INFLAMMATORY BOWEL DISEASE (IBD) IMMUNOMODULATOR TREATMENT PATHWAY (ADULTS)

Approved by NHS Surrey Heartlands ICS Area Prescribing Committee - October 2023

Patient has progressed through treatment from Inflammatory Bowel Disease:

Immunosuppression in crohn's disease (Pathway 3) - December 2018.pdf (res-systems.net)

Carry out pre-screen tests.

If no clear indication for a specific agent, then use the most cost-effective.

See over for the most cost-effective choices.

START NEW TREATMENT LINE

There are FOUR different modes of action in Crohn's disease and FIVE different modes of action in UC.

For first three treatment lines, apply via Blueteq.

For 4th and subsequent treatment , requests must be considered by an external MDT via the Gastroenterology Network (see below for process).

Assess response at 8-12 weeks.

For primary intolerance/adverse effects, use another option from the SAME treatment line.

Good response

Continue treatment and monitor patient 12 months post initiation and then every 12 months thereafter.

If remission achieved consider trial of stopping biologic. Continue with immunosuppression.

Patient can restart treatment at any time if stopped in remission.

For secondary intolerance/adverse effects, move to another treatment line.

Poor response

Good response

Loss of response

Alternatives available:

Consider **dose intensification** (temporary dose/frequency escalation to recapture response with return to standard dosing).

See over for commissioned dose intensification regimens

Maintenance of escalated dose will be funded if patient loses response once the patient has returned to the standard dosing within a short time period.

OR

switch to next treatment line.

Poor response

The most cost-effective drug choices are:

TNFα inhibitor: Biosimilar adalimumab

JAK inhibitor for ulcerative colitis: Filgotinib

Where sub-cut and iv infusion presentations are available (infliximab and vedolizumab), the preference is for the sub-cut presentation.

Pathway definitions:

	Definition	Action
Primary intolerance/adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side-effects of that treatment that occurs **during the initial time period defined by the NICE TA**	Change to a new mode of action which will NOT count as a new treatment line
Secondary intolerance/adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side effects of that treatment that occurs **after the initial time period defined by the NICE TA**	Change to a new mode of action which will count as a new treatment line OR discuss at GN meeting
Conception	If conception plans or pregnancy indicate a change of drug is advisable, it is agreed that this **does not constitute a change in line of treatment**	Please update Blueteq accordingly

Requests for additional lines of treatment to external network MDT

The 'Additional lines of treatment application form' is available at [Profile : Additional lines of treatment process - various (res-systems.net)]

- Each consultation will last for seven days.
- Agreement requires **3 positive** endorsements (from clinicians of **at least 3 trusts other** than from the requesting clinician) **+ no negative/severe concerns.**
- If there are negative/severe concerns then decision should be postponed until the next face-to-face Gastroenterology Network meeting. The requesting clinician should attend this meeting, or be prepared to dial into the meeting, with access to the patient's notes (in case of further questions).

Drug choices: Ulcerative colitis and Crohn's disease

Mode of action		Drug	Indication	
			Ulcerative colitis	**Crohn's disease**
TNF alpha inhibitor		Adalimumab biosimilar	✓	✓
		Infliximab biosimilar #	✓	✓
		Golimumab	✓	✘
Integrin α4β7 receptor antagonist		Vedolizumab #	✓	✓
Interleukin (IL) inhibitor	IL 12/23	Ustekinumab	✓	✓
	IL 23	Risankizumab	✘	✓
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 / Subtype 5	Ozanimod	✓	✘

SC and IV presentations available (IV should be used at clinician's discretion)

Ulcerative colitis

Drug	Ulcerative colitis		
	TA	Date	Place in pathway
Adalimumab biosimilar **Infliximab biosimilar** **Golimumab**	TA329	Feb-15	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. **DOSE INTENSIFICATION** (maintenance to be reviewed): Adalimumab: ✓ 40mg once weekly for 12 weeks **or** 80mg every two weeks for 12 weeks Infliximab IV*: ✓ 10mg/kg every 8 weeks for 3 doses (24 weeks), 5mg/kg every 4 weeks for 3 doses (12 weeks) **or** 5mg/kg every 6 weeks for 2 doses (12 weeks) Golimumab: ✘
Infliximab biosimilar	TA163	Dec-08	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.
Vedolizumab	TA342	Jun-15	Treating moderately to severely active ulcerative colitis in adults. ✘ **DOSE INTENSIFICATION is NOT commissioned.**
Ustekinumab	TA633	Jun-20	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, 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. **DOSE INTENSIFICATION** (maintenance to be reviewed): ✓ 90mg every 8 weeks for 2 doses
Tofacitinib	TA547	Nov-18	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. **DOSE INTENSIFICATION:** ✓ **LOSS OF RESPONSE:** Reinduction with tofacitinib 10 mg twice daily may be considered. Efficacy may be regained by 8 weeks of 10 mg twice daily therapy.
Filgotinib	TA792	Jun-22	Treating 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. ✘ **DOSE INTENSIFICATION is NOT commissioned.**
Upadacitinib	TA856	Jan-23	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. ✘ **DOSE INTENSIFICATION is NOT commissioned.**
Ozanimod	TA828	Oct-22	Treating moderately to severely active ulcerative colitis in adults when 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. ✘ **DOSE INTENSIFICATION is NOT commissioned.**

Notes:

1. 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.

2. If patients on JAK inhibitors need to change therapy due to the MHRA alert[2] issued 26th April 2023, then this would be considered a change **within** the same treatment line.

3. Ustekinumab is commissioned as per the SmPC i.e. at either 8 or 12 weekly intervals.

* Local commissioning agreement (not licensed).

NICE TA and place in pathway

Crohn's disease

Drug	Crohn's disease		
	TA	Date	Place in pathway
Adalimumab biosimilar	TA187	May-10	Treating 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. **DOSE INTENSIFICATION** (maintenance to be reviewed): Adalimumab: ✓ 40mg once weekly for 12 weeks **or** 80mg every two weeks for 12 weeks Infliximab IV*: ✓ 10mg/kg every 8 weeks for 3 doses (24 weeks), 5mg/kg every 4 weeks for 3 doses (12 weeks) **or** 5mg/kg every 6 weeks for 2 doses (12 weeks)
Infliximab biosimilar			
Vedolizumab	TA352	Aug-15	Treating 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. ✘ **DOSE INTENSIFICATION is NOT commissioned.**
Ustekinumab	TA456	Jul-17	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. **DOSE INTENSIFICATION** (maintenance to be reviewed): ✓ 90mg every 8 weeks for 2 doses (16 weeks)
Upadacitinib	TA905	June-23	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. ✘ **DOSE INTENSIFICATION is NOT commissioned.**
Risankizumab	TA888	May-23	Treating 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. ✘ **DOSE INTENSIFICATION is NOT commissioned.**

Notes:

1. The clinical definition for severe active disease normally but not exclusively, corresponds to a Crohn's Disease Activity Index (CDAI) score of 300 or more, or a Harvey-Bradshaw score of 8 to 9 or above or an alternative QOL score.

2. Treatment should be given until treatment failure (including the need for surgery) 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.

3. For vedolizumab - 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.

4. If patients on JAK inhibitors need to change therapy due to the MHRA alert[2] issued 26th April 2023, then this would be considered a change **within** the same treatment line.

* Local commissioning agreement (not licensed).

References:

1 NICE Technical Guidance TA 187, TA352, TA456, TA329, TA163, TA342, TA633, TA547, TA792, TA828, TA856,TA888. Available at https://www.nice.org.uk

2 Drug Safety Update. Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality. Available at: Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality

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Agreed date: Area Prescribing Committee October 2023 **Review date:** October 2026