DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Adult with moderately to severely active Ulcerative Colitis

Does the patient have an acute exacerbation of severely acute ulcerative colitis

- Yes → Treat according to NICE TA163 (Infliximab (TNFi))
- No

Has the patient's disease responded inadequately **or** is the patient intolerant of **or** does the patient have contraindications to conventional therapy, including:

- Mercaptopurine/azathiopurine **and/or**
- Corticosteroid treatments?

First line treatment option:

Adalimumab biosimilar (TNFi) (TA329)

Alternate treatment options if first line biologic is clinically inappropriate. Use the less expensive drug as a planned course of treatment (see note 1):

- Etrasimod (S1P) (TA956)
- Filgotinib (JAK1) (TA792) or
- Upadacitinib (JAK1) (TA856) (at 15mg maintenance dose) or
- Tofacitinib[1] (JAK1 JAK3) (TA547) or
- Infliximab biosimilar SC/IV (TNFi) (TA329) or
- Golimumab (TNFi) (TA329) or
- Ozanimod (S1P) (TA828) or
- Mirikizumab (IL23) (TA925) (at standard maintenance dose) or
- Upadacitinib (JAK1) (TA856) (at 30mg maintenance dose) or
- Ustekinumab biosimilar (IL12/IL23) (TA633) or
- Vedolizumab SC or IV[12] (Anti-integrin) (TA342)

Note 1: 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 active disease. This should be determined by

- Clinical symptoms and
- biological markers and
- investigation, including endoscopy if necessary

Please note:
Dose escalation of biologic drugs is not currently recommended by NICE

[1] The following treatments may be given to patients who have had an inadequate response or lost response to, or who were intolerant to either conventional therapy or a TNF inhibitor.

- Adalimumab (TNFi) (TA329) or
- Etrasimod (S1P) (TA956) or
- Filgotinib (JAK1) (TA792) or
- Upadacitinib (JAK1) (TA856) (at 15mg maintenance dose) or
- Tofacitinib (JAK1 JAK3) (TA547) or
- Ozanimod (S1P) (TA828) or
- Mirikizumab (IL23) (TA925) (at standard maintenance dose) or
- Upadacitinib (JAK1) (TA856) (at 30mg maintenance dose) or
- Ustekinumab biosimilar (IL12/IL23) (TA633) or
- Vedolizumab SC or IV (Anti-integrin) (TA342)

[2]Continued therapy for patients with UC should be carefully reconsidered if no evidence of therapeutic benefit is observed by week 10.

The ICB will only commission 4 treatment options (3 switches) per patient - this includes treatment failure and contra-indication/ intolerance. JAPC recognises the RMOC statement. Further sequential use outside of the commissioning algorithm should be undertaken after advice via MDT in-line with Trust processes but is limited by clinical appropriateness and safety

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery)? (See appendix 1 for adequate response time)

- Yes → Cease treatment with the biologic/advanced treatment drug used.
- No

At 12 months after the start of treatment, reassess the disease.

- No

Is the patient in stable clinical remission?

- Yes
- No

Discuss the risks and benefits of continued treatment. Is a trial withdrawal considered appropriate?

- Yes → Trial withdrawal from biologic/ advanced treatment drug used. Restart treatment if patient relapses after treatment is stopped.
- No
- No → Maintain treatment and reassess patient at least every 12 months.

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Appendix 1- Dosing schedule in UC

Biologic/advanced treatment		Induction phase	Maintenance phase	Adequate response time (weeks)
Subcutaneous/intravenous injections				
Adalimumab (SC)	Adalimumab is a recombinant human monoclonal antibody that binds specifically to tumour necrosis factor alpha (TNF-α)	Week 0 - 160mg SC Week 2 - 80mg SC	40mg every other week thereafter.	2 - 8 weeks after starting treatment
Golimumab (SC) *Only recommended if the company provides the 100mg dose of golimumab at the same cost as the 50mg dose, as agreed in the patient access scheme.*	Human IgG1κ monoclonal antibody produced by a murine hybridoma cell line with recombinant DNA technology	**<u>if patient weighs <80kg</u>** Week 0 - 200mg SC Week 2 - 100mg SC	50mg every 4 weeks thereafter.	12 - 14 weeks after starting treatment
		<u>if patient weighs >80kg</u> Week 0 - 200mg SC Week 2 - 100mg SC	100mg every 4 weeks thereafter.	
Infliximab (SC)	Infliximab is a chimeric human-murine IgG1 monoclonal antibody	Week 0, 2 – 5mg/kg IV Week 6 – 120mg SC	120mg SC every 2 weeks	Within the first 14 weeks
Infliximab (IV)		Week 0 - 5mg/kg IV Week 2 - 5mg/kg IV Week 6 - 5mg/kg IV	5mg/kg IV every 8 weeks	
Mirikizumab (IV/SC)	Mirikizumab is a monoclonal antibody and is designed to attach to interleukin-23 and block its activity.	Week 0 – 300mg IV Week 4 – 300mg IV Week 8 – 300mg IV	200mg SC every 4 weeks	12 weeks after starting treatment For patients who do not achieve adequate therapeutic benefit at week 12 of induction dosing, mirikizumab 300 mg by intravenous infusion may be continued at weeks 12, 16 and 20. If therapeutic benefit is achieved with the additional intravenous therapy, patients may initiate mirikizumab subcutaneous maintenance dosing (200 mg) every 4 weeks, starting at week 24. Mirikizumab should be discontinued in patients who do not show evidence of therapeutic benefit to extended induction therapy by week 24. Patients with loss of therapeutic response during maintenance treatment may receive 300 mg mirikizumab by intravenous infusion every 4 weeks, for a total of 3 doses (re-induction). If clinical benefit is achieved from this additional intravenous therapy, patients may resume mirikizumab subcutaneous dosing every 4 weeks. The efficacy and safety of repeated re-induction therapy have not been evaluated.

Ustekinumab biosimilar (IV/SC)	Ustekinumab is a fully human IgG1κ monoclonal antibody to interleukin (IL)-12/23	Week 0 - 6 mg/kg IV	Week 8 – 90mg SC Thereafter every 12 weeks	Patients who have not had an adequate response 8 weeks after the first subcutaneous dose (week 16) may have a second subcutaneous dose at this time, to allow for delayed response. Patients who lose response on dosing every 12 weeks may benefit from an increase in dosing frequency to every 8 weeks. Patients may subsequently have ustekinumab every 8 weeks or every 12 weeks according to clinical judgement.
Vedolizumab (SC)	Vedolizumab is a humanised IgG1 monoclonal antibody that binds to the human α4β7 integrin.	Week 0 - 300mg IV Week 2 - 300mg IV Week 6 - 300mg IV*	108mg SC every 2 weeks thereafter	Observed by week 10. *The recommended dose regimen of subcutaneous vedolizumab as a maintenance treatment, following at least 2 intravenous infusions, is 108 mg administered by subcutaneous injection once every 2 weeks.
Vedolizumab (IV)	Vedolizumab is a humanised IgG1 monoclonal antibody that binds to the human α4β7 ntegrin.	Week 0 - 300mg IV Week 2 - 300mg IV Week 6 - 300mg IV	300mg IV every 8 weeks thereafter	Observed by week 10.
Oral preparations				
Etrasimod (Oral)	Etrasimod is a sphingosine 1-phosphate receptor modulator that binds to S1P receptors 1, 4 and 5 (S1P1,4,5) and is a balanced G-protein and beta-arrestin agonist at S1P1	2mg once daily	2mg once daily	Effectiveness assessed at 12 weeks in clinical trials
Filgotinib (Oral)	Filgotinib is an inhibitor of JAK1	200mg OD for 10 weeks	200mg OD	10 weeks after starting treatment If adequate therapeutic benefit is not achieved by week 10 the induction dose can be taken for an additional 12 weeks (22 weeks in total). If no therapeutic benefit is shown after 22 weeks, treatment should be discontinued.
Ozanimod (Oral)	Ozanimod is a selective sphingosine 1-phosphate (S1P) receptor modulator with specificity for receptor subtypes 1 and 5	Days 1 to 4 - 0.23 mg once daily Days 5 to 7 - 0.46 mg once daily Days 8 and thereafter - 0.92 mg once daily	0.92 mg once daily	Effectiveness assessed at 10 weeks in clinical trials
Tofacitinib (Oral)	Tofacitinib is an inhibitor of JAK1 and JAK3	10mg BD for 8 weeks 10 mg twice-daily dose of tofacitinib must **not** be prescribed in patients with	5mg BD	If adequate therapeutic benefit is **not** achieved by week 8 the induction dose can be taken for an additional 8 weeks (16 weeks in total). Induction therapy should be stopped if there is no evidence of therapeutic benefit by week 16.

		one or more risk factors for pulmonary embolism. See MHRA warning here 10 mg twice-daily dose of tofacitinib should **not** be used in patients who are at high risk of blood clots unless there is no suitable alternative treatment. Patients older than 65 years of age should be treated with tofacitinib only when there is no alternative treatment. See EMA warning here Tofacitinib should not be used in patients older than 65 years of age, people who are current or past smokers, or individuals with other cardiovascular (such as diabetes or coronary artery disease) or malignancy risk factors unless there are no suitable treatment alternatives See MHRA warning here		For patients whose disease has responded inadequately to tumour necrosis factor antagonist therapy, consider continuing the 10-mg twice-daily dose for maintenance in order to maintain therapeutic benefit.
Upadacitinib (Oral)	Selective and reversible inhibitor of the Janus-associated tyrosine kinase JAK1.	45mg once daily for 8 weeks	15mg once daily 30mg once daily 30mg dose maybe appropriate for patients with high disease burden or requiring 16-week induction or those patients who do not show adequate therapeutic benefit to 15mg OD.	For patients who do not achieve adequate therapeutic benefit by week 8, upadacitinib 45 mg once daily may be continued for an additional 8 weeks. Upadacitinib should be discontinued in any patient who shows no evidence of therapeutic benefit by week 16.