Moderately to Severely Active Ulcerative Colitis Biologic Pathway

NHS Bath and North East Somerset, Swindon and Wiltshire Integrated Care Board

NICE criteria to start treatment with a biologic: Patients with moderately to severely active UC, whose disease has responded inadequately to conventional therapy (including corticosteroids/mercaptopurine/azathioprine), or who cannot tolerate, or have medical contraindications for these.

1ST LINE TREATMENT OPTIONS (Anti-TNF)

Adalimumab biosimilar is the cheapest and preferred 1st line option. Vedolizumab can be used 1st line, however is the most expensive option and in practice it is anticipated that anti-TNFs will be 1st & 2nd line options unless otherwise inappropriate. NICE TA 329 recommends if more than one treatment is suitable the least expensive should be chosen.

TA329

Adalimumab (TNF inhibitor) BIOSIMILAR (prescribe by brand) S/C 160mg loading then 80mg week 2 then 40mg every 2 weeks. Review at week 12. **Blueteq required at initiation**

OR

TA329

Infliximab (TNF inhibitor) BIOSIMILAR (prescribe by brand) IV 5mg/kg at 0, 2, and 6 weeks then every 8 weeks or S/C 120mg every 2 weeks following IV loading. Review at week 12 to 14. Prescribe alongside immunosuppressant. **Blueteq required at initiation**

2ND LINE TREATMENT OPTIONS

NICE does not make any specific recommendations regarding sequential use of anti-TNFs for UC. The greatest evidence base for 2nd line anti-TNFs relates to adalimumab. Infliximab & golimumab as 2nd line treatments should be reserved for those patients who have had adalimumab as a 1st line anti-TNF ONLY. Ustekinumab or Vedolizumab may be a suitable alternative for patients who experience intolerance, primary or secondary failure to anti-TNF. Use of an Anti-TNF as a 3rd line biologic for patients who have experienced treatment failure or intolerance to a 2nd biologic is not recommended.

TA329

Alternative TNF inhibitor –
Adalimumab **OR** Infliximab BIOSIMILAR **OR** Golimumab (TNF inhibitor) < 80mg/kg 200 mg s/c wk 0, then 100 mg at wk 2, then 50 mg every 4 wks. >80mg/kg mg, 200mg wk 0 then 100 mg at wk 2, then 100 mg every 4 wks. Review at wk 12-14. **Blueteq at initiation and annual review for golimumab**

OR

TA633

Ustekinumab (IL12 & IL23 inhibitor) IV loading dose then 90mg s/c at wk 8 and every 12 wks.

≤55kg	260mg	2 vials of 130mg
> 55 kg to ≤ 85 kg	390mg	3 vials of 130mg
> 85 kg	520mg	4 vials of 130mg

Blueteq required at initiation and annual review

OR

TA342

Vedolizumab IV 300mg at week 0, 2 and 6 then every 8 weeks or S/C 108 mg once every 2 weeks as maintenance following IV loading Review at week 14 to 16
Blueteq required at initiation and annual review

3RD LINE TREATMENT OPTIONS

To be used when alternative options contraindicated, or patient has experienced inadequate/lost response or intolerance to 1st and 2nd line options. Mirikizumab is recommended by NICE only when treatment with a TNF inhibitor has failed, cannot be tolerated or is contraindicated.

TA925

Mirikizumab (IL23 inhibitor) IV loading 300mg at week 0, 4 and 8. Maintenance: 200mg S/C every 4 weeks. Review at week 12. If inadequate response IV induction may be extended to week 12, 16 and 20. **Blueteq required at initiation and annual review**

ORAL OPTIONS - Can be used PRE or POST biologics - choice will be driven by patient factors e.g. co-morbidities, age, pregnancy, alongside any previously tried therapies, including lost response or intolerance. Where a range of suitable options is available the least expensive should be chosen.

TA792

Filgotinib (JAK inhibitor) **Preferred 1st line oral option** 200mg once daily. Review at week 10, the induction dose may be extended for an additional 12 weeks (total 22 weeks). Not rec > age 75 yrs. NB. MHRA update **Blueteq required at initiation & annual review**

TA828

Ozanimod (S1P agonist) Reserved for when JAK unsuitable. For anti-TNF naive patients ozanimod should only be offered if infliximab unsuitable. 0.23mg once daily days 1-4 , then 0.46mg once daily days 5-7 , then 0.92mg once daily day 8 and thereafter. Review at 10 wks. **Blueteq required at initiation & annual review**

TA856

Upadacitinib (JAK inhibitor) 45mg once daily for 8 wks, induction dose may be extended for a further 8 wks if required. Review at 16 wks. Maintenance dose 15-30mg once daily. Age> 65 yrs 15mg once daily. NB. MHRA update **Blueteq required at initiation & annual review**

TA547

Tofacitinib (JAK inhibitor) 10mg twice daily for 8 wks, induction dose may be extended for a further 8 wks if required. Review at 16 wks. Maintenance dose 5mg twice daily. NB. See MHRA update **Blueteq required at initiation & annual review**

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. 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 should have the option to start treatment again.

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Crohn's Disease Biologic Pathway

NHS Bath and North East Somerset, Swindon and Wiltshire Integrated Care Board

NICE criteria to start treatment with a biologic: Patients with severe active CD, which has responded inadequately to conventional therapy (steroids, 5-ASA, immunosuppressant) or who cannot take/tolerate, or have medical contraindications for these are eligible for treatment with a biologic. Severe CD is defined as very poor general health & 1 or more symptoms e.g. weight loss, fever, severe abdominal pain and usually frequent (3–4 or more) diarrhoeal stools daily. This normally, but not exclusively, corresponds to a Crohn's Disease Activity Index (CDAI) score of 300 or more, or Harvey- Bradshaw score of 8 to 9 or more.

1ST LINE TREATMENT OPTIONS (Anti-TNF)

Adalimumab biosimilar is the cheapest and preferred 1st line option. Ustekinumab can be used 1st line, however is a more expensive option and in practice it is anticipated that anti-TNFs will be 1st line biologic options unless otherwise inappropriate. NICE TA 329 recommends if more than one treatment is suitable the least expensive should be chosen (taking into account drug administration costs, required dose and product price per dose).

TA187

Adalimumab (TNF inhibitor) BIOSIMILAR (prescribe by brand) S/C 160mg loading then 80mg week 2 then 40mg every 2 weeks. Review at week 12. **Blueteq required at initiation**

OR

TA187

Infliximab (TNF inhibitor) BIOSIMILAR (prescribe by brand) IV 5mg/kg at 0, 2, and 6 weeks then every 8 weeks or S/C 120mg every 2 weeks following IV loading. Prescribe alongside immunosuppressant. Review at week 12 to 14. **Blueteq required at initiation**

2ND LINE TREATMENT OPTIONS

NICE does not make any specific recommendations regarding sequential use of anti-TNFs. For patients who experience intolerance, secondary failure or primary failure with a 1st Anti-TNF, a 2nd approved Anti-TNF may be tried. Ustekinumab may be a suitable alternative for patients who experience intolerance, primary or secondary failure to anti-TNF.

TA187

Alternative TNF inhibitor –
Adalimumab **OR** Infliximab BIOSIMILAR **OR**
Blueteq required at initiation

OR

Ustekinumab (IL12 & IL23 inhibitor) IV loading dose then 90mg s/c at week 8 and every 12 weeks. TA456

≤55kg	260mg	2 vials of 130mg
> 55 kg to ≤ 85 kg	390mg	3 vials of 130mg
> 85 kg	520mg	4 vials of 130mg

Blueteq required at initiation and annual review

3RD LINE TREATMENT OPTION

To be used when alternative options contraindicated, or patient has experienced inadequate/lost response or intolerance to 1st and 2nd line options. Use of an Anti-TNF as a 3rd line biologic for patients who have experienced treatment failure or intolerance to a 2nd biologic is not recommended.

TA905

Upadacitinib (JAK inhibitor) **Oral option** 45mg once daily for 12 wks. Review at 12 wks. Maintenance dose 15-30mg once daily. Age> 65 yrs 15mg once daily. NB. **MHRA update** **Blueteq required at initiation & annual review**

OR

TA352

Vedolizumab IV 300mg at week 0, 2 and 6 then every 8 weeks. or S/C 108 mg once every 2 weeks as maintenance following IV loading Review at wk 14 to 16. **Blueteq required at initiation and annual review**

OR

TA888

Risankizumab (IL23 Inhibitor) 600mg IV week 0, 4 and 8 followed by 360mg SC at week 12 and every 8 weeks thereafter. Review at week 12. **Blueteq required at initiation and annual review**

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. 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 should have the option to start treatment again.

Use of Biologics Post Surgery - Routine use of biologics as post surgery prophylaxis in CD is not recommended (insufficient evidence). In patients at high risk of recurrence (e.g. more than one resection, or penetrating or fistulising disease), prophylaxis with thiopurine should be considered where appropriate. An approved biologic may be considered in these high risk patients upon recurrence, or if thiopurine treatment is not tolerated

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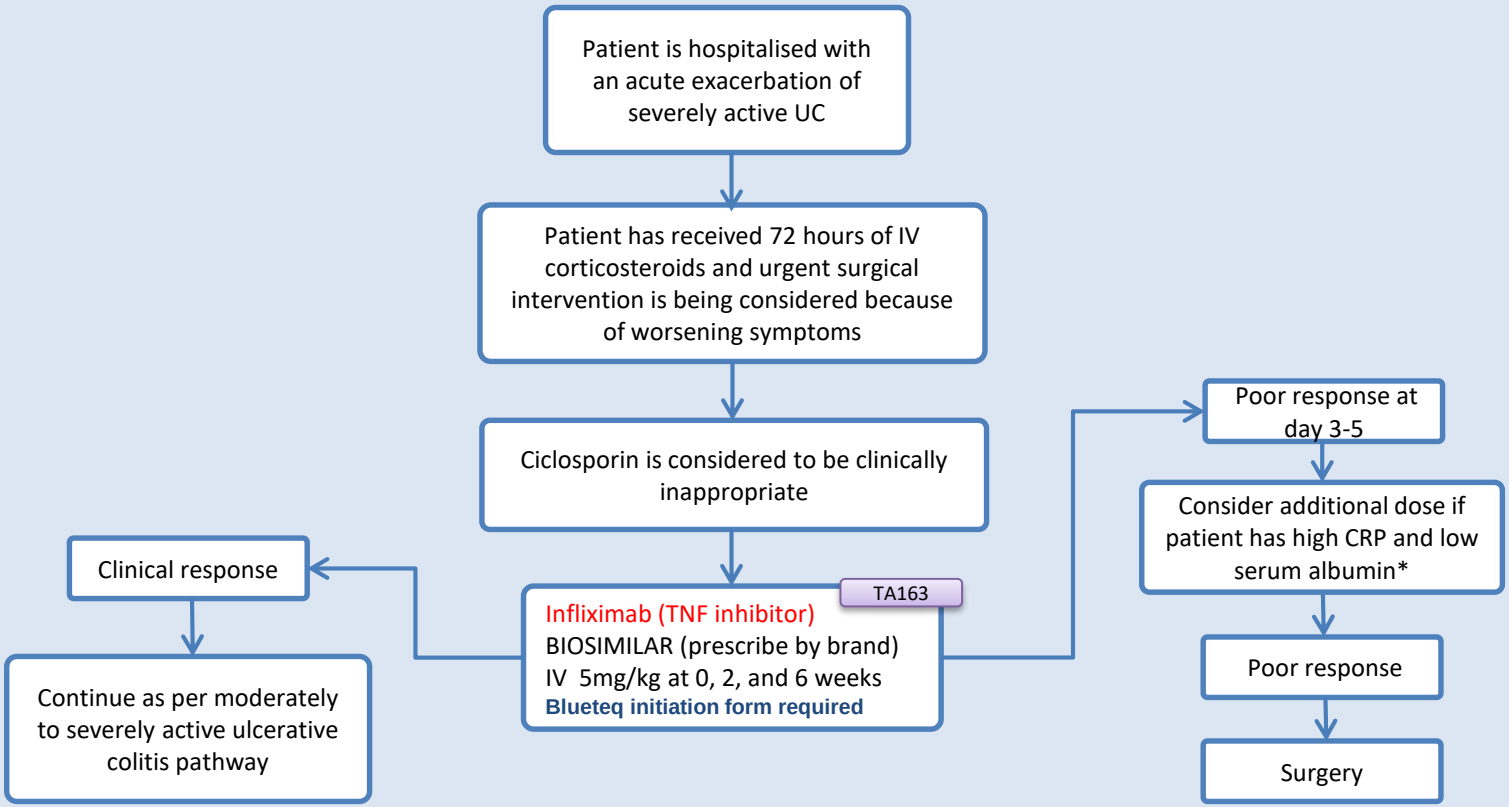
Jan 2024

Acute Exacerbation of Severely Active Ulcerative Colitis Biologic Pathway

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

NICE criteria to start treatment with a biologic: An acute exacerbation of severely active ulcerative colitis requires hospitalisation and urgent consideration for surgery and is defined by the following symptoms (Truelove & Witts) • Bowel movements > 6 plus at least one of the features of systemic upset (marked with *) • Blood in stools – visible blood • *Pyrexia (temperature greater than 37.8C) • *Pulse > 90 bpm • *Anaemia < 10g/100ml • *ESR > 30 mm/hr.



Acceleration & Continuation

*Patients who are not responding sufficiently to a 5mg/kg dose of infliximab **after 3–5 days can be treated with an early repeat infusion at week 1**, particularly in those with a low albumin (below 35g/L). Some clinicians use an initial 10mg/kg dose as salvage therapy but there is as yet insufficient data to demonstrate the value of this in comparison to a 5mg/kg dose. Accelerated dosing should only be given after colorectal surgical review, with agreement that colectomy is not required imminently. BSG IBD Guidelines 2019

Continue as per moderately to severely active ulcerative colitis criteria only if there is evidence of response as determined by clinical symptoms, biological markers and investigation. Review post induction at weeks 12-14.

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Proactive IBD TDM – Post-induction /maintenance review of anti-TNF therapy

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

Therapeutic Drug Monitoring (TDM) is a helpful tool for optimising the use and effectiveness of TNF inhibitors and can identify patients in whom it may be possible to reduce or even withdraw anti-TNF biologic treatment without adversely affecting clinical outcomes. Results should be interpreted alongside other relevant clinical findings and assessments to aid clinical decision making, evidence for clinical management based on TDM results alone has not been established. Please note that in the presence of therapeutic drug levels, free anti-drug antibody cannot be detected and therefore its measurement is not indicated.

SFT use only
TDM services via
Viapath Lab- London
www.viapath.co.uk/

Routine TDM indicated in asymptomatic patient
-End of induction (usually wk 12-14)
-Annual review of maintenance therapy
-After dose adjustment (pre 4th dose)

Anti-TNF drug trough levels

Supra-therapeutic drug levels
undefined. Anecdotally:
Infliximab: ≥12 µg/mL
Adalimumab: ≥12 µg/mL

If asymptomatic and clinically stable consider de-escalating anti-TNF
- Consider reducing dose
- Consider reducing frequency

Therapeutic drug levels
Infliximab: ≥2.5 µg/mL
(Intermediate= 1.2-2.4 µg/mL)
Adalimumab: ≥5 µg/mL

Continue anti-TNF
- If maintenance, no change to dose/frequency
- If dose escalated, aim to reduce
- If in remission consider stopping anti-TNF, maintain immunosuppressant

Sub therapeutic drug levels
Infliximab: <1.2 µg/mL
Adalimumab: <5 µg/mL

Anti-drug antibodies

Detected >50 ng/mL

Stop anti-TNF
-Switch anti-TNF
-Switch to non anti-TNF
-Surgery

Detected 10-50 ng/mL

Undetected or <10 ng/mL

Escalate anti-TNF
-Increase dose as below
-Increase frequency as below
-Add immunosuppressant/ check compliance

If asymptomatic and in clinical remission consider stopping anti-TNF, and maintain immunosuppressant

Trial Dose Escalation:
For patients who have responded to induction and maintenance treatment regime but then lost response, the following temporary dose escalations may be indicated in an attempt to recapture response:

Drug	Standard dosing	Commissioned dose escalation
Adalimumab	40mg every 2 weeks	40mg every week or 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks or 10mg/kg every 8 weeks or 10mg/kg every 6 weeks (off licence) No dose escalation for S/C
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (off licence) (On MDT agreement) Blueteq dose escalation form required
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On MDT agreement) Blueteq dose escalation form required. No dose escalation for S/C

NB. Dose escalations not listed above are not routinely commissioned and therefore require an IFR.

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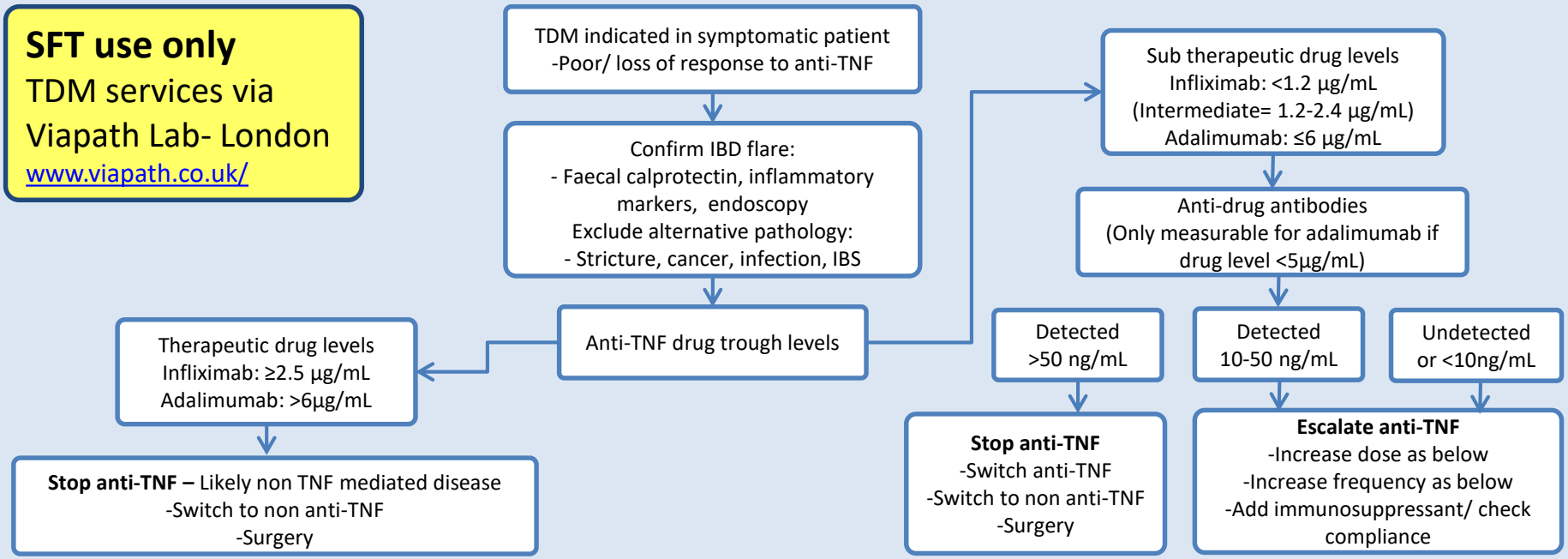
Reactive IBD TDM - Poor response or loss of response to anti-TNF therapy

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

Therapeutic Drug Monitoring (TDM) is a helpful tool for optimising the use and effectiveness of TNF inhibitors and can identify patients in whom dose escalation may benefit clinical outcomes and help recapture response to treatment. Results should be interpreted alongside other relevant clinical findings and assessments to aid clinical decision making, evidence for clinical management based on TDM results alone has not been established.
Please note that in the presence of therapeutic drug levels, free anti-drug antibody cannot be detected and therefore its measurement is not indicated.

SFT use only
TDM services via
Viapath Lab- London
www.viapath.co.uk/



Trial Dose Escalation:
For patients who have responded to induction and maintenance treatment regime but then lost response, the following temporary dose escalations may be indicated in an attempt to recapture response:

Drug	Standard dosing	Commissioned dose escalation
Adalimumab	40mg every 2 weeks	40mg every week or 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks or 10mg/kg every 8 weeks or 10mg/kg every 6 weeks (off licence) No dose escalation for S/C
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (off licence) (On MDT agreement) Blueteq dose escalation form required
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On MDT agreement) Blueteq dose escalation form required. No dose escalation for S/C

NB. Dose escalations not listed above are not routinely commissioned and therefore require an IFR.

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Proactive IBD TDM – Post-induction /maintenance review of anti-TNF therapy

NHS Bath and North East Somerset, Swindon and Wiltshire Integrated Care Board

Therapeutic Drug Monitoring (TDM) is a helpful tool for optimising the use and effectiveness of TNF inhibitors and can identify patients in whom it may be possible to reduce or even withdraw anti-TNF biologic treatment without adversely affecting clinical outcomes. Results should be interpreted alongside other relevant clinical findings and assessments to aid clinical decision making, evidence for clinical management based on TDM results alone has not been established.

RUH/GWH use only
TDM services via Exeter Lab*(published July21)
www.exeterlaboratory.com/

Routine TDM indicated in asymptomatic patient
-End of induction (usually wk 12-14)
-Annual review of maintenance therapy
-After dose adjustment (pre 4th dose)

Anti-TNF drug trough levels

Sub therapeutic drug levels
Infliximab: <7 mg/L*
Adalimumab: <12 mg/L*

Anti-drug antibodies

Detected >58 Au/mL

Detected 10-57 Au/mL

Undetected or <10 Au/mL

Stop anti-TNF
-Switch anti-TNF
-Switch to non anti-TNF
-Surgery

Escalate anti-TNF
-Increase dose as below
-Increase frequency as below
-Add immunosuppressant/ check compliance

If asymptomatic and in clinical remission consider stopping anti-TNF, and maintain immunosuppressant

Therapeutic drug levels
Infliximab: ≥7 mg/L*
Adalimumab: ≥12 mg/L*

Continue anti-TNF
- If maintenance, no change to dose/frequency
- If dose escalated, aim to reduce
- If in remission consider stopping anti-TNF, maintain immunosuppressant

Supra-therapeutic drug levels undefined. No additional clinical benefit observed for:
Infliximab: >7 mg/L*
Adalimumab: >12 mg/L *

If asymptomatic and clinically stable consider de-escalating anti-TNF
- Consider reducing dose
- Consider reducing frequency

Trial Dose Escalation:
For patients who have responded to induction and maintenance treatment regime but then lost response, the following temporary dose escalations may be indicated in an attempt to recapture response:

Drug	Standard dosing	Commissioned dose escalation
Adalimumab	40mg every 2 weeks	40mg every week or 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks or 10mg/kg every 8 weeks or 10mg/kg every 6 weeks (off licence) No dose escalation for S/C
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (off licence) (On MDT agreement) Blueteq dose escalation form required
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On MDT agreement) Blueteq dose escalation form required. No dose escalation for S/C

NB. Dose escalations not listed above are not routinely commissioned and therefore require an IFR.

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Reactive IBD TDM - Poor response or loss of response to anti-TNF therapy

NHS Bath and North East Somerset, Swindon and Wiltshire Integrated Care Board

Therapeutic Drug Monitoring (TDM) is a helpful tool for optimising the use and effectiveness of TNF inhibitors and can identify patients in whom dose escalation may benefit clinical outcomes and help recapture response to treatment. Results should be interpreted alongside other relevant clinical findings and assessments to aid clinical decision making, evidence for clinical management based on TDM results alone has not been established.

RUH/GWH use only
TDM services via Exeter Lab *(published July21)
www.exeterlaboratory.com/

TDM indicated in symptomatic patient
- Poor/ loss of response to anti-TNF

Confirm IBD flare:
- Faecal calprotectin, inflammatory markers, endoscopy
Exclude alternative pathology:
- Stricture, cancer, infection, IBS

Anti-TNF drug trough levels

Therapeutic drug levels
Infliximab: ≥7 mg/L*
Adalimumab: ≥ 12mg/L*

Stop anti-TNF – Likely non TNF mediated disease
-Switch to non anti-TNF
-Surgery

Sub therapeutic drug levels
Infliximab: <7 mg/L*
Adalimumab: <12 mg/L *

Anti-drug antibodies

Detected >58 Au/mL

Stop anti-TNF
-Switch anti-TNF
-Switch to non anti-TNF
-Surgery

Detected 10-57 Au/mL

Undetected or <10 Au/mL

Escalate anti-TNF
-Increase dose as below
-Increase frequency as below
-Add immunosuppressant/ check compliance

Trial Dose Escalation:
For patients who have responded to induction and maintenance treatment regime but then lost response, the following temporary dose escalations may be indicated in an attempt to recapture response:

Drug	Standard dosing	Commissioned dose escalation
Adalimumab	40mg every 2 weeks	40mg every week or 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks or 10mg/kg every 8 weeks or 10mg/kg every 6 weeks (off licence) No dose escalation for S/C
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (off licence) (On MDT agreement) Blueteq dose escalation form required
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On MDT agreement) Blueteq dose escalation form required. No dose escalation for S/C

NB. Dose escalations not listed above are not routinely commissioned and therefore require an IFR.

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