Inflammatory Bowel Disease Biologic Pathway

Immunosuppressant to Biologic

Gloucestershire Hospitals NHS Foundation Trust

Patient requiring escalation of IBD therapy

Start azathioprine (AZA) based on TPMT result (corticosteroids will also likely be required) and EBV if male and <30 years

High risk IBD[1] ?

Yes → **Pathway A or B**

No

AZA monotherapy
(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

Response at 12 weeks

Yes → Request shared care at 16 weeks
Annual review by IBD nurse and access to advice line

No (or bloods abnormal [3])

Evidence of ongoing active IBD (on clinical assessment)?

Yes → **Pathway A or B**

No → Likely will continue with thiopurine with annual review and blood monitoring[2]

Hospitalised patient

"Acute severe" ulcerative colitis → **Refer to Pathway A**

Note 1: High risk/Complex IBD

- Young patients (<40 years)
- Fulminant disease
- Previous surgery for Crohn's disease / early recurrence
- Fistulising / penetrating Crohn's disease
- Unable to use steroids as a bridge to immunosuppression
- Previous admission for ulcerative colitis

Note 2:
Reasons for 6TGN/MMPN monitoring (earliest check at 4 weeks)
- Non-adherence suspected or failing treatment
- Abnormalities in bloods especially low WCC or rising ALT
- Prior to progressing to biologic

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Approved by: Drugs and Therapeutics Committee
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Pathway A: Ulcerative Colitis

Patient requiring biologic (from page 1)

Moderate-severe chronic UC

Hyrimoz® SC (adalimumab)[4,5]
OR **Remsima® IV** (infliximab)[4,5] (if patient unsuitable for SC/Homecare therapy or if clinically preferred)

If these therapies are unsuitable refer to Pathway C for second/third line biologic options which may be used first line

Clinical assessment +/-FCal 6-12 weeks

Partial or no response

Pathway C

Recurrence

Good response

Continue with blood montoring and annual review to include:
-Clinical assessment
- Fcal
- Anti-TNF TDM

Remission

Consider stopping biologic
Maintain immunosuppressant

Note 3
10mg/kg dose may be considered by a Consultant Gastroenterologist only in patients with a high risk of colectomy, and where infliximab levels are likely to be low e.g:
-Age <30 years
-Non-smoker
-Extensive disease/deep ulcerations seen at endoscopy
-CRP >45
-Albumin <30g/L
->8 bloody stools by day 3 of admission

Note 4:
Contraindications to anti-TNF
-Demyelinating disease
-Heart failure
-Caution in previous malignancy

Note 5: Use of immunosuppressants whilst on biologics
Refer to note on Pathway B: Crohn's disease

"Acute severe" UC

OR **Ciclosporin IV** (as per GHT policy) if Remsima is unsuitable

Remsima® IV (infliximab) 5mg/kg
Or consider 10mg/kg[3,4]

No response

Consider repeat 5mg/kg dose (not if 10mg/kg given initially)

No response

Colectomy

Response

Continue with doses at week 2, 6 and consider week 14
Add thiopurine[5]

Loss of response at 12 weeks

Pathway C

Good response at 12 weeks +/- FCal

Stop infliximab if established on AZA but consider continuing infliximab to week 52 in patients previously established on a thiopurine at the time of acute flare

Recurrence

Option to restart biologic - follow moderate-severe chronic pathway

Pathway B: Crohn's disease

Patient requiring biologic (from page 1)

Anti-TNF treatment[4-5]
Yuflyma® SC (biosimilar adalimumab)
OR **Remsima® IV (biosimilar infliximab)** (if patients unsuitable for SC/ Homecare therapy or if clinically preferred)

If these therapies are unsuitable refer to Pathway C for second and subsequent line biologic options which may be used first line

Consider clinical trial if available

Clinical assessment with Fcal
Week 8 – Adalimumab
Week 12-Infliximab

Partial or no response → **Pathway C**

Good response

Continue treatment with blood monitoring and annual review to include:
-Clinical assessment
-Fcal
-Anti-TNF TDM
May also consider endoscopy and imaging

Remission → Consider stopping biologic
Maintain immunosuppressant

Loss of response/ recurrence → **Pathway C**

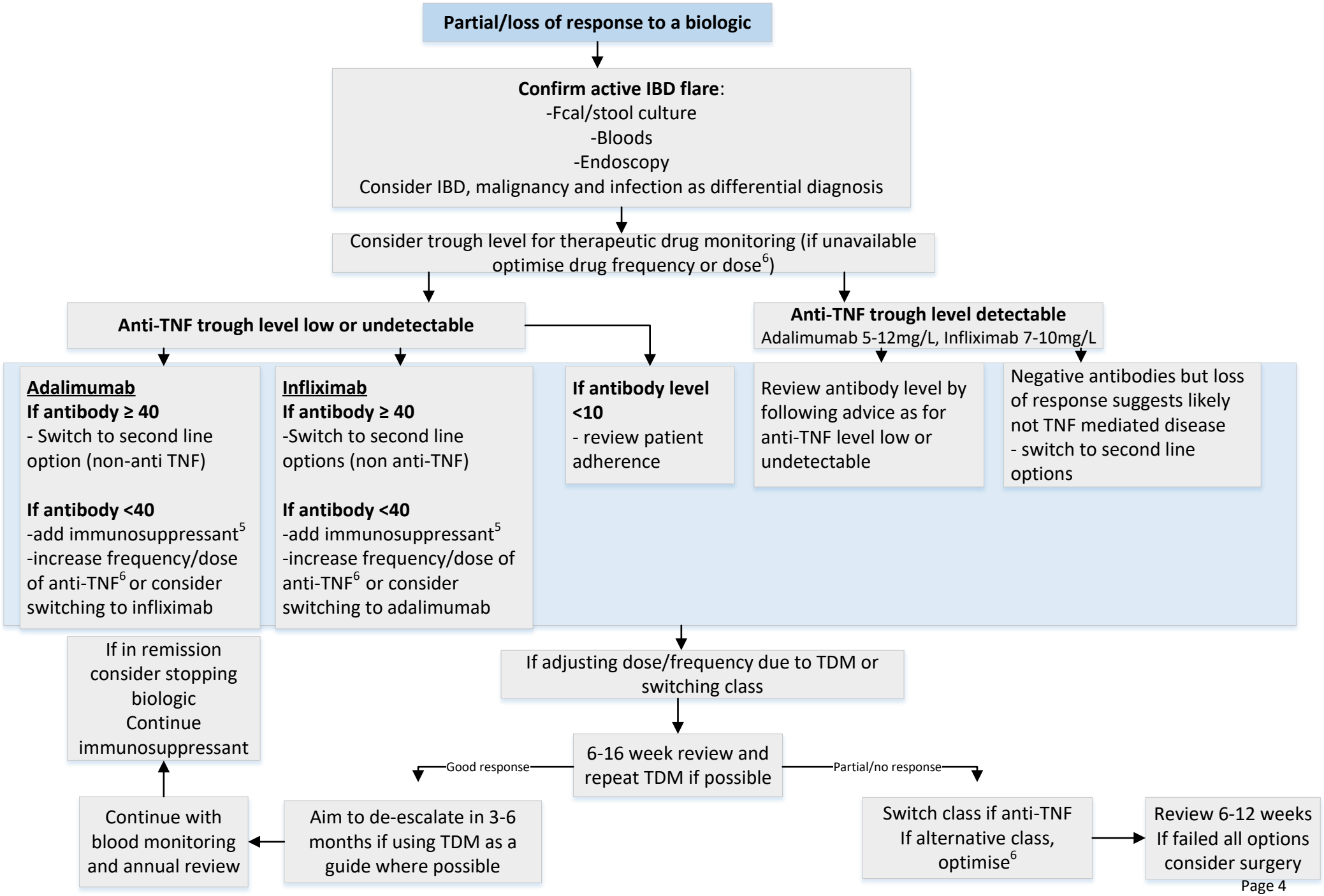
Note 4:
Contraindications to anti-TNF
-Demyelinating disease
-Heart failure
-Caution in previous cancer

Note 5: Use of immunosuppressants whilst on biologics
Anti-TNF: Continue/start a thiopurine or consider methotrexate (only for CD) if thiopurines are contraindicated

This is due to evidence showing that outcomes with anti-TNF plus thiopurines are improved compared to anti-TNF monotherapy. This effect can also be assumed with methotrexate due to reduced risk of immunogenicity.

Ustekinumab/risankizumab/ mirikizumab/vedolizumab/JAK inhibitors/ozanimod:
There is currently no evidence that continuing immunosuppressants is beneficial whilst on these medications

Pathway C: Partial response/Loss of response to anti-TNF



Pathway C: Second and subsequent line options

Second and subsequent choices following anti-TNF failure or contraindications

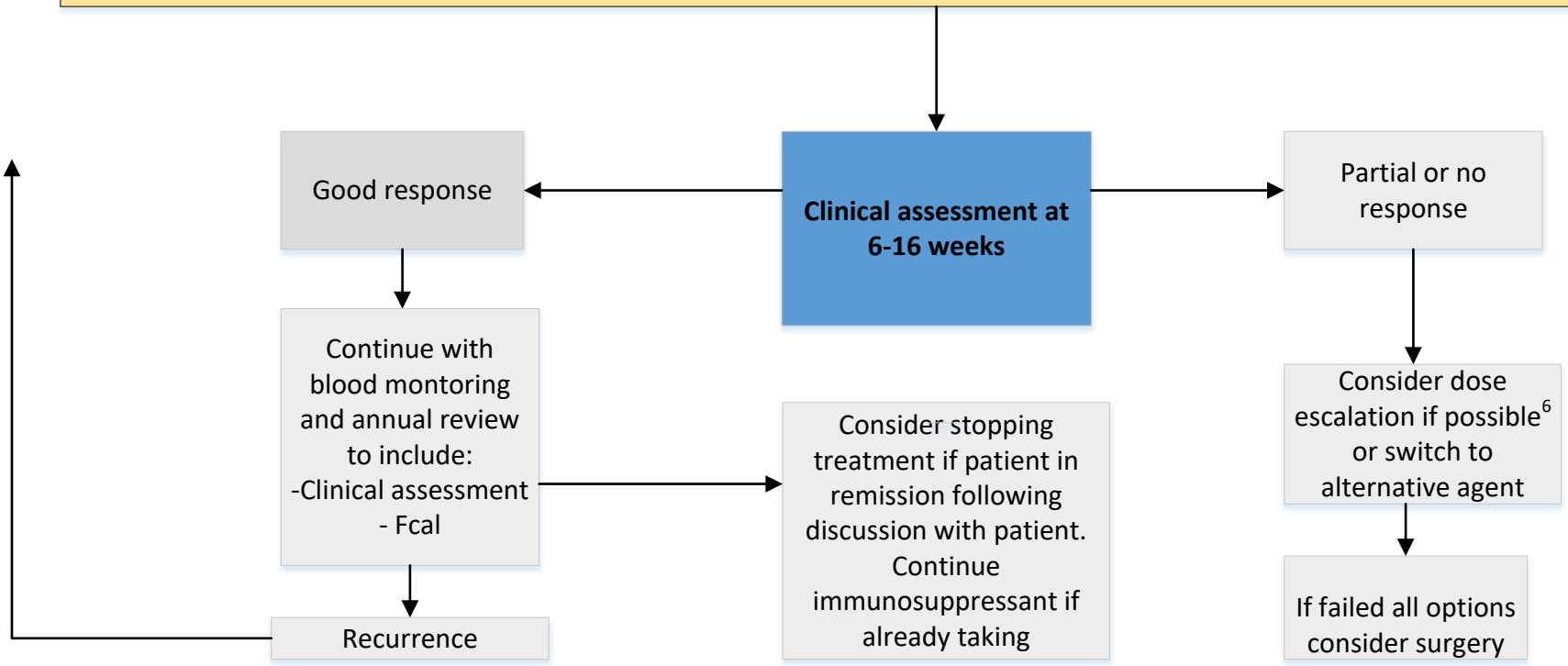
In UC: Switch to either **Jyseleca® PO** (filgotinib) or **Entyvio® SC** (vedolizumab, IV is also available for patients in whom SC is unsuitable)

Further options in order of preference are:
-**Omvoh® SC** (mirikizumab) 4 weekly or **Rinvoq® PO** (upadacitinib)
-**Zeposia® PO** (ozanimod), **Xeljanz® PO** (tofacitinib), **Velsipity® PO (etrasimod) or Stelara® SC** (ustekinumab) 8 weekly (aim to reduce to 12 weekly dosing if possible)

In Crohn's disease: Switch to **Rinvoq® 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)
- Pyzchiva® SC (biosimilar 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