North Central London
Joint Formulary Committee

Adult (age≥18 years) high-cost drug pathway for moderately to severely active ulcerative colitis

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Document control

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April 2019	1.0	New guideline

Document management

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Note 1: Moderately to severely active UC
- Corresponds to a Mayo score of 6-12

If alternative disease severity scoring system used, evidence of correlation with disease severity and response criteria to be provided.

Note 2: Conventional immunosuppressive therapy
Usual Adult maintenance treatment dose ranges:
- Azathioprine - 2 mg/kg/day to 2.5 mg/kg/day.
- Mercaptopurine - 0.75 mg/kg/day to 1.5 mg/kg/day

Note 3: Choice and Less expensive drug
When considering both drug and administration costs, the treatment cost hierarchy is expected to be:
- SC biosimilar (lowest cost)
- IV biosimilar
- SC originator
- IV originator (highest cost)

Note 4: Response definitions
Complete Mayo:
- decrease in full Mayo score from baseline by ≥3 points and ≥30%, AND
- decrease in rectal bleeding sub-score from baseline by ≥1 point, OR absolute rectal bleeding sub-score of 0 or 1.

Partial Mayo (where further endoscopy not considered necessary/appropriate):
- decrease in partial Mayo score from baseline of ≥2 points and ≥25% AND
- decrease in rectal bleeding sub-score from baseline of ≥1 point OR absolute rectal bleeding sub-score of 0 or 1.

If alternative disease severity scoring system used, evidence of correlation with disease severity and response criteria to be provided.

Note 5: Disease reassessment
At 12 months after the start of treatment, people should have their disease reassessed to determine whether ongoing treatment is still clinically appropriate. Treatment should only be continued if there is clear evidence of ongoing adequate response (Note 4) and active disease. This should be determined by:
- Clinical symptoms and
- Biological markers and
- Investigation, including endoscopy if necessary.

Clinical Remission:
- complete or partial Mayo score of ≤2 points and no individual subscore >1

Note 6: Trial Dose Escalation
For patients who have responded to induction and maintenance treatment regime of a TNF inhibitor but then lost response an attempt to recapture response with a temporary period of increased dose / shortened interval between doses may be made†:
- 3 doses of infliximab‡ dose of 10mg/kg 8 weekly and then back to 5mg/kg; or
- 3 doses of infliximab‡ 5mg/kg given 4-6 weekly and then back to 8 weekly; or
- Up to 12 weeks on weekly adalimumab 40mg then back to every other week.

Vedolizumab dose escalation is not routinely commissioned (submit IFR)§

Note 7: Anti-TNF drug and antibody levels

If response to treatment not seen, only partial response or loss of response; consider anti-TNF drug and antibody levels to guide further biologic therapy. See Appendix 1 for guidance on interpreting anti TNF drug and antibody levels

Does the adult have moderately to severely active UC (See note 1)?

Yes

Has there been lack/loss of response, intolerance or contraindication to optimised conventional therapy (Note 2) taken for an adequate period, including;
- corticosteroids and
- azathioprine/6-mercaptopurine

Yes

- **Adalimumab biosimilar or**
- **Infliximab biosimilar or**
- **Golimumab**

If more than 1 suitable, treatment the least expensive should be chosen (see Note 3). **Provide detail of individual patient factors if more expensive treatment chosen.**

Yes

Vedolizumab
- Inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF inhibitor.
- May be used 1st line where TNF inhibitor is not preferred

Is the adult hospitalised with an acute exacerbation of severely active UC (Mayo score >8)?

Yes

Has there been lack/loss of response, intolerance or contraindication to optimised conventional therapy (Note 2) taken for an adequate period, including;
- 5-aminosalicylates and
- corticosteroids (including IV for 72 hours) and/or
- azathioprine/6-mercaptopurine

Yes

Either*: Infliximab biosimilar (3 dose induction course). Continued treatment indicated when criteria for moderately to severely active UC fulfilled after induction. The indication course may be administered over 4 weeks for patients who experience an inadequate response to the first-dose‡.
Or ciclosporin

Response (Note 4) within 12 weeks (3 doses) infliximab, 12 weeks adalimumab, 14 weeks (4 doses) golimumab or 14 weeks‡ vedolizumab treatment?

No

Consider switch to alternative TNF inhibitor or vedolizumab if no response or intolerance to initial biologic.

GO TO BOX 1

Yes

BOX 1

Give as a planned course of treatment until treatment failure (including the need for surgery), or until 12 months after the start of treatment, whichever is shorter.

Continue maintenance dose.

At any point before 12 months of treatment has passed, has treatment failed (including the need for surgery)?

No

Consider switch to alternative TNF inhibitor or vedolizumab

GO TO BOX 1

Yes

BOX 2

If adalimumab/infliximab‡ consider dose escalation or interval reduction to recapture response (Note 6). Where available consider anti-TNF drug and antibody levels (Note 7).

Response to escalated dose?

Yes

De-escalate to standard dose after period shown in Note 6†

No

Patients whose disease has relapsed after trial de-escalation may continue escalated dose†

Reassess patient after 6 months and then at least every 12 months to determine if ongoing escalated dose is still clinically appropriate (see note 5)†.

Trial of de-escalation in patients without active disease in stable clinical remission†

At 12 months after start of treatment reassess the disease (Note 5).
Where there is an ongoing adequate response is there evidence of ongoing active disease?

Yes

Discuss the risks and benefits of continued treatment.

Maintain treatment.

Reassess patient at least every 12 months to determine if ongoing treatment is still clinically appropriate.

If loss of response at any time, consider:
- Trial dose escalation of adalimumab/infliximab to recapture response (Go to Box 2) (Where available consider anti-TNF drug and antibody levels (Note 7))
- Consider switch to alternative TNF inhibitor or vedolizumab (Go to box 1)

(See note 3)

No

Discuss the risks & benefits of continued treatment.

Trial withdrawal of patients in stable clinical remission.

If intolerance/contraindication to maintenance conventional therapy & only maintenance treatment option is TNF inhibitor/vedolizumab a trial withdrawal does not need to be attempted

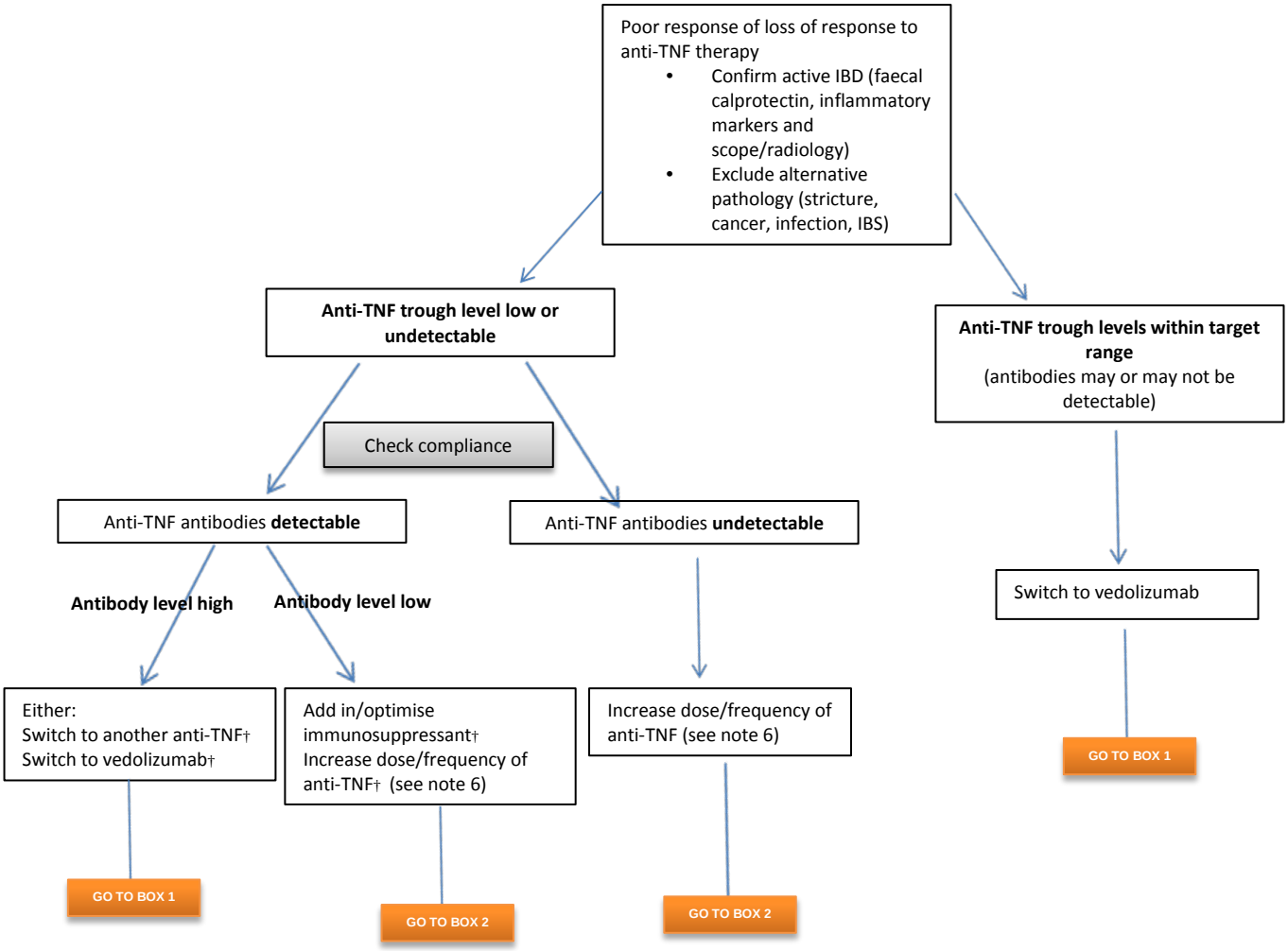
Patients without active disease in stable clinical remission should have trial withdrawal

Patients whose disease has relapsed after treatment is stopped may restart treatment **(go to box 1)**

Patients whose disease has relapsed on previous trial withdrawal may continue maintenance treatment without further trial withdrawal even if in stable clinical remission

† In the absence of robust published evidence, a pragmatic view was taken by the IBD working group
‡ An unlicensed use/dose of the medicine. Clinically approved by NCL JFC and/or IBD working group.
§ Licensed however not included within economic assessment of NICE TA342 therefore not routinely commissioned
* Deviation from NICE TA. Clinically approved by NCL JFC and IBD working group.

Appendix 1: Poor response or loss of response to anti-TNF therapy



Appendix 2: Tofacitinib use in Ulcerative Colitis

Tofacitinib will be considered as a treatment choice for patients who have failed on (at least one) anti-TNF therapy and/or Vedolizumab, in line with NICE TA547. Tofacitinib will only be considered as first line treatment of ulcerative colitis where the most cost effective choices (anti-TNF's) are contraindicated, or where the patient has a treatment-limiting needle phobia, resulting in an oral therapy being the most appropriate choice.

The place in therapy for tofacitinib will be reviewed in 6 months from the date of publication of this document, with the view to incorporate into the above clinical pathway.

Appendix 3: Clinical trials

An investigative medicinal product (IMP) will be considered part of the commissioned pathway, and subsequently reimbursed by NCL commissioners if all the following criteria are met:

- IMP has a positive NICE Technology Appraisal (NHS funding will commence 90 days after TA publication)
- Patient met NICE criteria when initiating IMP

Appendix 4: Review and Stop updates on Blueteq

Blueteq will be used for funding requests, as well as to record/capture patients that have stopped drug treatment as a result of clinical review and/or remission

Acknowledgements

This pathway is based on a version developed by Hertfordshire CCG and has been updated, with permission, for use within North Central London.