North Central London
Joint Formulary Committee

Adult (age≥18 years) high-cost drug pathway for active Crohn's disease

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Document control

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Document management

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Note 1: Severe Active Crohn's Disease

- Severe active Crohn's disease is defined as very poor general health and one or more symptoms such as weight loss, fever, severe abdominal pain and usually frequent diarrhoeal stools (≥3 daily).
- People with Severe Active Crohn's Disease may or may not develop new fistulae or have extra-intestinal manifestation of the disease.
- This clinical definition normally, but not exclusively, corresponds to:
  - o Crohn's disease activity index (CDAI) score ≥300
  - o Harvey-Bradshaw (HBI) score of ≥ 8-9.

Where HBI/CDAI is not a relevant indicator of disease severity alternative objective measures (e.g. colonoscopy, stoma output, CRP, ESR, faecal calprotectin) to be provided that demonstrate severe active Crohn's Disease.

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
- Methotrexate - 15 mg to 25 mg once weekly.

Note 3: 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

Severe Active Crohn's Disease

- Response - decrease in HBI ≥3 points or CDAI ≥70 points
- No response - decrease in HBI ≤2
- Where HBI is not a relevant indicator of disease severity the 'on treatment' alternative objective measures will be used (compared to baseline) to demonstrate response.

Active fistulising Crohn's

- Response - ≥50% improvement in fistula drainage
- No response - <50% improvement in fistula drainage

'On treatment' HBI scores or alternative objective measures can also be used (compared to baseline) to demonstrate response.
Patients prescribed vedolizumab who have not shown a response may benefit from a dose at week 10 (see SPC)

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 and active disease. This should be determined by:

- Clinical symptoms and
- Biological markers e.g. CRP, ESR and
- Investigation, including endoscopy if necessary.

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.
- Up to 16 weeks of 8 weekly ustekinumab and then back to 12 weekly

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 ant TNF drug and antibody levels.
The decision to use drug and antibody levels will be a clinical decision based on individual patient factors and is not required routinely.

Does the adult have Severe Active Crohn's disease (See Note1)?

Yes

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

- Immunosuppressive and/or
- Corticosteroid treatments?

Yes

- **Adalimumab biosimilar (preferred first-line)**
- **Infliximab biosimilar (preferred first-line)**
- **Ustekinumab**

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

Does the adult have active **fistulising** Crohn's disease

Yes

Has there been lack/loss of response, intolerance or contraindication to conventional therapy (Note 2) taken for an adequate period, including;

- Antibiotics and
- Drainage and
- Immunosuppressive treatments?

Yes

Ustekinumab or vedolizumab if TNF inhibitor contraindicated
If more than 1 treatment is suitable, the least expensive should be chosen (see Note 3).

Infliximab biosimilar
If patients are not able to receive infliximab (due tolerability or practicality concerns), adalimumab‡ is indicated. Ustekinumab‡ is indicated where both anti-TNFs are contraindicated or have previously failed.

Response (Note 4) within 12 weeks infliximab, 12 weeks adalimumab, 16 weeks for ustekinumab or 14 weeks vedolizumab (severe active Crohn's disease only) treatment?

No

Consider switch to alternative TNF inhibitor, ustekinumab or vedolizumab if no response or intolerance to initial TNF inhibitor. If more than 1 treatment is suitable, the least expensive should be chosen (see Note 3).

For vedolizumab, an additional dose can be considered if no response at week 10

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.

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

No

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 current TNF inhibitor or ustekinumab to recapture response (Go to Box 2)
- switch to alternative TNF inhibitor, ustekinumab 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 immunosuppressive treatment & only maintenance treatment option is biologic agent, a trial withdrawal does not need to be attempted

Patients without active disease in stable 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

Yes

Consider switch to alternative TNF inhibitor, ustekinumab or vedolizumab
If more than 1 treatment is suitable, the least expensive should be chosen (see Note 3).

GO TO BOX 1

BOX 2

If TNF inhibitor or ustekinumab consider dose escalation or interval reduction (Note 6).
Where available consider anti-TNF drug and antibody levels (Note 7).

No

Response to escalated dose?

Yes

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

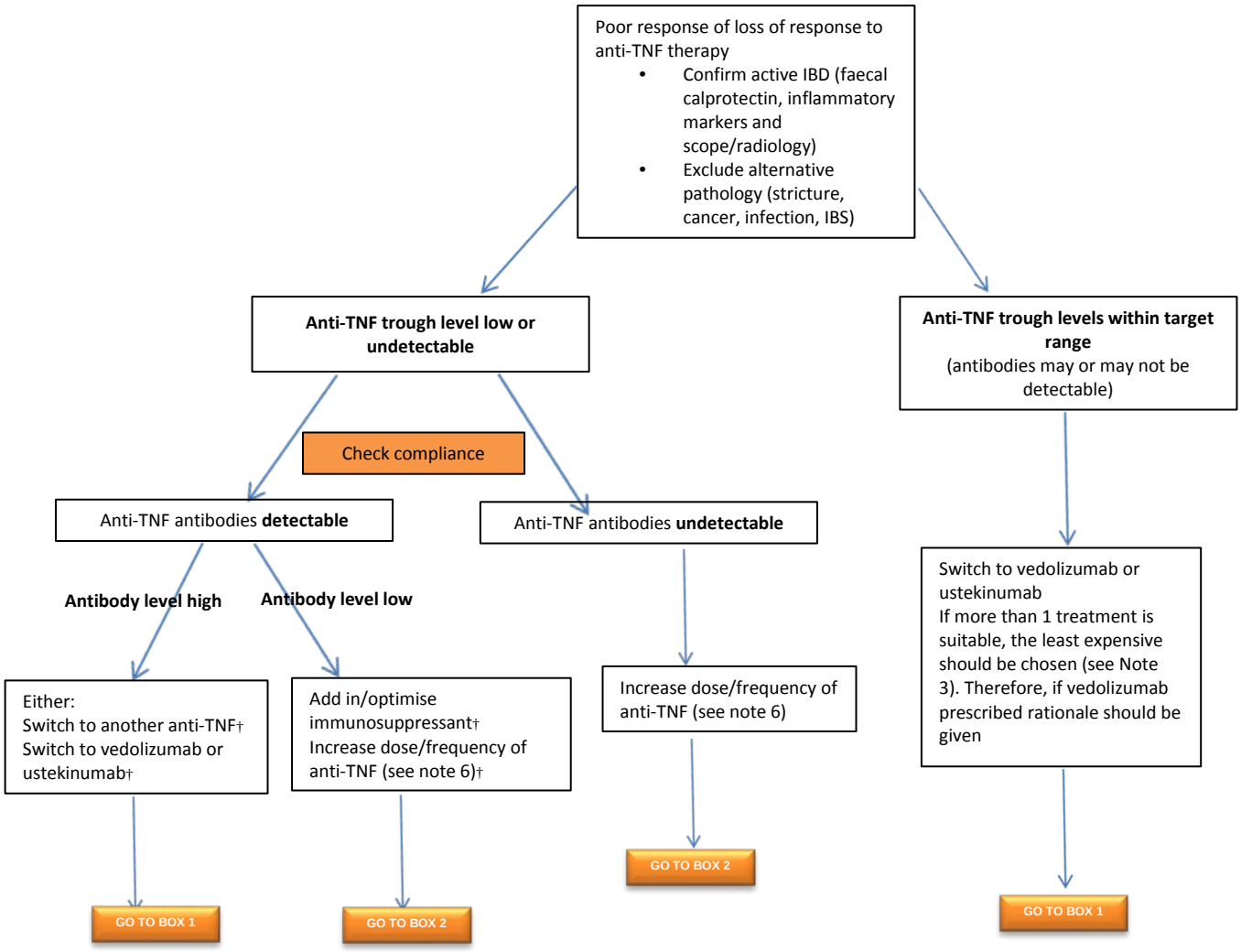
Patients whose disease has relapsed after trial de-escalation may continue escalated dose†

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)†. Consider anti-TNF drug and antibody levels to guide de-escalation (Note 7)

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

† In the absence of robust published evidence, a pragmatic view was taken by the authors of this guideline
‡ An unlicensed use/dose of the medicine,. Clinically approved by NCL JFC.
§ Licensed use/dose however not included within the NICE TA therefore not routinely commissioned

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



Appendix 2: Clinical trials

An investigative medicinal product (IMP) will be considered part of the commissioned pathway, and subsequently post-trail access will be reimbursed by 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
- The IMP may displace any single therapy routinely commissioned.

Appendix 3: 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 the version developed by Hertfordshire CCG and has been updated, with permission, for use within North Central London.