High cost drug treatment pathway

INFLAMMATORY BOWEL DISEASE in adults

GUIDELINE

Ulcerative colitis

Adult with **moderately to severely active ulcerative colitis** (defined normally, but not exclusively, by Truelove and Witts criteria). Other criteria, such as adapted Mayo score, may also be used.

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Inadequate response, intolerance or contraindication to optimised conventional therapy including corticosteroids and azathioprine/6-mercaptopurine

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When more than one treatment is suitable, the least expensive should be chosen

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Adalimumab, **infliximab**, **golimumab** (TA329)

Tofacitinib (TA547), **filgotinib** (TA792), **upadacitinib** (TA856)

Option if TNF α INHIBITOR therapy has failed, cannot be tolerated or is unsuitable: **ustekinumab** (TA633)

Option if infliximab is not suitable or a biological treatment cannot be tolerated or is not working well enough: **ozanimod** (TA828)

Vedolizumab (TA342)

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Adequate clinical response

Yes ↓

Continue treatment for 12 months or until treatment failure (whichever is shorter). Treatment should only continue if there is clear evidence of response as determined by clinical symptoms, biological markers and investigation, including endoscopy if necessary. People should be reassessed at least every 12 months. A trial withdrawal should be considered for patients in stable clinical remission at 12 months.

No ↓

Depending on clinical grounds consider an alternative therapy or surgery

Ulcerative Colitis[1]

Post-surgery prophylaxis
High cost drugs should not be offered to maintain remission after surgery.

Sequential use
NICE does not make any recommendations on sequential use of biologics treatment for ulcerative colitis, although it recommends ustekinumab if TNF α INHIBITOR therapy has failed and ozanimod if infliximab is not suitable or a biological treatment cannot be tolerated or is not working well enough.

When more than one treatment is available, the least expensive should be chosen.

Acute exacerbations of ulcerative colitis
For acute exacerbations, NICE TA163[2] recommends that infliximab is used if IV ciclosporin is contraindicated or clinically inappropriate. For reasons of safety and efficacy, NHS Cheshire and Merseyside recognises that infliximab will normally be used in preference to ciclosporin, after steroid treatment has been unsuccessful, for this indication.

References

1. Ulcerative colitis: management. NICE NG130 May 2019. Accessed 18/02/2020.
2. Infliximab for acute exacerbations of ulcerative colitis NICE TA163 December 2008. Accessed 3/02/2021
3. NICE TA 329. Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy
4. NICE TA 547. Tofacitinib for moderately to severely active ulcerative colitis
5. NICE TA792. Filgotinib for treating moderately to severely active ulcerative colitis
6. TA856. Upadacitinib for treating moderately to severely active ulcerative colitis
7. TA342. Vedolizumab for treating moderately to severely active ulcerative colitis
8. TA633. Ustekinumab for treating moderately to severely active ulcerative colitis
9. TA828. Ozanimod for treating moderately to severely active ulcerative colitis

Crohn's disease

Adult with **moderately to severely active Crohn's disease** (defined normally, but not exclusively, corresponds to a Harvey Bradshaw Index (HBI) of >/=8-9)

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Inadequate response, intolerance or contraindication to optimised conventional therapy including corticosteroids and/or immunosuppressant treatments

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When more than one treatment is suitable, the least expensive should be chosen

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Adalimumab, **infliximab** (TA187)

Ustekinumab (TA456)

Option if the disease has not responded well enough or lost response to a previous biological treatment, a previous biological treatment was not tolerated or TNF α inhibitor therapy is not suitable: **risankizumab** (TA888), **upadacitinib** (TA905)

Option if a TNF α inhibitor therapy is ineffective or not suitable: **vedolizumab** (TA352)

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Adequate clinical response

↓ Yes

Continue treatment for 12 months or until treatment failure (whichever is shorter). Treatment should only continue if there is clear evidence of response as determined by clinical symptoms, biological markers and investigation, including endoscopy if necessary. People should be reassessed at least every 12 months. A trial withdrawal should be considered for patients in stable clinical remission at 12 months.

Adult with **active fistulising Crohn's disease**

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Inadequate response, intolerance or contraindication to conventional therapy including immunosuppressive treatments, antibiotics and drainage

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Infliximab (TA187)

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Adequate clinical response

↓ No

Depending on clinical grounds consider an alternative therapy or surgery.

Running out of treatment options does not confer clinical exceptionality.

Crohn's Disease[10]

Post-surgery prophylaxis

Biologics should not be offered to maintain remission after complete macroscopic resection of ileocolonic Crohn's disease. Azathioprine should be considered, in combination with up to 3 months post-operative metronidazole. Biologics would only continue if surgery does not remove all the diseased area.

Subsequent disease flares

If the patient subsequently relapses post successful surgery, a biologic may be considered. The choice of biologic would usually be made at an MDT meeting, choosing the drug with the best chance of success and striving to use the most cost-effective agent.

Sequential use

NICE does not make any recommendations on sequential use of biologics although it recommends that ustekinumab and vedolizumab are used after failure of treatment with TNF α inhibitors and risankizumab and upadacitinib are used if the disease has not responded well enough or lost response to a previous biological treatment, a previous biological treatment was not tolerated or TNF α inhibitor therapy is not suitable.

When more than one treatment is available, the least expensive should be chosen.

Response to TNF α inhibitor therapy[11]

For patients with primary nonresponse to one TNF α inhibitor the likelihood that they will respond to a second is small but is dependent on the clinical context. Switching to a drug that acts through a different mechanism is more likely to be successful.

Secondary loss of response to TNF α inhibitor therapy can occur as a consequence of immune-mediated neutralising antibodies to the drug (although there are likely to be other mechanisms including non-neutralising, drug-clearing antibodies, or non-immune-mediated mechanisms).

Measurement of drug and antibody levels may be helpful in guiding individual treatment choices and next steps[12].

References

10. NICE NG129. Crohn's disease: management
11. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. June 2019. Accessed 18/02/2020.
12. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut BMJ 2021
13. TA187. Infliximab and adalimumab for the treatment of Crohn's disease
14. TA456. Ustekinumab for moderately to severely active Crohn's disease after previous treatment
15. TA888. Risankizumab for previously treated moderately to severely active Crohn's disease
16. TA905. Upadacitinib for previously treated moderately to severely active Crohn's disease
17. TA352. Vedolizumab for treating moderately to severely active Crohn's disease after prior therapy
18. TA187. Infliximab and adalimumab for the treatment of Crohn's disease