

KENT AND MEDWAY INFLAMMATORY BOWEL DISEASE (IBD) (ADULTS) HIGH-COST DRUG (HCD) PATHWAY

Developed by the Kent and Medway IBD HCD
working group
Version 1.13

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Version Control		
Date	Amendment	Author
22/06/2023	Pathway agreed by group V1.0	Thelma Okunuga
22/08/2023	Pathway approved by IMOC	Thelma Okunuga
30/10/2023	Inclusion of mirikizumab (TA925) to pathway V1.1	Thelma Okunuga
24/11/2023	Inclusion of yuflyma to cost indicator table V1.11 (cost indicator to be reviewed)	Thelma Okunuga
26/03/2024	Inclusion of etrasimod to pathway NICETA956 V1.12	Thelma Okunuga
02/05/24	Inclusion of pregnancy requirement for etrasimod (note 9 UC pathway) V1.13	Thelma Okunuga

Moderate to Severe UC NICE NG 130

It is best practice to review patient treatment at complex IBD MDT after five lines of treatment (there are 5 different mode of action for treatment of ulcerative colitis)

2. Moderate to severe UC defined by disease severity scoring system

- Mayo score ≥ 6
- Partial Mayo score ≥ 5
- SCCAI ≥ 6
- UCEIS ≥ 5
- Faecal calprotectin can be used to detect inflammation and check for biochemical response.

3a. If there is more than 1 suitable second choice treatment, the least expensive treatment should be chosen, unless clinically inappropriate.

3b. Ustekinumab dosing post induction:

Ustekinumab can be administered Q8 or Q12. Patients suitable for Q8 dosing include the following:

- Previous biologic failure
- Poor prognostic factors (note 7)

Response to patients receiving Q8 ustekinumab should be reviewed at 6/12, so that dose de-escalation can be considered

3c. Contraindications to all JAK-1 (MHRA alert):

- Lymphocyte count < 0.75
- Neutrophil count < 1
- Active infection
- Hb $< 9g/L$
- Use if no other alternative drug available in patients at risk of CVD, > 65 yrs, smoker, high risk of cancer, prior MI / VTE. Trial lowest dose first

3d. Contraindication to Anti-TNF: Moderate-severe heart failure and active infections. Check SPC for further information and screening requirements

4. Dose escalation for an initial period of 16 weeks following MDT discussion. Then review at 6-12 months.

Infliximab dose escalation is allowed if partial response during initial induction period:

- Infliximab IV (unlicensed)
 - 10mg/kg Q8 or
 - 5mg/kg Q4 or
 - 5mg/kg Q6

Drug levels to aid decision making please refer to loss of response to anti-TNF pathway (IFX aim 3 – 7 mcg/ml)

- Tofacitinib 10mg twice daily (consider VTE risk) (licensed)
- Ustekinumab 90mg Q8 (licensed)
- Vedolizumab 300mg Q4 (licensed) Q6 (unlicensed)

5. Disease response definitions:

Adequate response

Complete Mayo Score:

Decrease in Mayo score from baseline ≥ 3 and $\geq 30\%$, AND
Decrease in rectal bleeding sub-score from baseline by ≥ 1 point, OR absolute rectal bleeding sub-score 0 – 1.

Partial Mayo Score:

Decrease in partial Mayo score from baseline ≥ 2 points and $\geq 25\%$ AND
Decrease in rectal bleeding sub-score from baseline of ≥ 1 point OR absolute rectal bleeding sub-score 0 – 1.

UCEIS:

Change in UCEIS ≥ 3 points (associated with better colectomy-free survival)

Partial response

Any improvement in complete or partial Mayo score from baseline that does not meet adequate response criteria

No response

Deterioration or no change in full or partial Mayo score from baseline
If alternative disease severity scoring systems used, evidence of treatment response (e.g. endoscopy, radiology results, biochemical markers e.g. FCP/CRP) to be provided.

6. Poor prognostic indicators: Progression of disease extension, higher Mayo score, higher endoscopic score, corticosteroid use, younger age at diagnosis, presence of PSC, failure of biologic

Poor prognostic factors may be taken into account when considering continued dose escalation. Clinicians should provide details in Blueteq funding requests to assist with audits.

7. Disease reassessment at 12 months

Treatment should only be continued if there is evidence of on-going adequate or partial response and active disease, determined by:

- Clinical symptoms / physicians assessment and
- Biological markers or
- Investigations, including endoscopy as needed

Clinical remission: Normally defined by complete Mayo ≤ 2 with no subscore > 1 , partial Mayo ≤ 1 , SCCAI ≤ 2 , UCEIS 0 – 1.
Proactive monitoring: Partial Mayo score, FCP, CRP, FBC

8. Escalated doses post induction

Continuing escalated doses of treatment may be appropriate for some patients. This should be discussed at the internal gastroenterology MDT meeting. These patients should be monitored every 6 – 12 months, dependant on clinical need, with the aim to de-escalate or switch therapy where appropriate. Dose escalation will only be funded for 12 months and a new blueteq form will be required for funding to continue past 12 months

9. Ozanimod & etrasimod screening requirements: ECG screening for all patients prior to commencement of Ozanimod or etrasimod to detect cardiac abnormality First-dose, 6-hour observation is recommended for certain patients (refer to SPC). Ophthalmology screening for macular oedema is required for patients with diabetes uveitis or a history of retinal disease prior to initiation and during treatment. Patients treated with etrasimod must have a negative pregnancy test for all women of childbearing potential.

Inadequate response, intolerance or contraindication to optimised conventional therapy, taken for an adequate period, including:

- Corticosteroids and
- Thiopurine drug (> 14 weeks) – If appropriate

Risk of disease related complications:

- Note 6 – Poor prognostic indicators

First line therapy:

- Infliximab +/- thiopurine (severe disease, extraintestinal manifestations) or Golimumab or Adalimumab

• Etrasimod

- Vedolizumab (moderate disease) (Switch to SC if adequate response)

Second line therapy (if intolerant or failed first line biologic):

- Alternative TNF antagonist (for patients with loss of response due to immunogenicity, or intolerance, to first TNF antagonist please refer to loss of response to anti-TNF pathway)
- Vedolizumab (switch to SC if adequate response) or ustekinumab or Mirikizumab
- Filgotinib / Upadacitinib / Tofacitinib (Note 3c)
- Ozanimod (Note 9)

Risk of treatment related complications:

- Prior serious infections
- Prior malignancy
- > 65 yrs, multiple co-morbidities

First line therapy:

- Vedolizumab (switch to SC if adequate response) or Ustekinumab or Mirikizumab

Second line therapy (if intolerant or failed on first line biologic):

- Filgotinib Upadacitinib or Tofacitinib (Note 3c)
- Etrasimod/Ozanimod (Note 9)
- Anti-TNF monotherapy i.e., Infliximab, golimumab or adalimumab (Note 3d)

Assess initial induction response at 12 – 16 weeks (NICE review)

If responding to treatment and criteria for moderate to severe UC met, complete BlueTeq funding request

No response to therapy

Partial response to therapy

Adequate response to therapy

Stop therapy
Initiate alternative drug from Box 1.
Consider referral for surgical intervention or clinical trial at any stage

Optimise treatment
Aim target IFX drug trough level of 3-7 mcg/mL. See note 3 and loss of response to anti-TNF α pathway.

Continue escalated dose
Monitor response at 6-12 month intervals

Response at 16 weeks after initial trial of dose escalation? (notes 3 and 7)

No or inadequate response

Adequate response AND/OR Poor prognostic factors

Reduce to standard dose of treatment

Clinical remission

Option to optimise therapy? See note 3

Check for secondary loss of response
Review every 6-12 months dependent on clinical need

Review at 12 months post initiation (note 6)
Is there evidence of on-going active disease?

YES

NO

Reassess patient
Follow pathway for secondary loss of response
Reassess patient every 12 months or 6-12 months if on escalated dosing

Is the patient in stable clinical remission?

YES

YES

Patient on escalated dosing

Patient on standard dosing

Consider trial of standard dosing

Consider trial of withdrawal
Withdrawal may be inappropriate if: Intolerance / contraindication to conventional maintenance therapy & only maintenance option is a biologic or JAK-1
Previous failure of therapy withdrawal

- Reduce to standard dosing and follow pathway above
- 3/12 proactive monitoring
- If disease relapse, consider dose escalation and follow pathway above

- Stop biologic
- 3/12 proactive monitoring
- Restart Rx if disease relapse

Moderate to Severe Active Crohn's NG129

Inadequate response, intolerance or contraindication to optimised conventional therapy, taken for an adequate period, including:

- Corticosteroids and
- Thiopurine drug / methotrexate (> 14 weeks) – If appropriate

It is best practice to review patient treatment at complex IBD MDT after five lines of treatment (there are 5 different mode of action for Crohn's disease)

Active Fistulising Crohn's Disease

Lack or loss of response, intolerance or contraindication to conventional therapy taken for an adequate period, including:

Antibiotics and Drainage +/- seton and Immunosuppressants

First line: Infliximab IV, +/- thiopurine
Second line: Adalimumab
Third line: Ustekinumab (If both anti-TNFs are contraindicated / previous failure)
Biosimilars available. Use best value brand. Can switch from IV infliximab to subcut for maintenance once stable

BOX 1

Risk of disease related complications:

- Note 6 – Poor prognostic indicators

First line therapy:

- Infliximab or adalimumab, ideally in combination with an immunomodulator

Second line therapy (in patients with prior exposure to infliximab or adalimumab):

- Alternative TNF antagonist (for patients with loss of response due to immunogenicity, or intolerance, to first TNF antagonist please refer to loss of response to anti-TNF pathway)
- Vedolizumab (switch to SC if adequate response) (note 3c)
- Risankizumab or Ustekinumab
- Upadacitinib (when available) (Note 3c in UC pathway)

Risk of treatment related complications:

- Prior serious infections
- Prior malignancy
- >65yrs, multiple co-morbidities
- TNF antagonist contraindicated (note 3d of UC pathway)

First line therapy

- Vedolizumab - (switch to SC if adequate response) (note 3c)
- TNF antagonist contraindicated (note 3d of UC pathway)
- Risankizumab
- Upadacitinib - (note 3c UC pathway)

Assess initial induction response at 12 – 16 weeks (NICE review)

No response to therapy

Partial response to therapy

Adequate response to therapy

Stop therapy
Initiate alternative drug
Consider referral for surgical intervention or clinical trial at any stage

Optimise treatment
Aim target IFX drug trough level of >3-7, ADA > 4.9 mcg/ml. Note 3&7 and loss of response to anti-TNF α pathway

Adequate response AND / OR Poor prognostic factors

Continue escalated dose
Monitor response at 6-12 month intervals

Response at 16 weeks after initial trial of dose escalation? (notes 3, 4&7)

No or inadequate response

Clinical remission

Reduce to standard dose of treatment

Option to optimise therapy? See note 3

Check for secondary loss of response
Review every 6-12 months dependent on clinical need

5. Disease response definitions:

Moderate to Severe active Crohn's disease

Adequate response – Decrease in HBI \geq 3 points or CDAI \geq 70 points
 Partial response – Any improvement in HBI or CDAI that does not meet adequate response criteria
 No response – Worsening or no change in HBI or CDAI
 Where is HBI is not a relevant indicator of disease severity, alternative objective measure will be used (compared to baseline) to demonstrate response^{*}

Active fistulising Crohn's

Response – \geq 50% improvement in fistula drainage / closure
 No response < 50% improvement in fistula drainage
^{*} If alternative disease severity scoring systems used, evidence of treatment response (e.g. endoscopy, radiology results, biochemical markers e.g. FCP/CRP) to be provided.

6. Poor prognostic indicators: Complex disease (stricturing, penetrating or fistulising), perianal disease, previous surgery for Crohns disease, previous biologic failure, age of onset < 40 yrs, corticosteroid use / dependency

Poor prognostic factors may be considered in decisions around continued dose escalation. Clinicians should provide details in Blueteq funding requests to assist with audits.

7. Disease reassessment at 12 months

Treatment should only be continued if there is evidence of on-going adequate or partial response and active disease, determined by:
 Clinical symptoms / physicians assessment and Biological markers or Investigations, including endoscopy as needed
 Clinical remission: Normally defined by HBI \leq 4 or CDAI \leq 150

8. Escalated doses post induction:

Continuing escalated doses of treatment may be appropriate for some patients. This should be discussed at the internal gastroenterology MDT meeting. These patients should be monitored every 6 – 12 months, dependant on clinical need, with the aim to de-escalate or switch therapy where appropriate. Dose escalation will only be funded for 12 months and a new blueteq form will be required for funding to continue past 12 months.

Review at 12 months post initiation (note 7)

Is there evidence of on-going active disease?

YES

NO

Reassess patient
Follow pathway for secondary loss of response
Reassess patient every 12 months or 6-12 months if on escalated dosing

Is the patient in stable clinical remission?

YES

YES

Patient on escalated dosing

Patient on standard dosing

Consider trial of standard dosing

Consider trial of withdrawal

Reduce to standard dosing and follow pathway above

Withdrawal may be inappropriate if: Intolerance / contraindication to conventional maintenance therapy & only maintenance option is a biologic or JAK-1

3/12 proactive monitoring

Previous failure of therapy withdrawal

If disease relapse, consider dose escalation and follow pathway above

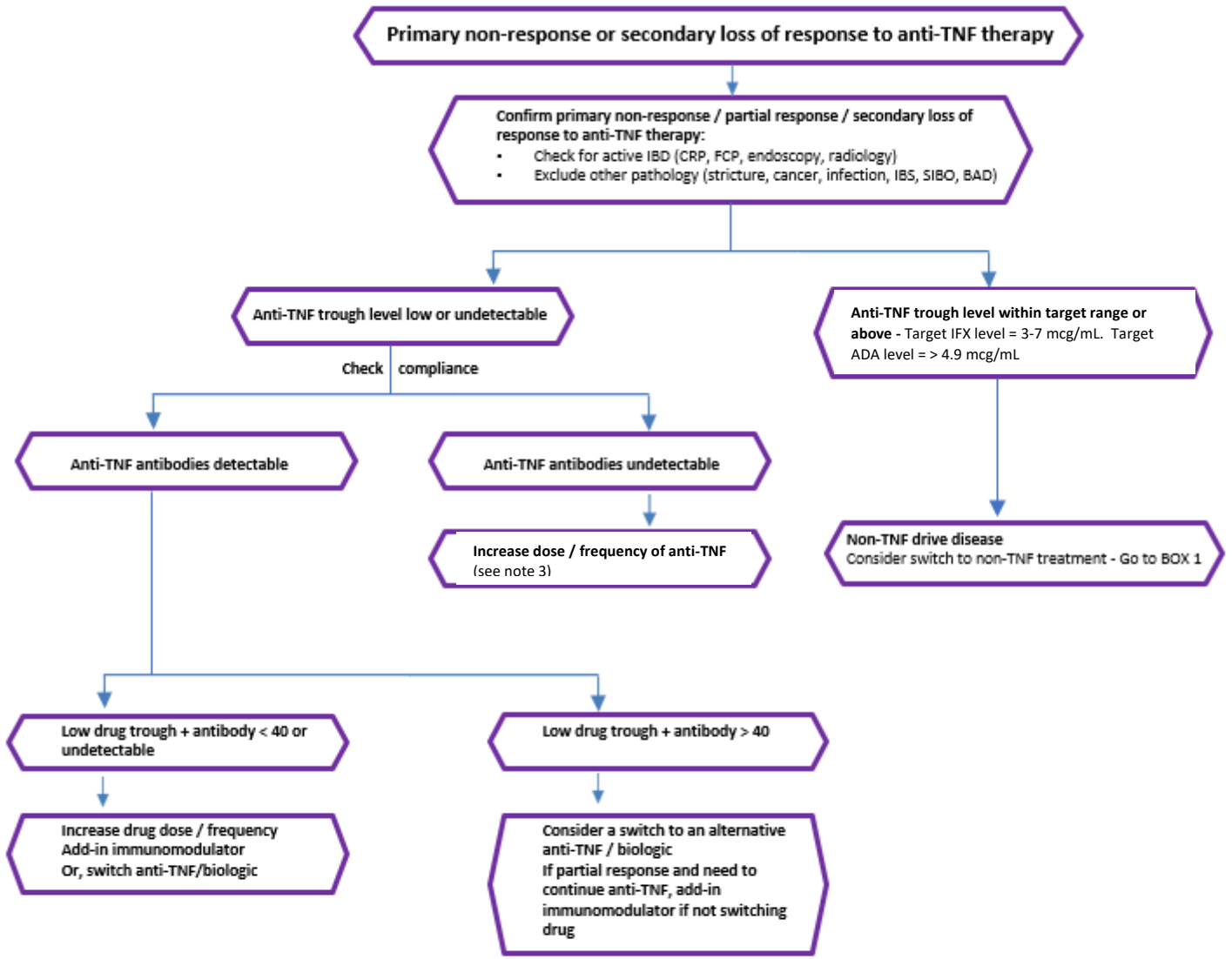
Restart Rx if disease relapse

Stop biologic

3/12 proactive monitoring

Restart Rx if disease relapse

Restart Rx if disease relapse



The precise level of antibody significance is yet to be defined
 Antibodies can be reduced by immunosuppression or anti-TNF dose adjustments
 An antibody level > 40 is unlikely to be cleared by immunosuppression or anti-TNF dose adjustments

Appendix 1:

NICE TA's and Evidence Based Treatment Outcomes:

CROHN'S DISEASE				
Drug	TA	DATE	Place in pathway	Evidence based treatment outcomes from clinical trials <i>(source NICE guidance)</i>
Adalimumab Infliximab	TA187	MAY-10	Infliximab and adalimumab, within their licensed indications, are recommended as treatment options for adults with severe active Crohn's disease whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments), or who are intolerant of or have contraindications to conventional therapy.	<p>Infliximab: Participants were randomised to infliximab 5 mg/kg, 10 mg/kg, 20 mg/kg or placebo for non-fistulating disease. The rate ratio (RR) for remission (the rate of remission in the 5 mg/kg group divided by the rate of remission in the placebo group; remission defined as CDAI score below 150) was 12.04 (95% confidence interval [CI] 1.70 to 85.44). There were also significantly greater rates of 70-point reductions in CDAI (referred to as response 70) in the infliximab 5 mg/kg group.</p> <p>The study of infliximab induction treatment in fistulating disease compared infliximab at a dose of 5 mg/kg or 10 mg/kg with placebo. Follow-up extended to at least week 18. The primary outcome was a 50% reduction in the number of draining fistulae; the rate difference between the infliximab 5 mg/kg and placebo groups was 0.42 (95% CI 0.19 to 0.64). The secondary outcome was complete absence of fistulae; the rate difference between the infliximab 5 mg/kg and placebo groups was 0.42 (95% CI 0.21 to 0.63). Infliximab groups had statistically significant improvements in CDAI and PCDAI scores at week #</p> <p>Adalimumab: For maintenance dose the CLASSIC II trial results for the point estimate for remission RR versus placebo at week 56 was 1.78 (95% CI 1.01 to 3.13) for the every other week schedule and 1.88 (95% CI 1.08 to 3.27) for the weekly schedule.</p>
Vedolizumab	TA352	Aug-15	Vedolizumab is recommended as an option for treating moderately to severely active Crohn's disease only if: <ul style="list-style-type: none"> • a tumour necrosis factor-alpha inhibitor has failed (that is, the disease has responded inadequately or has lost response to treatment) or • a tumour necrosis factor-alpha inhibitor cannot be tolerated or is contraindicated. Vedolizumab is recommended only if the company provides it with the discount agreed in the patient access scheme.	<p>The results for the primary outcomes of GEMINI II showed that at week 6, clinical remission rates (CDAI score 150 points or less) were significantly higher in patients having vedolizumab than in patients having placebo (14.5% [95% CI 9.9 to 19.2] and 6.8% [95% CI 2.7 to 10.8]) respectively. For maintenance treatments, i.e. patients receiving vedolizumab every 8 weeks, the treatment difference from placebo was 17.4% (95% CI 7.3 to 27.5, p=0.0007) and in patients receiving vedolizumab every 4 weeks, it was 14.7% (95% CI 4.6 to 24.7, p=0.0042).</p> <p>Clinical remission rates were higher for patients who had vedolizumab every 4 or 8 weeks compared with those who had placebo regardless of prior TNF-alpha inhibitor use.</p>
Ustekinumab	TA456	Jul-17	Ustekinumab is recommended, within its marketing authorisation, as an option for treating moderately to severely active Crohn's disease, that is, for adults who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha inhibitor or have medical contraindications to such therapies.	<p>In UNITI-1 at week 6, 33.7% of patients in the ustekinumab group at the licensed dose of approximately 6 mg/kg had a clinical response compared with 21.5% in the placebo group (p=0.003). In UNITI-2 (TNF naive) at week 6, 55.5% of patients in the ustekinumab group had a clinical response compared with 28.7% in the placebo group (p=0.001). The committee noted that at 44-week follow-up in the IM-UNITI maintenance trial, the proportion of patients in clinical remission (the primary outcome) was significantly greater in both the 90 mg every 12 weeks (48.8%) and 90 mg every 8 weeks (53.1%) ustekinumab groups than in the placebo group (35.9%, p=0.040 and p=0.005 respectively).</p>
Risankizumab	TA888	May-23	Risankizumab is recommended as an option for treating moderately to severely active Crohn's disease in people 16 years and over, only if: <ul style="list-style-type: none"> • the disease has not responded well enough or lost response to a previous biological treatment, or • a previous biological treatment was not tolerated, or • tumour necrosis factor (TNF)-alpha inhibitors are not suitable. 	<p>Induction:</p> <p>In ADVANCE trial, there were 219 people in the conventional care failure subgroup and 292 people in the biological treatment failure subgroup In MOTIVATE trial, there were 378 people who had a previous biological treatment.</p> <p>Maintenance:</p> <p>People whose disease responded to treatment entered FORTIFY, a phase 3 multicentre, double-blind, placebo-controlled maintenance trial. FORTIFY sub-study 1 (n=542): re-randomised people to subcutaneous 180 mg or 360 mg risankizumab or placebo (withdrawal) every 8 weeks for 52 weeks.</p>

				The results from the induction trials suggested that risankizumab is associated with higher rates of clinical remission and endoscopic response compared with placebo in the conventional care failure and biological treatment failure populations. The results from FORTIFY suggested that risankizumab is associated with higher rates of endoscopic response compared with placebo in the conventional care failure and biological treatment failure populations.
Upadacitinib	TA905	Jan-23	Upadacitinib is recommended as an option for treating moderately to severely active Crohn's disease in adults, only if: the disease has not responded well enough or lost response to a previous biological treatment or a previous biological treatment was not tolerated or tumour necrosis factor (TNF)-alpha inhibitors are contraindicated. Upadacitinib is only recommended if the company provides it according to the commercial arrangement.	U-EXCEL and U-EXCEED were studies of upadacitinib induction treatment. U-EXCEL (n=526 for part 1) included people whose disease had had inadequate response or were intolerant to conventional therapy only (conventional care failure) or to biological treatment (biological failure). U-EXCEED (n=495 for part 1) included only a biological failure population. For the biological failure population, both trials showed a statistically significant improvement in the rate of clinical remission and endoscopic response with a 45-mg induction dose of upadacitinib compared with placebo at 12 weeks. The third study, U-ENDURE, was a study of upadacitinib maintenance treatment. For the biological failure population, cohort 1 of U-ENDURE showed a statistically significant improvement in rates of clinical remission and endoscopic response with a 15-mg and 30-mg maintenance dose of upadacitinib compared with placebo at 52 weeks. The data is confidential and was not reported in the NICE guidance.

ULCERATIVE COLITIS

Drug	TA	DATE	Place in pathway	Evidence based treatment outcomes from clinical trials (source NICE guidance)
Adalimumab Infliximab Golimumab	TA329	Feb-15	Infliximab, adalimumab and golimumab are recommended, within their marketing authorisations, as options for treating moderately to severely active ulcerative colitis in adults whose disease has responded inadequately to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who cannot tolerate, or have medical contraindications for, such therapies.	The committee concluded that the TNF-alpha inhibitors were clinically effective compared with placebo in the randomised controlled trials (RCT). Ultra trial results: Adalimumab 16.5% vs 9.3% placebo on clinical remission at week 8. 8.5% adalimumab vs 4.1% placebo continued remission to week 52. ACT trial: Infliximab - week 8: 69% infliximab vs 31% placebo - week 54 46% vs 27% placebo. Pursuit trial result: Golimumab 51% vs 30% placebo at week 6 on clinical remission, 49.7% golimumab vs 31.2% placebo week 52 on clinical remission.
Infliximab	TA163	Dec-08	Infliximab is recommended as an option for the treatment of acute exacerbations of severely active ulcerative colitis only in patients in whom ciclosporin is contraindicated or clinically inappropriate, based on a careful assessment of the risks and benefits of treatment in the individual patient.	The probabilities of a patient undergoing colectomy were estimated to be 0.67, 0.23 and 0.58 for placebo, infliximab and ciclosporin, respectively, for the first 3 months. The respective probabilities during months 4–12 was 0.14, 0.27 and 0.18 for placebo, infliximab and ciclosporin respectively.
Vedolizumab	TA342	June-15	Vedolizumab is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults only if the company provides vedolizumab with the discount agreed in the patient access scheme.	Gemini trial: - % Clinical remission at week 6: 16.9% vedolizumab vs 5.4% placebo. - % Clinical remission at week 52: 8weekly 41%, 4weekly 44.8% vs placebo 15.9%.
Ustekinumab	TA633	June-20	Ustekinumab is recommended as an option for treating moderately to severely active ulcerative colitis in adults when conventional therapy or a biological agent cannot be tolerated, or the disease has	At the end of induction treatment, rates of clinical remission and response were statistically significantly higher in the ustekinumab 6 mg per kg and 130 mg groups than the placebo group. This was the case for both the non-biologic failure and biologic-failure subgroups, and for the overall ITT population. At week 44 of the maintenance phase, a statistically significantly greater proportion of patients who had had ustekinumab maintenance with either

			<p>responded inadequately or lost response to treatment, only if:</p> <ul style="list-style-type: none"> • a tumour necrosis factor-alpha inhibitor has failed (that is the disease has responded inadequately or has lost response to treatment) or • a tumour necrosis factor-alpha inhibitor cannot be tolerated or is not suitable, and • the company provides ustekinumab at the same price or lower than that agreed with the Commercial Medicines Unit. 	dose were in clinical remission than those who had had placebo. This was the case for both the non-biologic failure and biologic-failure subgroups, and for the overall ITT population.
Tofacitinib	TA547	Nov-18	Tofacitinib is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults when conventional therapy or a biological agent cannot be tolerated or the disease has responded inadequately or lost response to treatment. It is recommended only if the company provides tofacitinib with the discount agreed in the commercial arrangement.	<p>OCTAVE trial:</p> <p>Clinical remission at week 8: 18.5% Tofacitinib VS 8.2% Placebo.</p> <p>Clinical remission at week 52: 40.6% tofacitinib VS 11.1 placebo</p>
Filgotinib	TA792	June-22	<p>Filgotinib is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults:</p> <ul style="list-style-type: none"> • when conventional or biological treatment cannot be tolerated, or • if the disease has not responded well enough or has stopped responding to these treatments, and • if the company provides filgotinib according to the commercial arrangement. 	<p>Biologic naïve patients at week 8 had EBS remission of 26.1% filgotinib vs 15.6% on placebo.</p> <p>For biologic non-naïve patients, EBS remission at week 8 was 11.5% for filgotinib vs 4.2% for placebo and at week 52 was 37.2% for filgotinib vs 11.2% for placebo.</p>
Upadacitinib	TA856	Jan-23	Upadacitinib is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults: when conventional or biological treatment cannot be tolerated, or if the condition has not responded well enough or has stopped responding to these treatments, and if the company provides upadacitinib according to the commercial arrangement.	<p>U-achieve (induction): 26% of patients on rinvoq and 5% of patients on placebo had clinical remission respectively.</p> <p>U-accomplish (maintenance): 33% of patients on rinvoq and 4% of patients on placebo had clinical remission respectively.</p>
Ozanimod	TA828	Oct-22	<p>Ozanimod is recommended as an option for treating moderately to severely active ulcerative colitis in adults, only if:</p> <ul style="list-style-type: none"> • conventional treatment cannot be tolerated or is not working well enough and infliximab is not suitable, or • biological treatment cannot be tolerated or is not working well enough, and • the company provides it according to the commercial arrangement. 	<ul style="list-style-type: none"> • For both the TNF-alpha inhibitor-naïve and TNF-alpha inhibitor-experienced subgroups, a greater proportion of people who had ozanimod experienced clinical remission than those in the placebo group at the end of induction and maintenance (18.4% vs. 6.0%; P<0.001). These findings were all statistically significant except for the TNF-alpha inhibitor-experienced subgroup at the end of induction. • 47.8% (n=205) of patients in the Ozanimod group demonstrated clinical response compared with 25.9% (n=56) in the placebo group (P<0.001) • Endoscopic improvement was achieved in 27.3% (n=117) of Ozanimod patients compared with 11.6% (n=25) of placebo patients (p<0.001) • 12.6% (n=54) of Ozanimod patients showed mucosal healing vs. 3.7% (n=8) for placebo (p<0.001)
Mirikizumab	TA925	Oct-23	Mirikizumab is recommended as an option for treating moderately to severely active ulcerative colitis in adults when conventional or biological treatment cannot be tolerated, or the condition has not responded well enough or lost response to treatment, only if:	<p>Lucent-1 was an intravenous induction study with treatment of up to 12 weeks, followed by a 40 week subcutaneous randomised withdrawal maintenance study (LUCENT 2), representing at least 52 weeks of therapy.</p> <p>Lucent-1: Clinical remission: mirikizumab treatment group (n=210/868; 24.2%) vs placebo (n=39/294; 13.3%) at week 12 (P<0.001). Clinical response: mirikizumab treated group (n=551/868; 63.5%) vs placebo (n=124/294; 42.2%) at week 12 (P<0.001;</p>

			<p>a tumour necrosis factor (TNF)-alpha inhibitor has not worked (that is the condition has not responded well enough or has lost response to treatment) or</p> <p>a TNF-alpha inhibitor cannot be tolerated or is not suitable and</p> <p>the company provides it according to the commercial arrangement.</p>	<p>Lucent-2: Among patients who achieved a clinical response with mirikizumab at week 12 in LUCENT-1; Clinical remission (the primary endpoint) in the mirikizumab treated group (n=182/365; 49.9%) vs placebo group (n=45/179; 25.1%) at week 40 of LUCENT-2 (P<0.001).</p> <p>In biologic-naïve patients: Clinical response: mirikizumab treated group (n=118/229; 51.5%) vs placebo group (n=35/114; 30.7%) at week 40 of LUCENT-2.</p> <p>In biologic-failed patients: Clinical response: mirikizumab treated group (n=59/128; 46.1%) compared to the placebo group (n=10/64; 15.6%) at week 40 of LUCENT-2.</p>
Etrasimod	TA956	March-24	<p>Etrasimod is recommended, within its marketing authorisation, as an option for moderately to severely active ulcerative colitis in people aged 16 years and over when:</p> <p>conventional or biological treatments cannot be tolerated or</p> <p>the condition has not responded well enough, or lost response to treatment.</p> <p>Etrasimod is only recommended if the company provides it according to the commercial arrangement.</p>	<p>The studies involved a total of 743 people aged 16 years and over for whom standard treatment or other treatments did not work well enough or could not be used. 26% (129 out of 496) of those who received Velsipity had achieved clinical remission compared with 11% (27 out of 247) of those who received placebo. Awaiting further information from SmPC when published.</p>

Appendix 2:

Inflammatory Bowel Disease (IBD) HCD Pathway Cost profiling sheet for Advanced Therapies

Review in progress.

Appendix 3:

Kent and Medway IBD HCD Working Group attendees (8/11/22-31/5/23):

Thelma Okunuga (TO) (Lead medicines optimization pharmacist ICB)

Nicola Grasso (NG) (IBD nurse DVH)

Jonathan Bailey (JB) (Deputy chief pharmacist MTW)

Kris Jones (KJ) (Chief pharmacy technician MTW)

Krupesh Haria (KH) (Clinical Effectiveness Manager | Integrated Health and Care Services

NHS South, Central and West)

Golnaz Douraghi-zadeh (GD) (Lead pharmacist EKHUFT)

Dr Paul Blaker (Gastroenterologist MTW),

Glyn Scott (Consultant nurse EKHUFT),

Dr Arun Dhiman (Gastroenterologist EKHUFT)

Marie Owens (Lead Pharmacist MFT)

James Hartwell (Lead Pharmacist DVH)

Philip Mairs (Gastroenterology Consultant DVH)

Iona Bell (Gastroenterologist MTW)

Nevidita Ghosh (Gastroenterologist MFT)

References:

- NICE Guideline 129 (NG129), Crohn's disease: management. May 2019.2
- NICE Crohn's disease pathway (see: [https://pathways.nice.org.uk/pathways/crohns disease](https://pathways.nice.org.uk/pathways/crohns%20disease))
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