Ulcerative Colitis Biologic Pathway

5-ASA treatment to biologic

Gloucestershire Hospitals NHS Foundation Trust

Patient requiring escalation of UC therapy
-Ensure oral mesalazine maximised and consider topical therapies

Start **Jyseleca® PO** (filgotinib **£**)**(1)**
Or if the patient has extensive disease, severe presentation or at consultant discretion consider **Rinvoq® PO** (upadacitinib **££**) as an alternative **(1), consider reducing to 15mg dose when possible as long-term evidence suggests this dose is as effective as 30mg**

If patient has contraindications to JAK inhibitors start **Zeposia® PO** (ozanimod **£**) as an alternative

Clinical assessment +/-Fcal at 8-12 weeks

Partial or no response to first line options → **Pathway A**

Good response

Continue with blood monitoring and annual review to include:
-Clinical assessment
-FCal

Recurrence → **Pathway A**

Hospitalised patient

"Acute severe" ulcerative colitis

Refer to Pathway A

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Pathway A: Ulcerative Colitis

Patient requiring advanced therapy (from page 1)

Moderate-severe chronic UC

Second line options: If partial responder or loss of response to **filgotinib** consider switching to **Rinvoq® PO** (upadacitinib **££**) **(1)**

Alternatively consider:
Remsima® IV (biosimilar infliximab **£**) **(2) and azathioprine PO (consider stopping azathioprine after 1 year of treatment)**

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

Clinical assessment +/-Fcal 12 weeks
Infliximab TDM at week 14

Partial or no response → **Pathway B or C**

Good response → Continue with blood monitoring and annual review to include:
-Clinical assessment
- Fcal
- Infliximab TDM

Recurrence → **Pathway B or C**

"Acute severe" UC

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

Remsima® IV (biosimilar infliximab **£**) 5mg/kg
Or consider 10mg/kg **(2,3)**

No response → Consider repeat 5mg/kg dose (not if 10mg/kg given initially)

Response → Continue with doses at week 2, 6 and consider week 14
Add thiopurine (can consider stopping after 1 year) **(4)**

Loss of response at 12 weeks → **Pathway B/C**

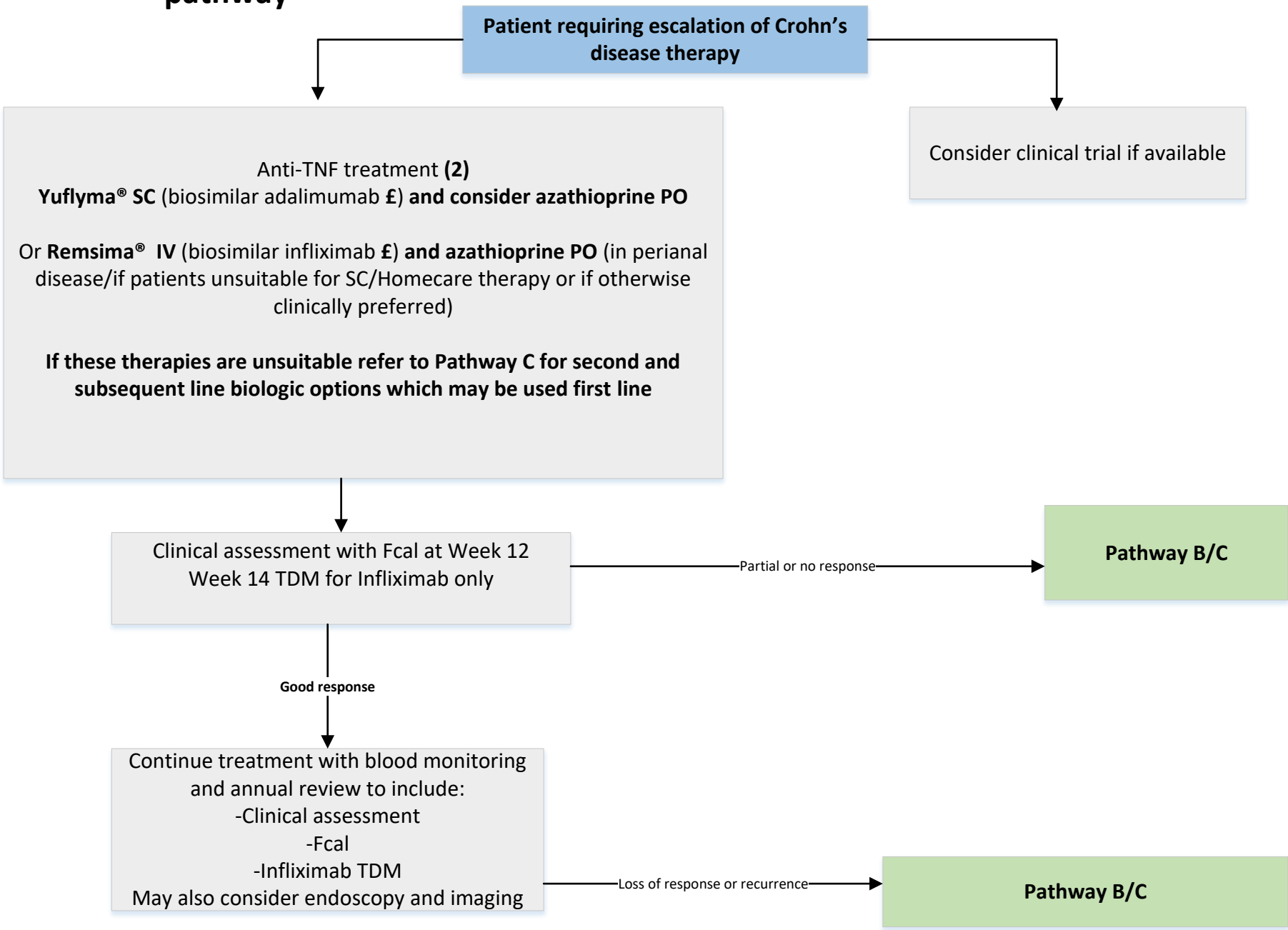
Good response at 12 weeks +/- Fcal Infliximab TDM at week 14

Continue with blood monitoring and annual review to include:
-Clinical assessment
-Fcal
- Infliximab TDM

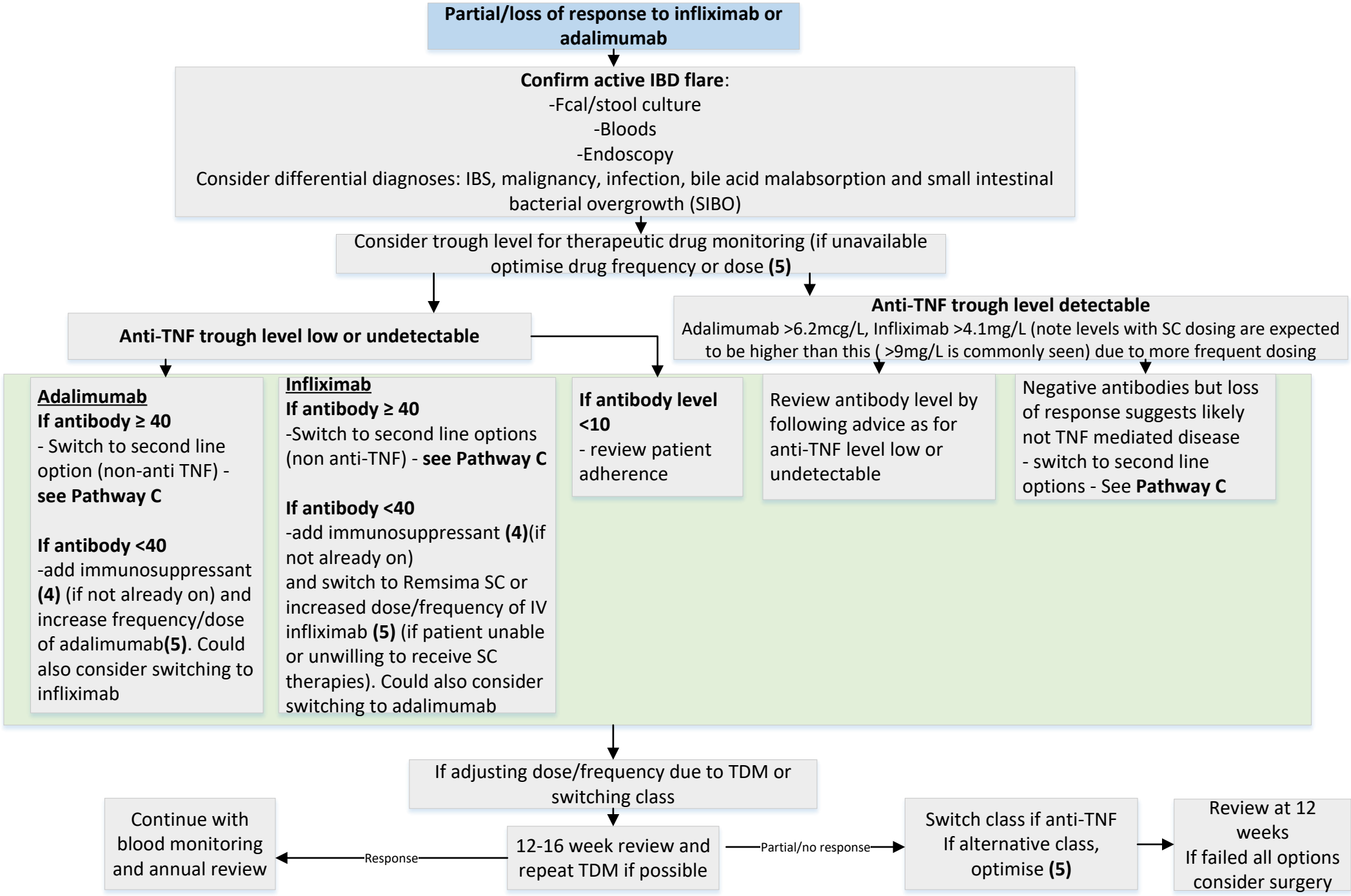
Recurrence → Follow moderate-severe chronic pathway

No response → Colectomy

Crohn's disease biologic pathway



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



Pathway C: Second and subsequent line options for patients who failed or who are unsuitable for initial therapies

ULCERATIVE COLITIS

Third line/fourth line:
Switch to either **Pyzchiva SC** 8 weekly (biosimilar ustekinumab **£**) or **Entyvio® SC** (vedolizumab) (SC is preferred **£££** but if patients are unsuitable for Homecare or decline SC, IV is available **££££**)

Last line:
Tremfya® SC (Guselkumab **£££**) (SC loading is preferred)

Other lines of treatment below this include:
Velsipity® PO (etrasimod **£**), **Xeljanz® PO** (tofacitinib **££**), **Omvoh® SC** (mirikizumab **£££**), **Gobivaz® SC** (biosimilar golimumab **£**) and **Skyrizi® SC** (risankizumab **££££**) (consider other autoimmune co-morbidities)

CROHN'S DISEASE

Second line: Switch to **Pyzchiva® SC** 8 weekly (biosimilar ustekinumab **£**) or refer to **note 6** for the criteria of those able to have an IL-23 agent in advance of ustekinumab

Third line: **Rinvoq® PO** (upadacitinib **££**) **(1)**

Or in patients unsuitable for a JAK-inhibitor:

Entyvio® IV/SC (vedolizumab **£££/££££**)– **only to be used in patients who are likely to be high-responders following the CDST criteria, defined by a score of >19 (7):**

1. No prior bowel surgery (+2 points)
2. No prior anti-TNF therapy exposure (+3 points)
2. No prior fistulising disease (+2 points)
3. Baseline albumin levels in g/L (+ 0.4 points per g/L)
4. Baseline CRP mg/L (-0.5 points if CRP 3.0-10.0 mg/L, -3.0 points if CRP >10mg/L)

Low probability of response = <13 points, high probability of response = >19 points

For patients who do not have a CDST score of >19 – **Tremfya® SC** (guselkumab **£££**) (SC loading is preferred) or **Skyrizi® SC** (risankizumab **££££**)

Other lines of treatment below this include **Omvoh® SC** (mirikizumab **££££**)

Response at 12-16 weeks?

Yes → Continue with blood monitoring and annual review to include:
-Clinical assessment
- Fcal

Partial or no response → Consider dose escalation if possible **(5)** or switch to alternative agent → If failed all options consider surgery

Notes and additional information

1. 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 suitable alternatives:
-Age 65 or over
-Current or past long-term 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 examination 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

2. Contraindications to anti-TNF:
-Demyelinating disease
-Heart failure
-Caution in previous malignancy

3. Infliximab dosing in acute severe colitis:

A 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

4. Use of immunosuppressants whilst on biologics:

-Infliximab and adalimumab:
Continue or start a thiopurine
This is due to evidence showing that outcomes with infliximab plus thiopurines are improved compared to anti-TNF monotherapy. Note evidence for combination therapy with adalimumab is not as clear and can be considered on a case by case basis.

-Other therapies:
There is currently no evidence that continuing immunosuppressants is beneficial whilst on these medications. Continuation alongside small molecules such as JAK inhibitors or ozanimod is not recommended due to the risks of additive immunosuppression.

Stopping immunomodulators:
In Crohn's disease, for patients on a combination on anti-TNF and immunomodulator, withdrawal of the immunomodulator is not associated with a significant risk of relapse at 2 years as long as withdrawal is attempted after >2 years of anti-TNF therapy and only if the patient is in corticosteroid-free remission for >6 months *(BSG IBD guidance 2025).* In UC, thiopurines may be stopped after 1 year if used as combination therapy with anti-TNF as immunogenicity is thought to be most problematic in the first year of treatment.

5. Dose escalation:
Yuflyma (biosimilar adalimumab): Increase to 40mg weekly **(£)**

Remsima IV (biosimilar infliximab): Consider switching to Remsima SC **(£**) as this provides higher levels due to more frequent dosing. If the patient wishes to continue with IV dosing or unsuitable for Homecare, increase IV dose to 10mg/kg 8 weekly **(££)** if levels are low. If the dose is wearing off too soon, consider 5mg/kg 6 weekly **(£)**

Pyzchiva SC (biosimilar ustekinumab): Doses may be increased to 90mg 6 weekly **(£)**

Rinvoq PO (upadacitinib): In UC only - continue 45mg induction dose for an additional 8 weeks. The dose can also be increased to 30mg in either condition, if taking 15mg as a maintenance dose **(££)**

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

Entyvio IV/SC (vedolizumab): In Crohn's disease only - can use a week 10 IV dose
In either condition - can escalate to 4 weekly maintenance dosing. If loss of response on SC preparation consider switching to 4 weekly IV as evidence suggests levels are higher on this regime **(£££££)**

Tremfya SC (guselkumab): If the patient does not have an adequate therapeutic benefit after induction, the dose may be increased to 200mg from week 12 and then given every 4 weeks **(£££££)**

Omvoh SC (mirikizumab): **In UC only** - for patients who do not achieve adequate therapeutic benefit at week 12 of induction dosing, a 300mg IV dose may be given at weeks 12, 16 and 20 (extended induction)(**£££££**). Patients with loss of therapeutic response during maintenance treatment may receive 300mg mirikizumab by IV infusion every 4 weeks for 3 doses **(£££££)**.

Xeljanz PO (tofacitinib): Continue 10mg BD induction phase for an additional 8 weeks, can also use 10mg BD as a maintenance dose but review VTE risk assessment **(££)**

6. Patients who may receive IL-23 agents prior to ustekinumab as a second-line option for Crohn's disease:
- patients with perianal or penetrating disease
- pan-enteric Crohn's disease
- > 1 resection surgery
- Younger than 16 years old at diagnosis
- Or at Consultant discretion

(Criteria taken with permission from University College London Hospitals IBD team)

7. Taken from the CDST criteria: Dulai PSD et al (2018); Development and Validation of a Scoring System to Predict Outcomes of Vedolizumab Treatment in Patients With Crohn's Disease; *Gastroenterology*; 155; 687-695