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 4 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[2]
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[2,3]

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:
Shared Care Guideline

Note 3:
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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Pathway A: Ulcerative Colitis

Patient requiring biologic (from page 1)

Note 4: It is the position of GHT that biosimilar preparations be used in preference to originators where there are multiple products in the same class

Moderate-severe chronic UC

Anti-TNF Treatment (NICE TA 329)[4,6,7]
Adalimumab SC
OR Infliximab IV (if patients unsuitable for SC/Homecare therapy or if clinically preferred)
Infliximab SC and Golimumab SC may also be considered

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
Week 14 anti-TNF therapeutic drug monitoring (TDM) if on anti-TNF

- Partial or no response → **Pathway C**
- Good response → Continue with blood montoring and annual review to include:
  -Clinical assessment
  - Fcal
  - Anti-TNF TDM
  - Recurrence → **Pathway C**
  - Remission → Consider stopping biologic
    Maintain immunosuppressant

Note 5:
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 6:
Contraindications to anti-TNF
-Demyelinating disease
-Heart failure
-Caution in previous malignancy

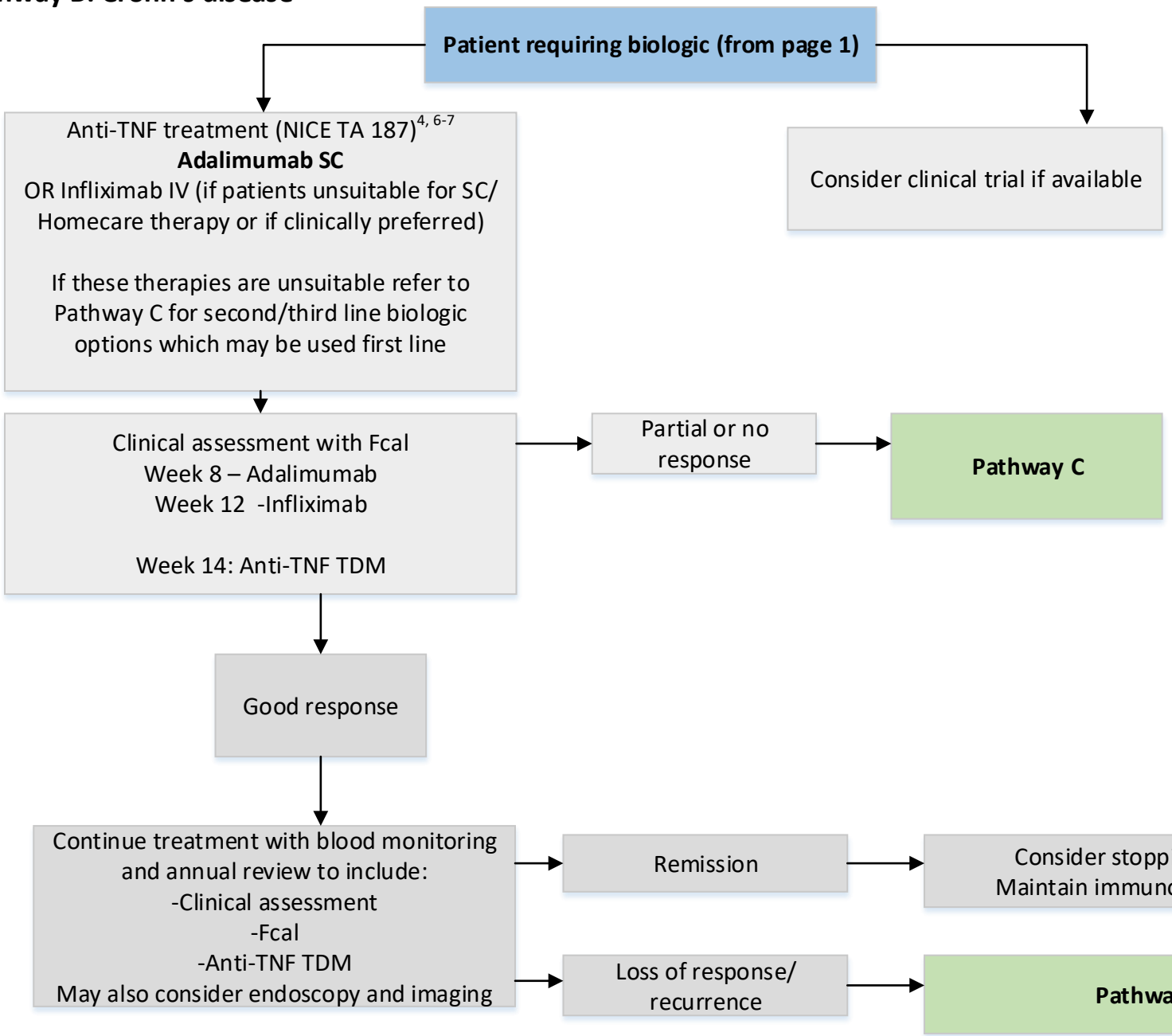
Note 7: Use of immunosuppressants whilst on biologics
Refer to note on Pathway B: Crohn's disease

"Acute severe" UC

Infliximab IV 5mg/kg [4] (NICE TA163)
Or consider 10mg/kg[5]

- No response → Consider repeat 5mg/kg dose[4] (not if 10mg/kg given initially)
  - No response → Colectomy
- Response → Consider continuing with doses at week 2, 6 and 14
  Add thiopurine [7]
  - 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



Note 4: **Biosimilars**
It is the position of GHT that biosimilar preparations be used in preference to originators where there are multiple products in the same class

Note 6:
Contraindications to anti-TNF
-Demyelinating disease
-Heart failure
-Caution in previous cancer

Note 7: Use of immunosuppressants whilst on biologics
Anti-TNF: Continue/start a thiopurine or consider methotrexate 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/vedolizumab/ tofacitinib:
There is currently no evidence that continuing immunosuppressants is beneficial whilst on these medications

Pathway C: Partial response/Loss of response

Note 9: Second/Third line choices following Anti-TNF
UC: Switch to vedolizumab (SC preferred) second line and then either ustekinumab 8 weekly (aim to dose reduce to 12 weekly if patient in remission) or tofacitinib as an alternative (or earlier if contraindications to other options)
Note risk of VTE with tofacitinib, refer to GHT policy for risk assessment.
Patients over the age of 65 should not receive tofacitinib due to risk of infections

Crohn's disease: Switch to vedolizumab (SC preferred) second line and then ustekinumab SC 8 weekly (aim to dose reduce to 12 weekly if patient in remission) (or earlier if contraindications to other options)

Note 8: Dose escalation

Adalimumab: Increase to 40mg weekly
Infliximab: If levels low, increase to 10mg/kg 8 weekly. If dose wearing off too soon, consider 5mg/kg 6 weekly
Golimumab: Increase to 100mg monthly if <80kg
Tofacitinib: Continue 10mg BD induction phase for an additional 8 weeks, if anti-TNF failure can use 10mg BD as maintenance
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

Partial/loss of response to a biologic

Confirm active IBD flare:
-Fcal/stool culture
-Bloods
-Endoscopy
Consider IBD, malignancy and infection as differential diagnosis

Send trough level for therapeutic drug monitoring (if unavailable optimise drug frequency or dose[8])

Anti-TNF trough level low or undetectable

Adalimumab
If antibody ≥ 58
- Switch to second line option (non-anti TNF)[9]

If antibody <58
-add immunosuppressant[7]
-increase frequency/dose of anti-TNF[8] or consider switching to infliximab

Infliximab
If antibody≥40
-Switch to second line options (non anti-TNF)[9]

If antibody <40
-add immunosuppressant[7]
-increase frequency/dose of anti-TNF[8] or consider switching to adalimumab

If antibody level <10
- review patient adherence

Anti-TNF trough level detectable
Adalimumab 5-12mg/L, Infliximab 5-10mg/L

Review antibody level by following advice as for anti-TNF level low or undetectable

Negative antibodies but loss of response suggests likely not TNF mediated disease
- switch to second line options[9]

If adjusting dose/frequency due to TDM or switching class

6-16 week review and repeat TDM if possible

Good response

Partial/no response

Aim to de-escalate in 3-6 months if using TDM as a guide where possible

Continue with blood monitoring and annual review

If in remission consider stopping biologic
Continue immunosuppressant

Switch class if anti-TNF[9]
If alternative class, optimise[8]

Review 6-12 weeks
If failed all options consider surgery