

Moderately to Severely Active Ulcerative Colitis Biologic Pathway

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 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).

TA329

Adalimumab (TNF inhibitor) BIOSIMILAR (prescribe by brand) S/C 80mg loading then 40mg every 2 weeks. (OR 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.
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 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 may be a suitable alternative for patients who experience intolerance, primary or secondary failure to anti-TNF.

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 required at initiation only for adalimumab and initiation and annual review for golimumab

OR

TA633

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

≤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.

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

ORAL OPTION - Can be used PRE or POST biologics due to an inadequate /lost response, or intolerance to either conventional therapy or a biologic agent

Tofacitinib (JAK inhibitor)

TA547

10mg twice daily for 8 wks then 5mg twice daily. If adequate benefit not achieved by wk 8, the induction dose 10mg twice daily can be extended for an additional 8 wks (16 wks total) Review at 16 weeks.
NB. See [MHRA update](#) **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.

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. 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 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).

Adalimumab (TNF inhibitor) BIOSIMILAR (TA187)
(prescribe by brand) S/C 80mg loading then 40mg every 2 weeks. (OR 160mg loading then 80mg week 2 then 40mg every 2 weeks).
Review at week 12
Blueteq required at initiation

OR

Infliximab (TNF inhibitor) BIOSIMILAR (TA187)
(prescribe by brand) IV 5mg/kg at 0, 2, and 6 weeks then every 8 weeks.
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.

Alternative TNF inhibitor – Adalimumab OR Infliximab BIOSIMILAR OR (TA187)
Blueteq required at initiation

OR

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

≤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.

Vedolizumab IV 300mg at week 0, 2 and 6 then every 8 weeks. or S/C 108 mg (TA352)
once every 2 weeks as maintenance following IV loading Review at week 14 to 16
Blueteq required at initiation and annual review

Continuation of Biologic Treatment

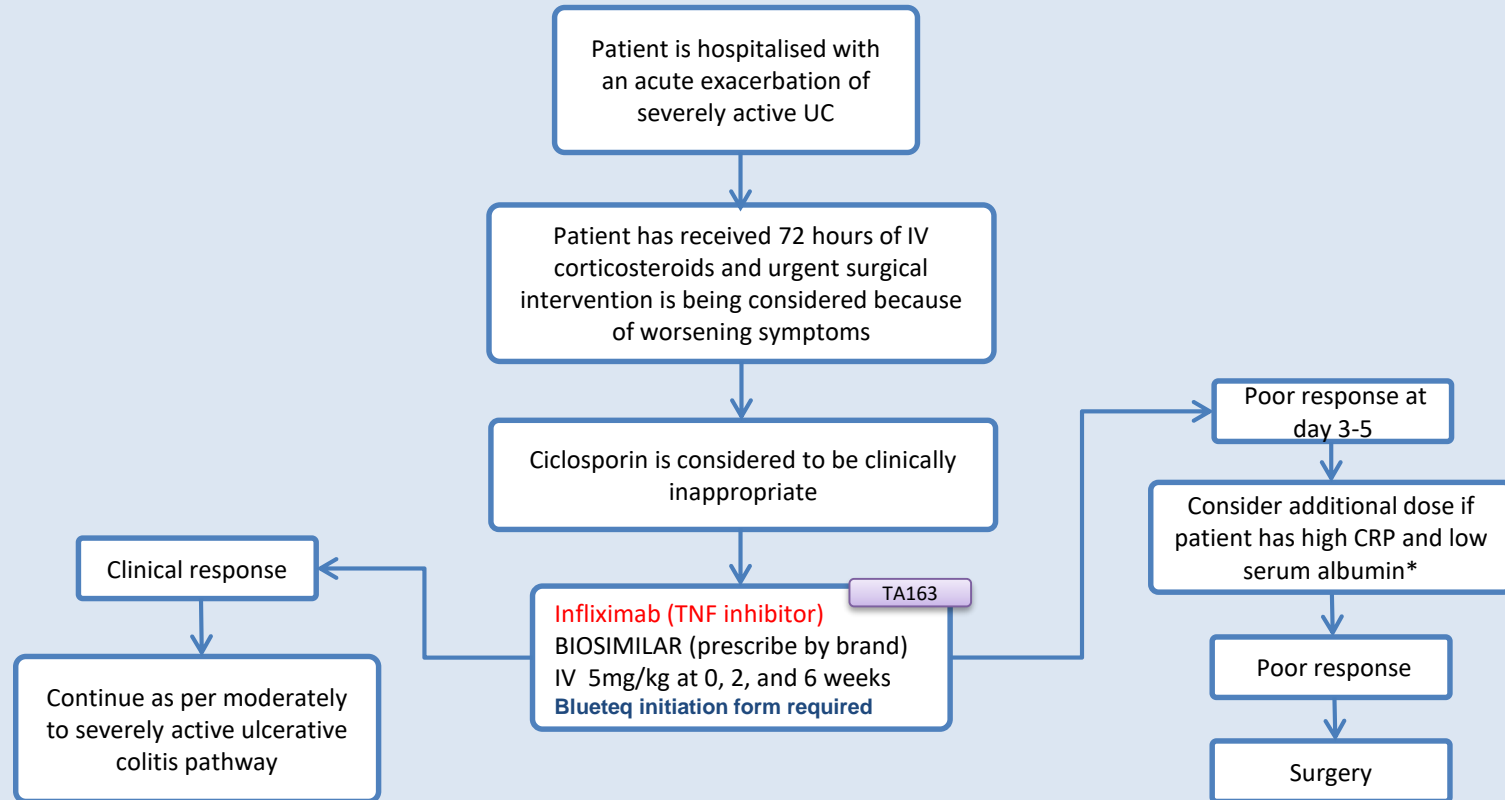
Treat for 12 months or until treatment failure (including the need for surgery), whichever is shorter, then review and discuss the risks and benefits of continued treatment. Continue only if there is evidence of response as determined by clinical symptoms, biological markers and investigation, including 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

Acute Exacerbation of Severely Active Ulcerative Colitis Biologic Pathway

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

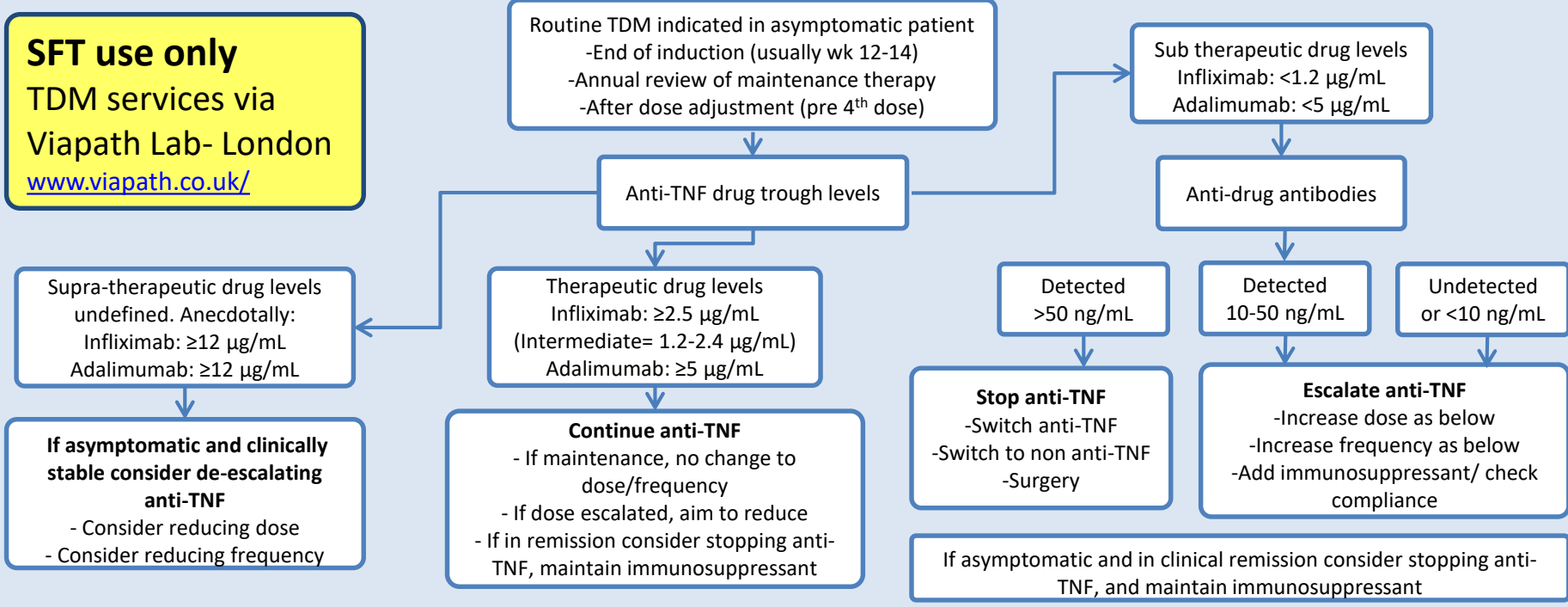
*Patients who are not responding sufficiently to a 5mg/kg dose of infliximab **after 3–5 days can be treated with an early repeat infusion at week 1**, particularly in those with a low albumin (below 35g/L). Some clinicians use an initial 10mg/kg dose as salvage therapy but there is as yet insufficient 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.

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

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/



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:

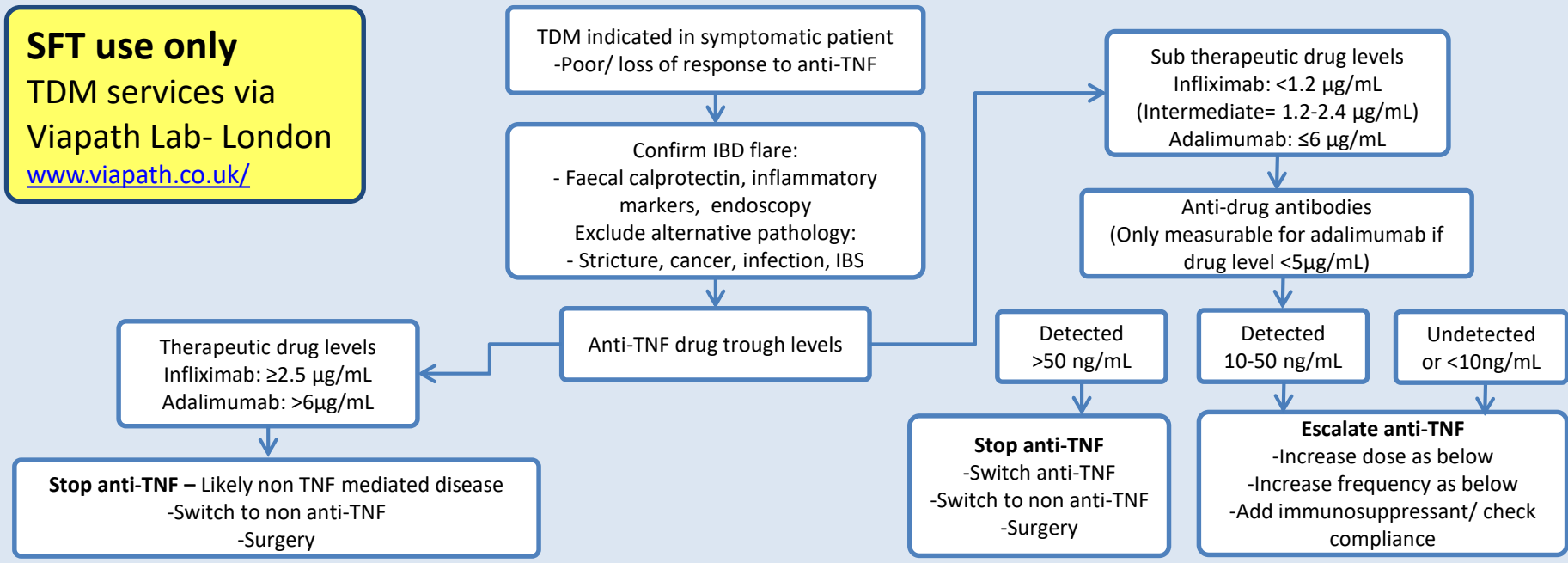
Drug	Standard dosing	Commissioned dose escalation
Adalimumab	40mg every 2 weeks	40mg every week <u>or</u> 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks <u>or</u> 10mg/kg every 8 weeks (off licence)
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (On tertiary centre advice only) Crohn's only as per BSW Policy Blueteq reqd dose escalation form
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On tertiary centre advice only) No dose escalation for S/C vedolizumab. Blueteq reqd dose escalation form

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

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

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.



Trial Dose Escalation:

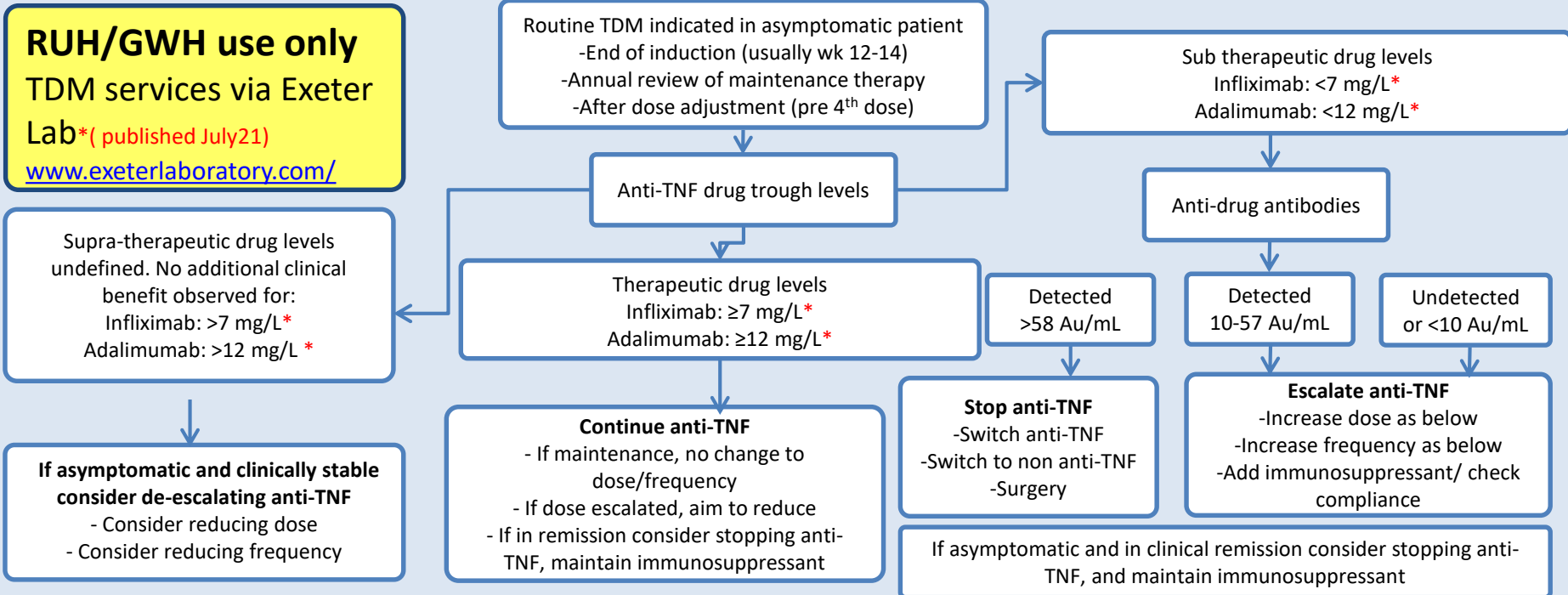
For patients who have responded to induction and maintenance treatment regime but then lost response, the following temporary dose escalations may be indicated in an attempt to recapture response:

Drug	Standard dosing	Commissioned dose escalation
Adalimumab	40mg every 2 weeks	40mg every week <u>or</u> 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks <u>or</u> 10mg/kg every 8 weeks (off licence)
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (On tertiary centre advice only) Crohn's only see BSW Policy Blueteq reqd dose escalation form
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On tertiary centre advice only) No dose escalation for S/C vedolizumab Blueteq reqd dose escalation form

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

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

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.



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 <u>or</u> 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks <u>or</u> 10mg/kg every 8 weeks (off license)
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (On tertiary centre advice only) Crohn's only see BSW Policy Blueteq reqd dose escalation
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On tertiary centre advice only) No dose escalation for S/C vedolizumab Blueteq reqd dose escalation

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

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

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/

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

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

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

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

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 <u>or</u> 80mg every 2 weeks
Infliximab	5mg/kg every 8 weeks	5mg/kg every 6 weeks <u>or</u> 10mg/kg every 8 weeks (off license)
Ustekinumab	90mg every 8 or 12 weeks	90mg every 6 weeks (On tertiary centre advice only) Crohn's only see BSW Policy Blueteq reqd dose escalation
Vedolizumab	300mg IV every 8 weeks	300mg IV every 4 weeks (On tertiary centre advice only) No dose escalation for S/C vedolizumab Blueteq reqd dose escalation

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