# South East Regional Medicines Optimisation Group (SERMOG) policy recommendation

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| **Title:** | Inflammatory bowel disease (IBD) high cost drug pathway for adults |
| **Number:** | SERMOG-06 |
| **Category:** | Treatment pathway |
| **Date determined by SERMOG:** | March 2025 |

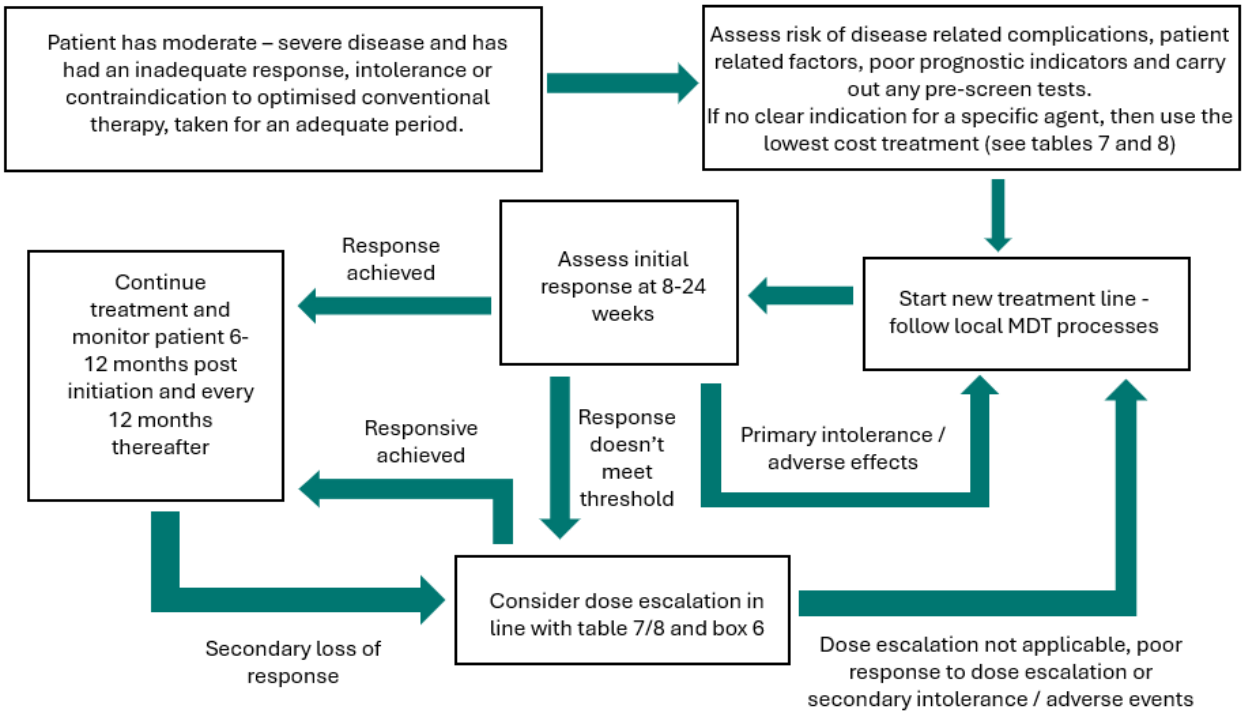
## Introduction

This pathway is a guideline for the initiation and maintenance of high cost drugs (biologicals and small molecules) for the treatment of inflammatory bowel disease (IBD) in adults where the patient has had an inadequate response, intolerance or contraindication to optimised conventional therapy (non-biological therapy e.g aminosalicylates, corticosteroids and immunomodulators), taken for an adequate period. The pathway follows NICE Technology Appraisal (TA) guidance alongside additional recommendations for dose escalation considered by the SERMOG. The use of HCDs for the treatment of IBD is only approved in line with this pathway and the dosing regimens outlined in tables 7 and 8. Any dose regimens outside of these recommendations are not routinely funded, as detailed in SERMOG-02. Where dose escalations are off-label, the guidance for off-label use of HCDs as detailed in box 6 should be followed. See Box 4 for considerations when choosing treatment and Box 5 on assessing response and effective maintenance. Definitions for terms used in the pathway are set out in Tables 1 and 2.

The use of dual-biological therapy for IBD is not routinely funded, as detailed in SERMOG-01.

Any new high cost drug (HCD) which receives a positive recommendation from NICE between document iterations will be approved through local ICB processes and will be included in future pathway updates.

## High cost drug pathway for IBD




## Table 1. Definitions of moderate – severe disease (one or more may be applicable)

| Crohn's disease | Ulcerative Colitis |
|---|---|
| • Crohn's disease activity index (CDAI) score ≥ 220<br>• Harvey Bradshaw Index (HBI) ≥ 8.<br>• Where CDAI / HBI is not a relevant indicator of disease severity alternative objective measures (e.g. colonoscopy, stoma output, C-reactive protein, Faecal calprotectin, video capsule) should be provided to confirm moderate to severe disease | • Mayo score ≥ 6<br>• Partial Mayo score ≥ 5<br>• Simple Clinical Colitis Activity Index (SCCAI) ≥ 6<br>• Ulcerative Colitis Endoscopic Index of Severity (UCEIS) ≥ 5<br>• Faecal calprotectin can be used to detect inflammation and check for biochemical response |

## Table 2. Pathway definitions and actions

| Description | Definition | Action |
|---|---|---|
| Response does not meet threshold | Level of improvement does not meet the thresholds above, or the agreed clinical outcome. Includes primary non response and partial response. | Dose escalate or switch mode of action. Switch within class acceptable if loss of response considered to be treatment specific. |
| Secondary loss of response | Where the improvement meets initial thresholds, but this response is lost over time | Dose escalate or switch mode of action. Switch within class acceptable if loss of |

| | | |
|---|---|---|
| | | response considered to be treatment specific. |
| Primary intolerance or adverse events | Where treatment is discontinued within the initial time period defined by the NICE TA due to inability to tolerate side-effects of treatment | If class specific or a severe adverse event change to a new mode of action. Otherwise consider changing to another option from the same treatment line. |
| Secondary intolerance or adverse events | Where treatment is discontinued outside of the initial time period defined by the NICE TA due to inability to tolerate side-effects of treatment | Change to a new mode of action. Switch within class acceptable if loss of response considered to be treatment specific. |

### Table 3. Drug treatment options (lowest acquisition cost option highlighted)

| Mode of action | | Drug | Indication | |
|---|---|---|---|---|
| | | | Ulcerative colitis | Crohn's disease |
| TNF alpha inhibitor | | Adalimumab | ✓ | ✓ |
| | | Infliximab | ✓ | ✓ |
| | | Golimumab | ✓ | × |
| Integrin α4β7 receptor antagonist | | Vedolizumab | ✓ | ✓ |
| Interleukin (IL) inhibitor | IL 12/23 | Ustekinumab | ✓ | ✓ |
| | IL 23 | Risankizumab | ✓ | ✓ |
| | | Mirikizumab | ✓ | × |
| Janus Kinase (JAK) inhibitor (oral) | JAK 1 and JAK 3 | Tofacitinib | ✓ | × |
| | JAK 1 | Filgotinib | ✓ | × |
| | JAK 1 | Upadacitinib | ✓ | ✓ |
| Sphingosine 1-phosphate (S1P) receptor modulator | Subtype 1 and 5 | Ozanimod | ✓ | × |
| | Subtype 1,4 and 5 | Etrasimod | ✓ | × |

### Box 4. Considerations when choosing and starting treatment

The most appropriate treatment should be chosen after discussing the advantages and disadvantages of the treatments available with the person having treatment. If patients and clinicians consider more than one treatment to be suitable, choose the least expensive treatment (taking into account drug administration costs, dose needed and frequency, and product price per dose). The lowest cost treatments are highlighted in table 3 and comparative indicators are given in tables 7 and 8.

Where subcutaneous and intravenous (IV) preparations are available, subcutaneous preparations are preferred where there is not a clinical need for an IV preparation.

Where biosimilars are available, these should be used, as detailed in SERMOG-03.

When initiating a treatment, the treatment aims should be discussed and agreed with the individual. This should include a specified outcome and a definition of achieving this. Examples include:

- CD – A decrease in HBI ≥ 3 points or a decrease in CDAI ≥ 70 points

- UC – Reduction of baseline Mayo score by ≥3 points and a decrease of 30% from the baseline score with a decrease of at least one point on the rectal bleeding subscale or an absolute rectal bleeding score of 0 or 1, or a decrease in partial Mayo score from baseline ≥ 2 points and ≥ 25% AND Decrease in rectal bleeding sub-score from baseline of ≥ 1 point OR absolute rectal bleeding sub-score 0 – 1, or a change in UCEIS ≥ 3 points, or a reduction in faecal calprotectin to less than 250 mcg/g

### Box 5. Assessing response and effective maintenance

Response should be initially assessed 8-24 weeks after initiation (specific time frame as detailed in NICE TA/SPC) where it should be ascertained if the response meets the treatment aims set out at initiation. If this aim has been met, treatment should be continued and reviewed again at 6-12 months. If the aim has not been met, consideration may be given to dose escalation or switching treatment.

Response should be re-assessed 6-12 months (or earlier if recommended by NICE TA) after treatment was commenced to determine whether ongoing treatment is still clinically appropriate.

Treatment should only be continued at this point if there is evidence of on-going adequate or partial response and active disease, determined by clinical symptoms / physicians' assessment and biological markers and/or evidence of endoscopic/imagery and histological disease activity,

If there is evidence of ongoing disease, the treatment may be dose escalated in line with pathway recommendations, or if more appropriate the patient may move to the next step in the treatment pathway.

If the patient is in a stable clinical remission, consideration may be given to stopping or dose tapering treatment. This decision should follow a discussion with the patient regarding the risk of inflammatory exacerbations (with and without drug treatment) and the potential side effects of drug treatment. Treatment may be re-started if the patient relapses.

Drug levels and antibody testing should be used where appropriate to guide optimal patient care, including the management of secondary loss of response and at annual review.

### Box 6. Using off-label dose escalations

The use of licenced dosing of high cost drugs (HCD) including biologics and small molecules for the treatment of inflammatory bowel disease (IBD) is the preferred treatment option. However, it is acknowledged that there are instances where off-label dose escalation may be most clinically appropriate for the individual.

The use of off-label dose escalations as detailed within the SER IBD HCD pathway is supported if all the following criteria are met, response is monitored and treatment discontinued if adequate response is not achieved. The prescribing doctor must take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring, and any follow up treatment.

#### Criteria for use

- There is ongoing active disease despite escalated dosing in line with the licenced, locally approved or TA recommended escalations.
- There is consensus at MDT that off-label dose escalation is the most clinically appropriate treatment option for the individual.
- If escalating anti-TNF medications, where antibody testing is available, the results are indicative that treatment escalation has a good chance of therapeutic effect

- There is clear reasoning for continuing the current treatment over switching to another treatment option (e.g. response has been previously achieved, and it is considered likely that escalation will recapture response)
- The individual has optimised concomitant treatment where appropriate (e.g. immunomodulators)
- There is recorded informed consent from the individual being treated

**Assessment of response**

- Response should be assessed after 3 months.
- If no improvement has been achieved (30% improvement in Mayo score point, a 70 point reduction in CDAI score or evidence of endoscopic response) treatment should be stopped and the individual switched to an alternative treatment option (if available).
- If the individual responds at 3 months, response should be re-assessed at 6-12 months in line with box 5.
- If there has been a secondary loss of response, then treatment should be stopped and the individual switched to an alternative treatment option.

**Monitoring**

The use of off-label dose escalations should be recorded. This record should include details on MDT approval, response, outcomes and adverse events.

**Table 7. TA recommendations and local dose escalation agreements for Crohn's disease**

| Treatment | TA | Can be used first line | NICE TA indication | Cost tier[1] | Biosimilar available | Maintenance dose | Approved dose escalations |
|---|---|---|---|---|---|---|---|
| Adalimumab | TA187 (2010) | Yes | 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[2] | £ | Yes | • 40mg every 2 weeks | • 40mg weekly or 80mg every 2 weeks<br>• 80mg every week (unlicensed) |
| Infliximab | | Yes | | £££ | Yes | • IV - 5mg/kg 8 weekly | • IV – 10mg/kg every 8 weeks<br>• IV – 5mg/kg every 4 or 6 weeks (off-label)<br>• IV – 10mg/kg every 4 or 6 weeks (off-label) |
| | | | | ££ | No | • SC – 120mg every 2 weeks | • SC – 240mg every 2 weeks |
| Upadacitinib[3] | TA905 (2023) | No | 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. | £££ | No | • 15 or 30mg daily | • N/A |

1. Legend assumes use of biosimilars where available.

2. Severe active Crohn's disease was classified in TA187 as Crohn's Disease Activity Index (CDAI) score of 300 or more and a Harvey-Bradshaw Index of 8/9 or above.

3. Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality.

| Treatment | TA | Can be used first line | NICE TA indication | Cost tier[1] | Biosimilar available | Maintenance dose | Approved dose escalations |
|---|---|---|---|---|---|---|---|
| Ustekinumab | TA456 (2017) | Yes | 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 | £££ | Yes | • 90mg every 12 weeks | • 90mg every 8 weeks<br>• 90mg every 4 or 6 weeks (off-label) |
| Risankizumab | TA888 (2023) | No | Moderately to severely active Crohn's disease in people 16 years and over, 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 not suitable. | £££££ | No | • 360mg SC every 8 weeks | N/A |
| Vedolizumab | TA352 (2015) | No | Moderately to severely active Crohn's disease only if 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[4] | £££££<br><br>£££££ | No | • IV – 300mg IV every 8 weeks after<br>• SC – 108mg every 2 weeks | • IV – 300mg IV every 4 (licenced) or 6 weeks (off-label)<br>• SC – N/A |

4. Vedolizumab should be given as a planned course of treatment until it stops working or surgery is needed, or until 12 months after the start of treatment, whichever is shorter. At 12 months, people should be reassessed to determine whether treatment should continue. Treatment should only continue if there is

**Table 8. TA recommendations and local dose escalation agreements for Ulcerative Colitis**

| Treatment | Can be used first line | TA | NICE TA indication | Cost tier | Biosimilar available | Maintenance dose | Approved dose escalations |
|---|---|---|---|---|---|---|---|
| Adalimumab | Yes | TA329 (2015) | 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. | £ | Yes | • 40mg every 2 weeks | • 40mg weekly or 80mg every 2 weeks<br>• 80mg weekly (off-label) |
| Infliximab | Yes | | | £££ | Yes | • IV - 5mg/kg 8 weekly | • 10mg/kg every 8 weeks (off-label)<br>• 5mg/kg every 4 or 6 weeks |
| | | | | ££ | No | • SC – 120mg every 2 weeks | • No escalation for SC preparation |
| Golimumab | Yes | | | ££££ | No | • 50mg every 4 weeks if weight < 80kg<br>• 100mg every 4 weeks if weight > 80kg | • 100mg every 4 weeks |

clear evidence of ongoing clinical benefit. For people in complete remission at 12 months, consider stopping vedolizumab, resuming treatment if there is a relapse. People who continue vedolizumab should be reassessed at least every 12 months to decide whether continued treatment is justified.

| Treatment | Can be used first line | TA | NICE TA indication | Cost tier | Biosimilar available | Maintenance dose | Approved dose escalations |
|---|---|---|---|---|---|---|---|
| Etrasimod | Yes | TA956 (2024) | Moderately to severely active ulcerative colitis in people aged 16 years and over when conventional or biological treatments cannot be tolerated or the condition has not responded well enough, or lost response to treatment. | ff | No | • 2mg daily | N/A |
| Filgotinib[5] | Yes | TA792 (2022) | Moderately to severely active ulcerative colitis in adults when conventional or biological treatment cannot be tolerated, or if the disease has not responded well enough or has stopped responding to these treatments | ff | No | • 200mg daily<br>• 100mg daily for adults at higher risk of VTE, MACE and malignancy | N/A |
| Ozanimod | Yes | TA828 (2022) | Moderately to severely active ulcerative colitis in adults, only if 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 | fff | No | • 0.92mg daily | N/A |
| Tofacitinib[5] | Yes | TA547 (2018) | 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 | fff | No | • 5mg twice daily | • 10mg twice daily |
| Upadacitinib[5] | Yes | TA856 (2023) | 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 | fff | No | • 15mg once daily | • 30mg once daily |

5. Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality.

| Treatment | Can be used first line | TA | NICE TA indication | Cost tier | Biosimilar available | Maintenance dose | Approved dose escalations |
|---|---|---|---|---|---|---|---|
| Ustekinumab | No | TA633 (2020) | 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, only if 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, | £££ | Yes | • 90mg every 12 weeks | • 90mg every 8 weeks<br>• 90mg every 4 or 6 weeks (off-label) |
| Vedolizumab | Yes | TA342 (2015) | Moderately to severely active ulcerative colitis[6] | ££££££<br><br>£££££ | No | • IV – 300mg every 8 weeks<br><br>• SC – 108mg every 2 weeks | • IV – 300mg every 4 (licenced) or 6 (off-label) weeks<br>• SC – N/A |
| Mirikizumab | No | TA925 (2023) | 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 a tumour necrosis factor (TNF)-alpha inhibitor has not worked (that is the condition has not responded well enough or | £££££ | No | • 200mg every 4 weeks | N/A |

6. Vedolizumab should be given until it stops working or surgery is needed. At 12 months after the start of treatment, people should be reassessed to see whether treatment should continue. Treatment should only continue if there is clear evidence of ongoing clinical benefit. For people in complete remission at 12 months, consider stopping vedolizumab, resuming treatment if there is a relapse. People who continue vedolizumab should be reassessed at least every 12 months to see whether continued treatment is justified.

| Treatment | Can be used first line | TA | NICE TA indication | Cost tier | Biosimilar available | Maintenance dose | Approved dose escalations |
|---|---|---|---|---|---|---|---|
| | | | has lost response to treatment) or a TNF-alpha inhibitor cannot be tolerated or is not suitable | | | | |
| Risankizumab | No | TA998 (2024) | 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 has lost response to treatment, only if 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 cannot be tolerated or is not suitable | £££££££ | No | • 180mg every 8 weeks<br>• 360mg every 8 weeks if inadequate initiation response | N/A |

| **Version control:** |
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| Version 1.0 – Circulated to ICBs for ratification on 9th April 2025 |
| **Notes:** |
| This policy recommendation will be reviewed when new information becomes available that is likely to have a material effect on the current recommendation.<br>South East region ICBs will always consider appropriate individual funding requests (IFRs) through their IFR processes. |