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)

No

Has the patient's disease failed to respond to **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)

As part of a planned course of treatment

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

- Tofacitinib[1] (JAK1/3) (TA547) (See MHRA warning and EMA warning) or
- Infliximab biosimilar (TNFi) (TA329) or
- Golimumab (TNFi) (TA329) 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 oral TNF inhibitor.

- Tofacitinib (JAK1/3) (TA547)
- Ustekinumab (IL12/IL23) (TA633)
- 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.

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

Yes → Cease treatment with the biologic drug used.

No

At 12 months after the start of treatment, reassess the disease. Is there evidence of response active disease?

Yes → Maintain treatment and reassess patient at least every 12 months.

No

Is the patient in stable clinical remission?

Yes → Maintain treatment and reassess patient at least every 12 months.

No

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

Yes → Trial withdrawal from biologic drug used. Restart treatment if patient relapses after treatment

No → Maintain treatment and reassess patient at least every 12 months.

The CCG's 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

Date updated: June 2020

Local variation to NICE | NICE approved treatment

Appendix 1- Dosing schedule in UC

Biologic		Induction phase	Maintenance phase	Adequate response time (weeks)
Adalimumab (SC)	Adalimumab is a recombinant human monoclonal antibody that binds specifically to tumour necrosis factor alpha (TNF-α)	Induction phase • Week 0 - 160mg SC • Week 2 - 80mg SC	Maintenance phase • 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	Induction phase- **<u>if patient weighs <80kg</u>** • Week 0 - 200mg SC • Week 2 - 100mg SC	Maintenance phase • 50mg every 4 weeks thereafter.	12 - 14 weeks after starting treatment
		Induction phase **<u>if patient weighs >80kg</u>** • Week 0 - 200mg SC • Week 2 - 100mg SC	Maintenance phase • 100mg every 4 weeks thereafter.	
Infliximab biosimilar IV (Inflectra)	Infliximab is a chimeric human-murine IgG1 monoclonal antibody	Induction phase • Week 0 - 5mg/kg IV • Week 2 - 5mg/kg IV • Week 6 - 5mg/kg IV	Maintenance phase • 5mg/kg IV every 8 weeks	Within the first 14 weeks
Infliximab originator IV (Remicade)	Infliximab is a chimeric human-murine IgG1 monoclonal antibody	Induction phase • Week 0 - 5mg/kg IV • Week 2 - 5mg/kg IV • Week 6 - 5mg/kg IV	Maintenance phase • 5mg/kg IV every 8 weeks	
Tofacitinib	Tofacitinib is an inhibitor of JAK1 and JAK3	Induction phase • 10mg BD for 8 weeks 10 mg twice-daily dose of tofacitinib must **<u>not</u>** be prescribed in patients with one or more risk factors for pulmonary embolism. See MHRA warning here 10 mg twice-daily dose of tofacitinib should **<u>not</u>** 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	Maintenance phase • 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. 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.
Ustekinumab	Ustekinumab is a fully human IgG1κ monoclonal antibody to interleukin (IL)-12/23	Induction phase • Week 0 - 6 mg/kg IV	Maintenance phase • 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.	Induction Phase • Week 0 - 300mg IV • Week 2 - 300mg IV • Week 6 - 300mg IV*	Maintenance phase • 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 integrin.	Induction Phase • Week 0 - 300mg IV • Week 2 - 300mg IV • Week 6 - 300mg IV	Maintenance phase • 300mg IV every 8 weeks thereafter	Observed by week 10.