can also consider methotrexate in Crohn's disease only Note 2: Reasons for 6TGN/MMPN monitoring (earliest check at 4 weeks) - Non-adherence suspected or failing Response at 12 treatment weeks - Abnormalities in bloods especially low WCC or rising ALT No (or bloods abnormal 3) - Prior to progressing to biologic Request shared care at 16 weeks Annual review by IBD nurse and access Evidence of ongoing active IBD (on clinical assessment)? to advice line Likely will continue with thiopurine

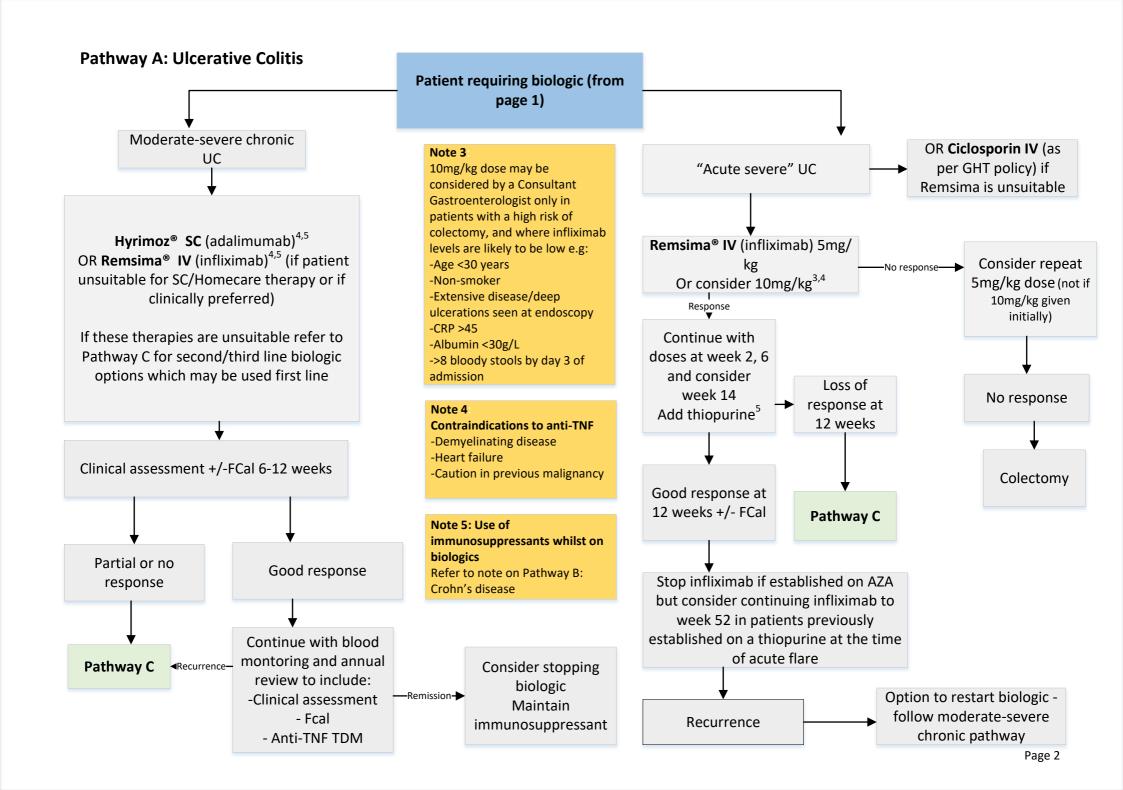
Authors: Dr Ian Shaw, Leela Terry & Sarah York

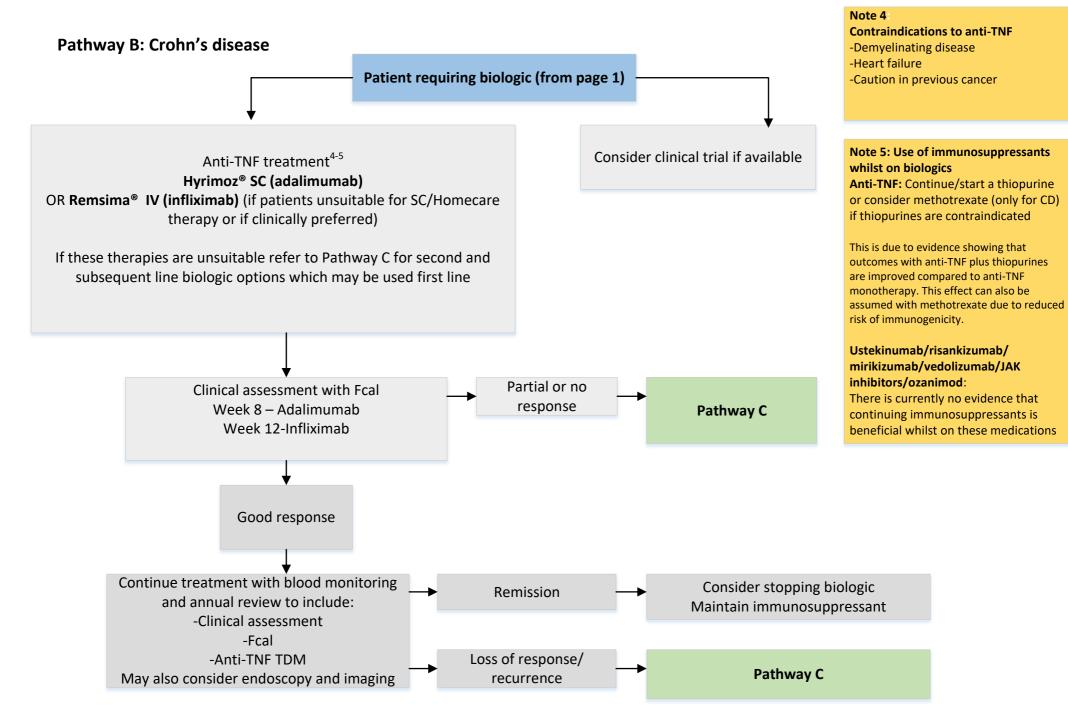
Approved by: Drugs and Therapeutics Committee

Review date: June 2025 (updated January 2024)

with annual review and blood

monitoring²





Pathway C: Partial response/Loss of response to anti-TNF Partial/loss of response to a biologic Confirm active IBD flare: -Fcal/stool culture -Bloods -Endoscopy Consider IBD, malignancy and infection as differential diagnosis Consider trough level for therapeutic drug monitoring (if unavailable optimise drug frequency or dose⁶) Anti-TNF trough level detectable Anti-TNF trough level low or undetectable Adalimumab 5-12mg/L, Infliximab 7-10mg/L Negative antibodies but loss **Adalimumab** If antibody level Review antibody level by Infliximab of response suggests likely If antibody ≥ 40 If antibody ≥ 40 <10 following advice as for not TNF mediated disease -Switch to second line - Switch to second line - review patient anti-TNF level low or - switch to second line option (non-anti TNF) options (non anti-TNF) adherence undetectable options If antibody <40 If antibody <40 -add immunosuppressant⁵ -add immunosuppressant⁵ -increase frequency/dose -increase frequency/dose of of anti-TNF⁶ or consider anti-TNF⁶ or consider switching to infliximab switching to adalimumab If in remission If adjusting dose/frequency due to TDM or consider stopping switching class biologic Continue immunosuppressant 6-16 week review and Good response Partial/no response repeat TDM if possible Switch class if anti-TNF Review 6-12 weeks Continue with Aim to de-escalate in 3-6 If alternative class, ▶ If failed all options blood monitoring ◀ months if using TDM as a optimise⁶ consider surgery guide where possible and annual review Page 4

Pathway C: Second and subsequent line options

Second and subsequent choices following anti-TNF failure or contraindications

In UC: Switch to either Jyseleca® PO (filgotinib) or Entyvio® SC (vedolizumab, IV is also available for patients in whom SC is unsuitable)

Further options in order of preference are:

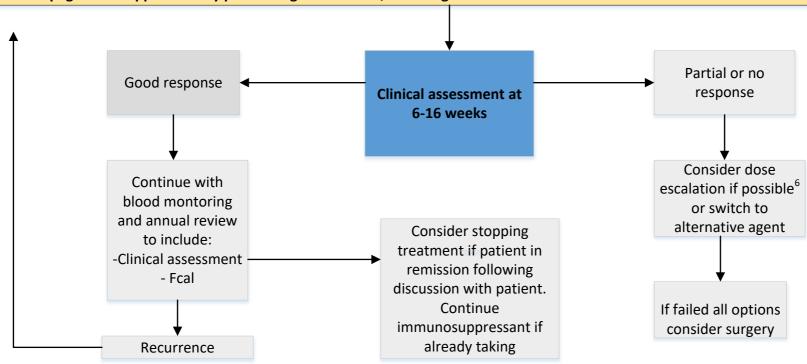
- -Omvoh® SC (mirikizumab) 4 weekly or Rinvoq® PO (upadacitinib)
- -Zeposia® PO (ozanimod), Xeljanz® PO (tofacitinib) or Stelara® SC (ustekinumab) 8 weekly (aim to reduce to 12 weekly dosing if possible)

In Crohn's disease: Switch to Rinvog® PO (upadacitinib)

Further options in order of preference are:

- Skyrizi®SC (risankizumab) or Entyvio® SC (vedolizumab, IV is also available for patients in whom SC is unsuitable)
- Stelara® SC (ustekinumab) 8 weekly (aim to reduce to 12 weekly dosing if possible)

Refer to page 6 for supplementary prescribing information, including dose escalation



Supplementary information

Note 6: Dose escalation

Adalimumab: Increase to 40mg weekly

Infliximab IV: If levels low increase IV dose to 10mg/kg 8 weekly. If dose wearing off too soon, consider 5mg/kg 6 weekly

Vedolizumab: Can use 300mg IV dose at week 10 in Crohn's disease and also 4 weekly maintenance dosing in both Crohn's disease and UC when using the IV preparation. If loss of response on SC preparation consider switching to 4 weekly IV as evidence suggests levels higher on this regime

Mirikizumab: Patients who do not achieve adequate therapeutic benefit at week 12 can receive additional IV loading doses at weeks 12,16 and 20 before commencing SC at week 24. If no benefit is seen by week 24treatment should be discontinued. Patients who lose response during the maintenance treatment may receive re induction with 3 IV doses given every 3 weeks for 4 doses.

Upadacitinib: Continue 45mg induction dose for an additional 8 weeks in UC only. Dose can also be increased to 30mg if initiated on 15mg daily as a maintenance dose

Tofacitinib: Continue 10mg BD induction phase for an additional 8 weeks, can use 10mg BD as maintenance but VTE risk assessment must be re-checked

In patients with risk factors for VTE on JAK inhibitors, use lower doses where possible

Janus kinase (JAK) inhibitors: measures to reduce the risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality:

JAK inhibitors (filgotinib, upadacitinib and tofacitinib) should not be used in patients with the following risk factors unless there are no other suitable alternatives:

- Age 65 or over
- Current or past long-time smoking
- Other risk factors for cardiovascular disease or malignancy

Use caution when prescribing in patients with other risk factors for VTE and prescribe lower doses where possible Carry out periodic skin examinations on all patients to check for skin malignancy (MHRA April 2023)

Patients should not receive maintenance treatment with tofacitinib 10mg twice daily if they have risk factors for VTE unless there are no other suitable options