Adult (age≥18 years) High Cost Drugs treatment pathway for moderately to severely active ulcerative colitis (UC) - based on NICE TAs 163, 329, 342, 547, 633, 792, 828, 856, 925, 998

Does the adult have moderately to severely active UC (see Note 1)?
(Go to page 2 for pathway 'adult hospitalised with an acute exacerbation of severely active UC'

Yes

Has there been lack/loss of response, intolerance or contraindication to optimised conventional therapy (Note 2) taken for an adequate period, including;
- 5-aminosalicylates and
- Corticosteroids (includes steroid dependence or requirement for regular repeat courses) and
- Azathioprine/6-mercaptopurine

BOX 1

Treatment options

Usually start treatment with least expensive appropriate drug: see Note 3
(options are listed by mechanism of action & overall cost [including admin costs])

TNF inhibitors
1. **Adalimumab (biosimilar)** **usual 1st line choice**
2. Infliximab IV (biosimilar)
3. Golimumab

Sphingosine 1-phosphate (S1P) receptor modulators
1. Ozanimod (first line option only if infliximab is not suitable)
2. Etrasimod

JAK inhibitors
1. Filgotinib
2. Upadacitinib
3. Tofacitinib

IL12/23 inhibitor
1. Ustekinumab
(first line option only if TNF inhibitor is not suitable/contraindicated)

IL 23 inhibitor
1. Mirikizumab
2. Risankizumab (*most costly option*)
(both first line option only if TNF inhibitor is not suitable/contraindicated)

α4β7 integrin antagonist
1. Vedolizumab Subcutaneous (SC)
2. Vedolizumab Intravenous (IV)

Give as a planned course of treatment until treatment failure (including the need for surgery), or until 12 months after the start of treatment, whichever is shorter.

Response (Note 4) **within 8 weeks adalimumab, 14 weeks (3 doses) infliximab, 14 weeks (4 doses) golimumab, 10 weeks filgotinib, 8 weeks upadacitinib** (if adequate response not achieved by week 8, induction can be extended for additional 8 weeks)**, 8 weeks tofacitinib** (if adequate response not achieved by week 8, induction can be extended for additional 8 weeks), **12 weeks etrasimod, 10 weeks ozanimod**, **16 weeks ustekinumab, 12 weeks mirikizumab** (if adequate response not achieved by week 12, induction can be extended for an additional 12 weeks), **12 weeks risankizumab** (if adequate response not achieved by week 12 the higher dose can be given for a further 12 weeks) **or 10 weeks vedolizumab treatment?**

No

Consider switch to alternative TNF inhibitor, JAK inhibitor, ozanimod, etrasimod, ustekinumab, mirikizumab, vedolizumab (SC/IV) or risankizumab if no response or intolerance to initial treatment
(If more than 1 treatment is suitable, the least expensive should be chosen, see note 3)

GO TO BOX 1

Yes

Continue maintenance dose.
Where a trial withdrawal at 12 months is likely, from 8 months consider the establishment of an optimised dose of conventional therapy unless intolerant/contraindicated.
At any point before 12 months of treatment has passed, has treatment failed (including the need for surgery)?

No

Yes

Where available, consider TNF inhibitor drug and antibody levels to support a decision to dose escalate or switch

Consider switch to alternative TNF inhibitor, JAK inhibitor, ozanimod, etrasimod, ustekinumab, mirikizumab, vedolizumab (SC/IV) or risankizumab
(If more than 1 treatment is suitable, the least expensive should be chosen, see Note 3)

GO TO BOX 1

BOX 2

Consider dose escalation or interval reduction of adalimumab/infliximab/ ustekinumab/ tofacitinib to recapture response. **Consider single re-induction of** mirikizumab.

At 12 months after start of treatment reassess the disease (Note 5).
Where there is an ongoing adequate response is there evidence of ongoing active disease?

Yes

Discuss the risks and benefits of continued treatment.
Maintain treatment.

Reassess patient at least every 12 months to determine if ongoing treatment is still clinically appropriate.

If loss of response at any time, consider: (Where available, consider TNF inhibitor drug and antibody levels to support a decision to dose escalate or switch):
- trial dose escalation of current adalimumab / infliximab / tofacitinib/ ustekinumab to recapture response or a single re-induction of mirikizumab (go to box 2)

No

Discuss the risks & benefits of continued treatment.
Consider trial withdrawal of patients in stable clinical remission.
If intolerance/contraindication to maintenance conventional therapy & only maintenance treatment option is a high-cost drug, a trial withdrawal does not need to be attempted.

Patients without active disease in stable clinical remission should be considered for a trial withdrawal

Patients whose disease has relapsed after treatment is stopped may restart treatment **(go to box 1)**

Patients whose disease has relapsed on previous trial withdrawal may continue maintenance treatment without further trial withdrawal even if in stable clinical remission

No

Response to re-induction?

Yes

De-escalate to standard subcutaneous dosing

No

OR

Response to escalated dose?

Yes

De-escalate to standard dose. **Response on return to standard dose?**

Yes

No

Consider trial of maintenance escalated dose for patients with clear objective evidence of response to escalated dose & loss of response on de-escalation to standard dose.
Alternatively consider alternative TNF inhibitor, JAK inhibitor, ozanimod, etrasimod, ustekinumab, mirikizumab, vedolizumab (SC/IV) or risankizumab **(go to box 1)**

Reassess patient after 6 months and then at least every 12 months to determine if ongoing escalated dose is still clinically appropriate (see Note 5).

Trial of de-escalation in patients without active disease in stable clinical remission

Patients whose disease has relapsed after trial de-escalation may continue escalated dose

Up to 7 sequential high-cost drugs, 6 treatment modalities, are routinely commissioned (including 2 TNF inhibitors)

Refer to individual SPC's for full prescribing information including dose restrictions, adverse drug reactions, contraindications and cautions; and to Drug Safety Updates for latest drug safety notices.

Adult (age≥18 years) High Cost Drugs treatment pathway for moderately to severely active ulcerative colitis (UC) - based on NICE TAs 163, 329, 342, 547, 633, 792, 828, 856, 925, 998

Note 1: Moderately to severely active UC
- Corresponds to a Mayo score of 6-12

If alternative disease severity scoring system used, evidence of correlation with disease severity and response criteria to be provided.

Note 2: Conventional immunosuppressive therapy
Usual Adult maintenance treatment dose ranges:
- Azathioprine - 2 mg/kg/day to 2.5 mg/kg/day
- Mercaptopurine - 0.75 mg/kg/day to 1.5 mg/kg/day

Note 3: Choice and Less expensive drug
Choice of treatment should be made on an individual basis after discussion between the responsible clinician and the patient about the advantages and disadvantages of the treatments available. This should take into consideration therapeutic need and whether or not the patient is likely to adhere to treatment.

If more than 1 treatment is suitable, the least expensive should be chosen (taking into account administration costs, dosage and price per dose). **This is usually adalimumab (biosimilar).**

If least expensive choice not selected rationale to be provided.

Note 4: Response definitions
Complete Mayo:
- decrease in full Mayo score from baseline by ≥3 points and ≥30%, AND
- decrease in rectal bleeding sub-score from baseline by ≥1 point, OR absolute rectal bleeding sub-score of 0 or 1.

Partial Mayo (where further endoscopy not considered necessary/appropriate):
- decrease in partial Mayo score from baseline of ≥2 points and ≥25% AND
- decrease in rectal bleeding sub-score from baseline of ≥1 point OR absolute rectal bleeding sub-score of 0 or 1.

If alternative disease severity scoring system used, evidence of correlation with disease severity and response criteria to be provided.

Note 5: 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. This should be determined by:
- Clinical symptoms and
- Biological markers and
- Investigation, including endoscopy if necessary.

Clinical Remission:
- complete or partial Mayo score of ≤2 points and no individual sub-score >1

Note 6: Dose Escalation adalimumab/infliximab / tofacitinib/ ustekinumab
When response to induction and maintenance treatment but then loss of response, an attempt to re-capture response with temporary period of increased dose / shortened interval between doses may be made: **infliximab** - 1 dose of 10mg/kg or 3 doses of 5mg/kg given 4-6 weekly and then stretch back to 8 weekly; **adalimumab** – 40mg weekly for up to 8 weeks then stretch back to every other week; **tofacitinib** 10mg twice daily for 8 weeks then reduce back to 5mg twice daily (*refer to SPC and Drug Safety Updates for restrictions for 10mg twice daily dose*); **ustekinumab** 2 doses 8 weekly, then stretch back to 12 weekly.

Note Off label use
- Infliximab dose escalation for UC is off label use
- Adalimumab use for acute exacerbation of severely active UC is off label

Re-induction with mirikizumab
When response to induction and maintenance treatment but then loss of response, a single attempt to recapture response with 300 mg mirikizumab by intravenous infusion every 4 weeks, for a total of 3 doses. If clinical benefit is achieved, resume subcutaneous dosing every 4 weeks.

Is the adult hospitalised with an acute exacerbation of severely active UC (Mayo score >8)?

Yes

Has there been lack/loss of response, intolerance or contraindication to optimised conventional therapy (Note 2) taken for adequate period, including;
- 5-aminosalicylates and azathioprine/6-mercaptopurine (not required if clinically inappropriate and rapid acting treatment required)
- corticosteroids (including IV for 72 hours)

Yes

Is ciclosporin contraindicated or clinically inappropriate?

Yes

Infliximab biosimilar (3 dose induction course).
Adalimumab (biosimilar) (for 6 weeks) may be considered if infliximab inappropriate or preference for s/c administration.
Continued treatment indicated when criteria for moderately to severely active UC fulfilled after induction.

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NICE recommends if patients and their clinicians consider a medicine to be one of a range of suitable treatments, the least expensive treatment should be chosen, taking into account administration costs, dosage, price per dose and commercial arrangements. Therefore, in line with this recommendation the order of preference of treatments in Box 1 will be updated accordingly as prices change or biosimilar medicines become available.