South West London Inflammatory Bowel Disease Pathway

Developed and agreed by the SWL IBD Medicines Optimisation Clinical Network

Version 5.2

Contents:

Approved by: SWL Integrated Medicines Optimisation Committee

Date: 18/09/2024

This pathway provides guidance to healthcare professionals in primary and secondary care for adult patients only. However, always use clinical judgement when a patient presents with IBD symptoms.

SWL IBD Pathway – Presenting with IBD symptoms

Version 5.2 (References: 1, 2, 3, 4 with local agreements)

Patient presenting with lower GI symptoms suggestive of IBD

Is the patient known to have IBD?

Yes

Go to:
- **CROHN'S DISEASE – Pathway 1: Inducing and maintaining remission (page 3)**
  OR
- **ULCERATIVE COLITIS – Pathway 1: Inducing and maintaining remission (page 9)**

No

Does patient have any of the following symptoms? (Red Flag Indicators)?
- Unintentional weight loss
- Rectal bleeding
- Family history of bowel/ovarian cancer
- Anaemia
- Abdominal/rectal mass
- Nocturnal symptoms
- Raised inflammatory markers
- Bloody diarrhoea
- Systemically unwell (tachycardia, fever, hypotension, nausea and vomiting, abdominal pain)

No

Primary diagnostics
- FBC
- CRP
- Coeliac screen
- Stool MCS (microbiology, culture and sensitivity)
- U&Es
- Bone profile
- LFTs
- Faecal calprotectin (FCP)

Yes

Suspected cancer → **Follow SWL cancer referral pathway**

Suspected acute severe IBD → **Discuss with IBD team**

Bloods abnormal and/or FCP > 150 → **New IBD referral** (to be seen within 4 weeks)

Refer if high suspicion

Bloods normal and FCP 50 - 150 → Repeat FCP in 4 weeks from first test
Consider IBS in meantime → FCP rising > 150

Yes → **New IBD referral** (to be seen within 4 weeks)

No → **Treat as IBS** (note: equivocal FCP can be monitored over a longer period every 4 – 6 weeks)

Bloods normal and FCP < 50 → **Treat as IBS** (note: equivocal FCP can be monitored over a longer period every 4 – 6 weeks)

IBD contact details for healthcare professionals:	Tel:	Switchboard:	E-mail:
Epsom and St. Helier Hospital (Epsom site)	IBD helpline: 01372 735363 Secretary: 01372 735129	02082962000 (ext:5129)	esth.cnsgastroegh@nhs.net
Epsom and St. Helier Hospital (St. Helier site)	IBD helpline: 07831 120969	02082962000 (ext:2340)	esth.ibdteamsth@nhs.net
Kingston Hospital	IBD helpline: 020 8934 2760	020 8546 7711	khft.ibdadviceline@nhs.net
St. George's Hospital	IBD helpline: 020 8725 2996	020 8672 1255	ibdadviceline@stgeorges.nhs.uk
Croydon University Hospital	IBD helpline: 020 8401 3000	020 8401 3000 (ext:4484)	ch-tr.ibdcuh@nhs.net

SWL IBD Pathway CROHN'S DISEASE - Pathway 1: Inducing and maintaining remission

Version 5.2 (Reference: NICE Guideline NG129[5])

Advice

Discuss treatment options and monitoring . Give advice on:

- Smoking cessation
- Patient experience
- Medicines adherence
- Fertility

If appropriate give information on:

- Diet and nutrition
- Fertility, pregnancy and sexual relationships
- Prognosis
- Side effects of treatment
- Cancer risk
- Surgery
- Support groups

INDUCING REMISSION

First presentation or single inflammatory exacerbation in a 12 months period

Monotherapy with conventional glucocorticosteroid:

- Prednisolone **or**
- Methylprednisolone **or**
- Hydrocortisone IV

Patients who decline, cannot tolerate or have a contraindication to conventional glucocorticosteroids:

- Budesonide (disto-ileal, ileo-caecal or right-sided colonic disease) **or**
- Aminosalicylate (*unlicensed*) - less effective than budesonide

Explain that budesonide and mesalazine are less effective than conventional glucocorticosteroids but may have fewer side-effects.

Do not offer:

- Budesonide or mesalazine for severe presentations or exacerbations
- Azathioprine, 6-mercaptopurine or methotrexate as monotherapy to induce remission

- 2 inflammatory exacerbations in a 12 months period **or**
- steroid dependent (glucocorticosteroid dose cannot be tapered)

Surgery (distal ileum):
Consider if disease is limited to distal ileum early in the course of the disease as an alternative to medical treatment

Balloon dilatation: Consider if strictures

Consider immuno-modulators

Consider biologics if severe active Crohn's disease
(HBI ≥ 8-9 or CDAI ≥ 300)

CROHN'S DISEASE – Pathway 2: Immuno-modulators (page 4)

CROHN'S DISEASE – Pathway 3: High Cost Drugs (page 5)

MAINTAINING REMISSION

Discuss options of treatment and no treatment, including the risk of inflammatory exacerbations and side effects

No treatment

- Agree follow-up plan and frequency
- Give advice on symptoms that may suggest a relapse and require medical attention e.g.
  - Unexplained weight loss
  - Adominal pain
  - Diarrhoea
  - General ill-health
- Emphasise importance of not smoking

After surgery i.e. ileocolonic Crohn's disease with complete macroscopic resection and no residual disease:

- Consider **azathioprine with up to 3 months metronidazole**
- Consider **azathioprine alone** (if metronidazole not tolerated)

Do not offer: biologics or budesonide

If residual active disease (see 'Inducing remission' above)

Immuno-modulator treatment

Do not offer: conventional glucocorticosteroids or budesonide

CROHN'S DISEASE – Pathway 2: Immuno-modulators (page 4)

Monitoring: Offer colonoscopic surveillance according to NICE Clinical Guideline CG118 [6]. Assess the risk of fragility fractures according to NICE Clinical Guideline CG146 [7] (adults).

SWL IBD Pathway CROHN'S DISEASE - Pathway 2: Immuno-modulators

Version 5.2 (References: 5, 8, 9, 10, 11, 12, 13 with local agreements)

Adult with Crohn's disease

After surgery in patients with adverse prognostic factors such as:
- > 1 resection
- Previously complicated/debilitating disease (e.g. abscess, involvement of adjacent structures, fistulating or penetrating disease)
- Ongoing smoking

- 2 or more inflammatory exacerbations in a 12 months period **or**
- steroid dependent (glucocorticosteroid dose cannot be tapered)

Consider immuno-modulator and discuss treatment choice with patient
- Vaccination and viral screen
- TPMT levels for thiopurines

Start immuno-modulator and increase gradually to maintenance dose – *all unlicensed*
- **1st choice:** Thiopurines (azathioprine or 6-mercaptopurine) +/- allopurinol (see dosing table)
- **2nd choice:** Methotrexate (subcutaneous or oral)
- **3rd choice:** Tioguanine (20 - 40mg daily) (if pancreatitis)[8] (subject to SWL formulary review/approval)

Is there a good response during first 12- 16 weeks at maximum tolerated doses?

Yes

Maintain treatment and consider initiation of shared care (for thiopurines/methotrexate only) after 3 months and if patient is stable (see shared care prescribing guidelines for monitoring frequency)

Consult with IBD service for advice if flare-up or side effects

No

Consider **alternative treatment/surgery**

No

Consider entry into **clinical trial**

No

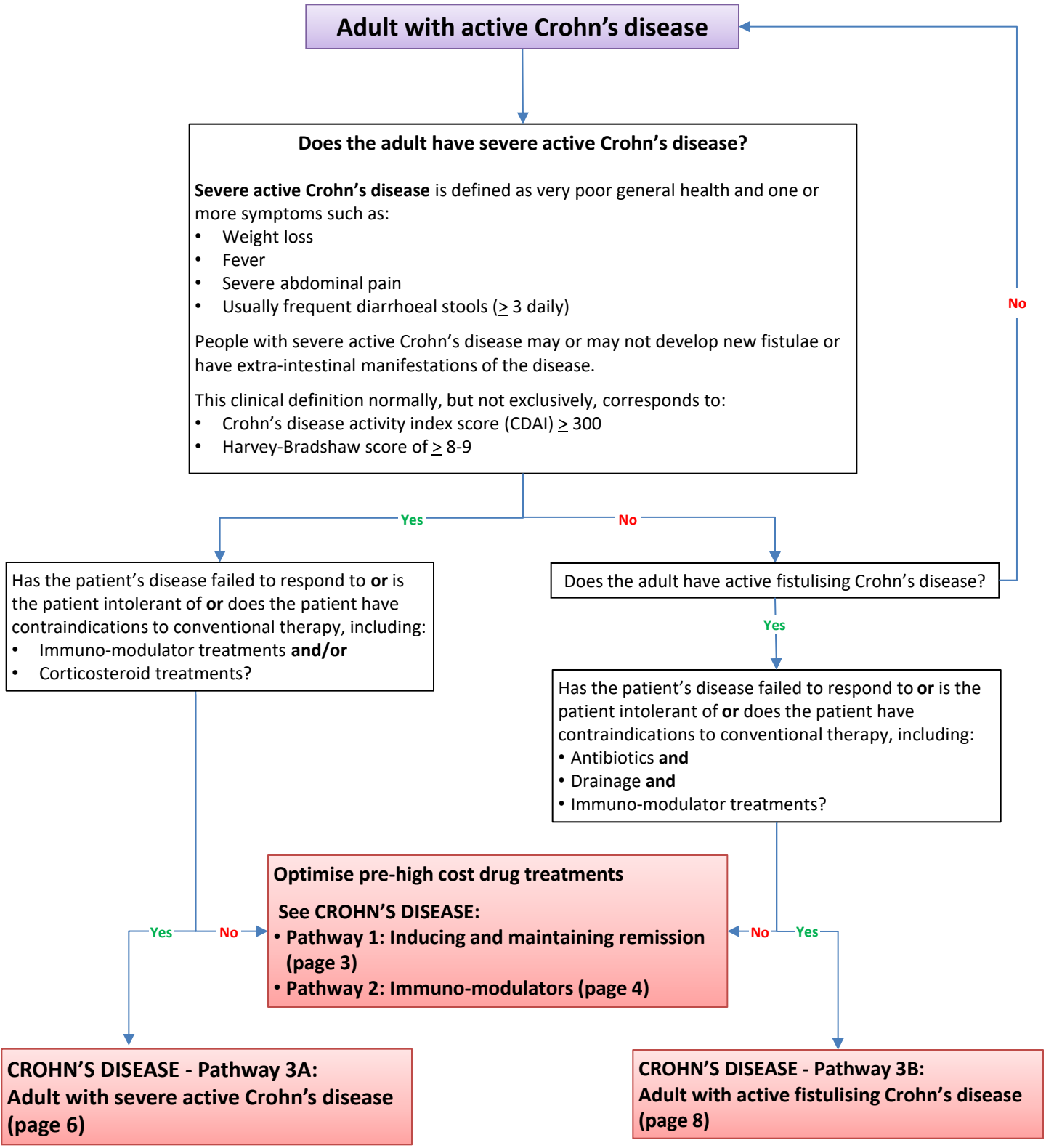
Consider **High Cost Drug** treatment alongside immunomodulator(s) where possible

CROHN'S DISEASE – Pathway 3: High Cost Drugs (page 5)

Dosing table [ref 8,9,10,11,12]	**TPMT normal activity (wild type)**	**TPMT intermediate activity (heterozygous)**	**TPMT low to no activity (homozygous)**
Azathioprine (AZA)	100% dose [2.0 - 2.5 mg/kg] [8,9,11]	50% dose [8,9,11] [1.0 - 1.25 mg/kg]	Not recommended [12]
Low dose azathioprine + allopurinol (100mg daily)	Initially 25% [8,12] of monotherapy dose [0.50 - 0.625mg/kg] Up to 50% [11] of monotherapy dose [1.0 -1.25mg/kg]	Initially 25% [8,12] of monotherapy dose [0.25 - 0.313mg/kg] Up to 50% [8] of monotherapy dose [0.5 - 0.625mg/kg]	Not recommended [12]
6-mercaptopurine (half of AZA dose)	100% dose [1.0 - 1.5 mg/kg] [8,9,11]	50% dose [11] [0.5 - 0.75mg/kg]	Not recommended [12]
Low dose 6-mercaptopurine + allopurinol (100mg daily)	Initially 25% [8,12] of monotherapy dose [0.25 - 0.375mg/kg] Up to 50% [11] of monotherapy dose [0.5 - 0.75mg/kg]	Initially 25% [8,12] of monotherapy dose [0.125 - 0.188mg/kg] Up to 50% [11] of monotherapy dose [0.25 - 0.375mg/kg]	Not recommended [12]

SWL IBD Pathway- CROHN'S DISEASE - Pathway 3: High Cost Drugs

Version 5.2 (Reference: NICE[14] with local agreements)



SWL IBD Pathway CROHN'S DISEASE - Pathway 3: High Cost Drugs

Version 5.2 (Reference: NICE[14] with local agreements)

Pathway 3A: Severe active Crohn's Disease

If there is more than one NICE approved treatment available, NICE recommends a discussion between the responsible clinician and the patient about the advantages and disadvantages of each treatment (considering therapeutic need and likely adherence to treatment).
If more than one treatment option is suitable, the least expensive will be chosen (taking into account administration costs, dosage and price per dose) unless an order of preference is stated in the NICE TAs. Drugs are listed in order of cost (including relevant administration costs, using list price or nationally (NICE) / locally (LPP) agreed contract prices).

Choose **ONE** option per step before moving onto the next step due to primary or secondary treatment failure. Select different drug class (see page 15) in each step (note 1,2,8)

STEP 1
Select from box A

*

STEP 2
Select from box B

*

STEP 3
Select from box B

*

Step 4 and subsequent steps
Multi-Trust MDT
Select from box B

*

Discontinue high cost drug treatment (note 9)

Box A: All listed drugs are available in step 1 (note 1,2,8)	
Adalimumab biosimilar (TA187) (note 3)	**£**
Ustekinumab biosimilar (TA456) Infliximab biosimilar SC/IV (TA187) (note 3) Upadacitinib (TA905) (only if TNF-inhibitors are contraindicated) (note 2)	**££**
Risankizumab (TA888) (only if TNF-inhibitors not suitable) (note 2)	**£££**
Vedolizumab SC/IV (TA352) (only if TNF-inhibitors are contraindicated or not tolerated) (note 2)	**££££**

Box B: All listed drugs are available in step 2 and subsequent steps (note 1,2,8)	
Adalimumab biosimilar (TA187) (note 3)	**£**
Ustekinumab biosimilar (TA456) Infliximab biosimilar SC/IV (TA187) (note 3) Upadacitinib (TA905)	**££**
Risankizumab (TA888)	**£££**
Vedolizumab SC/IV (TA352)	**££££**

***AFTER EACH STEP:** At any point **before 12 months** of treatment has passed, has treatment failed? (including the need for surgery) (note 3,4,5,7). IF

- **Yes** – Move to next step
- **No** – Maintain treatment and reassess **at 12 monthly intervals** after start of treatment (note 4,6) for evidence of on-going active disease.
  - **If evidence of on-going active disease**, maintain treatment and reassess at least every 12 months (note 3,4,5,6,7). If appropriate move to next step in treatment pathway if response is lost at any point during therapy.
  - **If no evidence of on-going active disease and patient is not in stable clinical remission**, maintain treatment and reassess at least every 12 months (note 3,4,5,6,7). If appropriate move to next step in treatment pathway if response is lost at any point during therapy.
  - **If no evidence of on-going active disease and patient is in stable clinical remission**, discuss the risks and benefits of continued treatment and whether a trial withdrawal is considered appropriate. If deemed appropriate, consider trial withdrawal and restart treatment if patient relapses after treatment is stopped

SWL IBD Pathway CROHN'S DISEASE - Pathway 3: High Cost Drugs

Version 5.2 (Reference: NICE[14] with local agreements)

Pathway 3A: Severe active Crohn's Disease - Notes

Note 1- Adverse event or new contra-indication: Consider alternative from the same step (using the same or different drug class) (in steps 1, 2 and 3 only) if treatment is stopped due to an adverse event or new contra-indication **AND**:

- patient was responding to the drug **OR**
- response was not yet assessed i.e. before 12 (adalimumab), 6 (infliximab), 14 (vedolizumab) or 16 (ustekinumab) weeks of initiating treatment.

Note 2- Contraindications and cautions: see page 15.

Note 3- Primary / secondary treatment failure with adalimumab or infliximab: An alternative TNF-alpha inhibitor may be chosen from the same step (in steps 1,2 and 3 only), if considered clinically appropriate. This is restricted to ONE switch within the TNF-alpha inhibitor class.

Note 4- Treatment response: At 12 weeks (adalimumab), 6 weeks (infliximab), 14 weeks (vedolizumab), 16 weeks (ustekinumab), 24 weeks (upadacitinib), clinician's discretion (risankizumab) after the start of treatment and at least at 12 monthly intervals thereafter, assess disease to determine if response is adequate and if ongoing treatment is still appropriate. Treatment should only be continued if there is clear evidence of response to drug treatment defined by a decrease in Harvey-Bradshaw Index by $\geq$ 3 points or CDAI by $\geq$ 70 points.

Note 5- Temporary dose escalation for patients with secondary treatment failure as follows:

- Adalimumab: 40mg / week for 3 months **or** 80mg / 2 weeks for 3 months
- Infliximab: 5mg/kg / 4-6 weeks for 3 doses **or** 10mg/kg / 8 weeks for 3 doses
- Ustekinumab: 90mg / 8 weeks for 4 months
- Vedolizumab: 300mg / 4 weeks for 3 months, ONLY if no alternative drug options exist and agreed through SWL multi-Trust MDT. Dose escalation is not commissioned if alternative drug options can be used.

For details and subsequent dose escalation requests see page 17.

Note 6- Disease reassessment: At 12 months after the start of treatment, reassess disease to determine whether ongoing treatment is clinically appropriate. Only continue treatment if there is clear evidence of ongoing active disease determined by:

- Clinical symptoms **and**
- Biological markers **and**
- Investigation, including endoscopy if necessary

Note 7- Drug levels and anti-drug antibodies: Consider where possible at clinician's discretion when considering switching drug within anti-TNF class or between classes.

Note 8- Immunomodulators: Optimise use before/ alongside biologics where possible.

Note 9- IFR: Requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process (see https://swlimo.southwestlondon.icb.nhs.uk/ for IFR policy and application form).

Clinicians and commissioners should refer to the relevant NICE TA and SPC for each drug for further information about their eligibility and prescription.

SWL IBD Pathway CROHN'S DISEASE - Pathway 3: High Cost Drugs

Version 5.2 (Reference: NICE [14] with local agreements)

Pathway 3B: Active fistulising Crohn's Disease

Note 4- Treatment response: At 6 weeks (infliximab) after the start of treatment and at least at 12 monthly intervals thereafter, asses disease to determine if response is adequate and if ongoing treatment is still appropriate. Treatment should only be continued if there is clear evidence of response to biologic treatment defined by a decrease in Harvey-Bradshaw Index by ≥ 3 points or CDAI by ≥ 70 points.

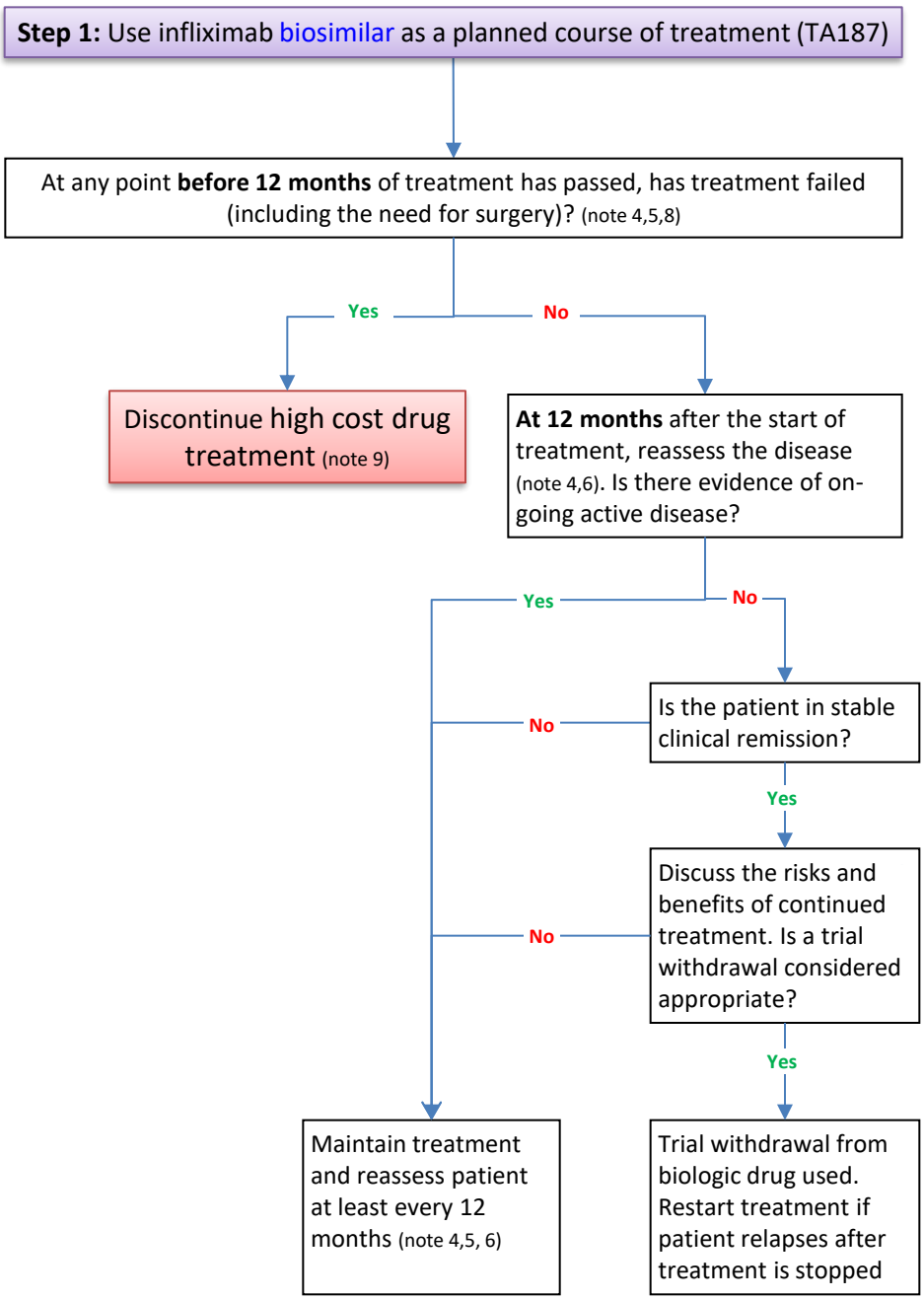
Note 5- Temporary dose escalation:
- Infliximab: 5mg/kg every 4-6 weeks for 3 doses **or** 10mg/kg every 8 weeks for 3 doses

For details and subsequent dose escalation requests see page 17.

Note 6- Disease reassessment: At 12 months after the start of treatment, reassess disease to determine whether ongoing treatment is clinically appropriate. Only continue treatment if there is clear evidence of ongoing active disease determined by:
- Clinical symptoms **and**
- Biological markers **and**
- Investigation, including endoscopy if necessary.

Note 8- Immunomodulators: Optimise use before/ alongside biologics where possible.

Note 9– IFR: Requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process to the relevant commissioning organisation (see https://swlimo.southwestlondon.icb.nhs.uk/ for IFR policy and application form).



SWL IBD Pathway ULCERATIVE COLITIS - Pathway 1: Inducing and maintaining remission

Version 5.2 (Reference: NICE Guideline NG130 [15] with local agreements)

Advice: Discuss the condition, associated symptoms, treatment options and monitoring with the patient and/or their parent or carer
Give advice on nature, frequency and severity of side effects of treatment and colorectal cancer risk

INDUCING REMISSION

Mild to moderate ulcerative colitis
For patients with a mild to moderate first presentation or inflammatory exacerbation

Proctosigmoiditis or left-sided ulcerative colitis:
- Topical aminosalicylate

If remission not achieved within 4 weeks:
- add oral aminosalicylate (high dose) **or**
- switch to oral aminosalicylate (high dose) + topical corticosteroid (time limited)

If further treatment needed:
- Stop topical treatments and offer oral aminosalicylate + oral corticosteroid (time limited e.g. prednisolone 40mg OD for 8 weeks)

If patient declines topical treatments:
- High dose oral aminosalicylate alone (not as effective as topical aminosalicylate)
- Add time limited course of oral corticosteroid (if remission not achieved within 4 weeks)

If patient cannot tolerate aminosalicylates:
- Topical or oral corticosteroid (time limited course)

Extensive disease:
- Topical aminosalicylate + high-dose oral aminosalicylate

If remission not achieved within 4 weeks:
- Switch to high dose oral aminosalicylate + oral corticosteroid (time limited)

If patient cannot tolerate aminosalicylates:
- Oral corticosteroid (time limited course)

Proctitis:
- Topical aminosalicylate

If remission not achieved within 4 weeks:
- Add oral aminosalicylate

If further treatment needed:
- Add topical or oral corticosteroid (time limited course e.g. prednisolone 40mg OD for 8 weeks)

If patient declines topical aminosalicylate:
- Oral aminosalicylate (not as effective as topical aminosalicylate)

If remission not achieved within 4 weeks:
- Add topical or oral corticosteroid (time limited course e.g. prednisolone 40mg OD for 8 weeks)

If patient cannot tolerate aminosalicylates:
- Topical or oral corticosteroid (time limited course e.g. prednisolone 40mg OD for 8 weeks)

If no improvement within 4 weeks of starting aminosalicylates or if symptoms worsen

Consider adding oral prednisolone (stop beclomethasone diproprionate)

If inadequate response after 2 - 4 weeks of oral prednisolone:

ULCERATIVE COLITIS - Pathway 2: Immuno-modulators (page 10)

Acute severe ulcerative colitis

Admit to hospital for treatment by gastroenterologist and colorectal surgeon (and paediatrician or obstetrics & gynaecology, paediatrician team if necessary)
Assess likelihood of needing surgery

ULCERATIVE COLITIS - Pathway 3: High Cost Drugs (page 11)

MAINTAINING REMISSION

Mild to moderate ulcerative colitis

Proctitis or proctosigmoiditis:
- Topical aminosalicylate (daily or intermittent) , with or without an oral aminosalicylate **or**
- Oral aminosalicylate alone (less effective)

Left-sided or extensive ulcerative colitis:
- Oral aminosalicylate (give a low maintenance dose in adults)

For patients with ≥ 2 inflammatory exacerbations in a 12 months period requiring systemic corticosteroids or in whom remission is not maintained with aminosalicylates

Consider immuno-modulators

For patients who decline, cannot tolerate or have a contraindication to immuno-modulators:
- Consider oral aminosalicylate

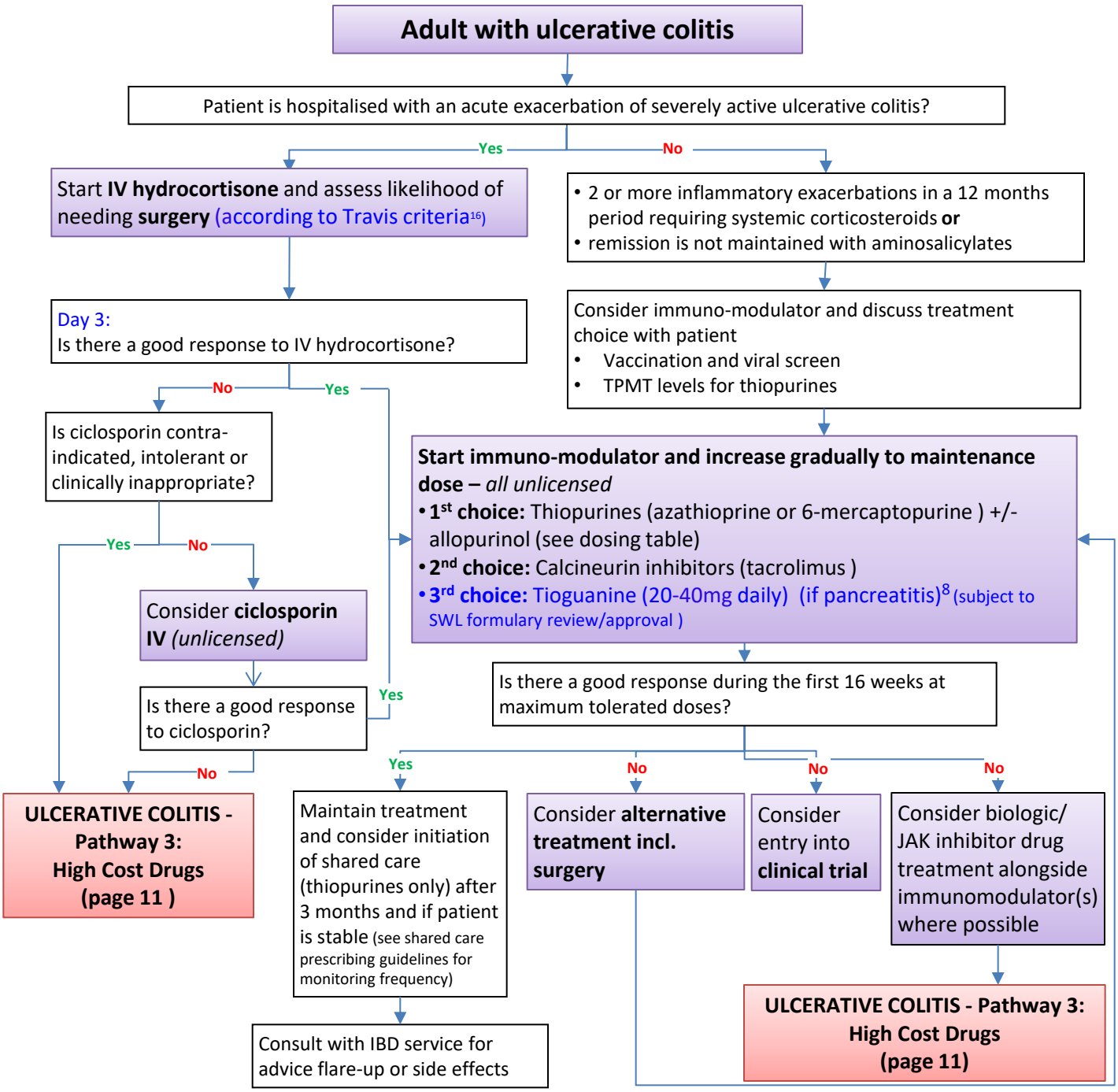
Acute severe ulcerative colitis (single episode)

ULCERATIVE COLITIS - Pathway 2: Immuno-modulators (page 10)

Monitoring:
Adults: Offer colonoscopic surveillance according to NICE CG118 [6]. Assess the risk of fragility fractures according to NICE CG146 [7].

SWL IBD Pathway ULCERATIVE COLITIS - Pathway 2: Immuno-modulators

Version 5.2 (References: 8, 9, 10, 11, 12, 15, 16 with local agreements)



Dosing table [ref 8, 9, 10, 11, 12]	**TPMT normal activity (wild type)**	**TPMT intermediate activity (heterozygous)**	**TPMT low to no activity (homozygous)**
Azathioprine (AZA)	100% dose [2.0 - 2.5 mg/kg] [8,9,11]	50% dose [8,9,11] [1.0 - 1.25 mg/kg]	Not recommended [12]
Low dose azathioprine + allopurinol (100mg daily)	Initially 25% [8,12] of monotherapy dose [0.50 - 0.625mg/kg] Up to 50% [11] of monotherapy dose [1.0 -1.25mg/kg]	Initially 25% [8,12] of monotherapy dose [0.25 - 0.313mg/kg] Up to 50% [8] of monotherapy dose [0.5 - 0.625mg/kg]	Not recommended [12]
6-mercaptopurine (half of AZA dose)	100% dose [1.0 - 1.5 mg/kg] [8,9,11]	50% dose [11] [0.5 - 0.75mg/kg]	Not recommended [12]
Low dose 6-mercaptopurine + allopurinol (100mg daily)	Initially 25% [8,12] of monotherapy dose [0.25 - 0.375mg/kg] Up to 50% [11] of monotherapy dose [0.5 - 0.75mg/kg]	Initially 25% [8,12] of monotherapy dose [0.125 - 0.188mg/kg] Up to 50% [11] of monotherapy dose [0.25 - 0.375mg/kg]	Not recommended [12]

SWL IBD Pathway ULCERATIVE COLITIS - Pathway 3: High Cost Drugs

Version 5.2 (Reference: NICE[17] with local agreements)

Adult with active ulcerative colitis

Does the adult have **moderately to severely active ulcerative colitis managed in outpatients** with no need for hospitalisation/surgery?

Moderately to severely active ulcerative colitis is usually managed in outpatients without requirement for hospitalisation/surgery and is defined by the following symptoms (Truelove & Witts)

- Bowel movements - 4 to 6
- Blood in stools – between mild and severe
- No pyrexia (temperature greater than 37.8C)
- Normal pulse rate (≤ 90 bpm)
- Absence of anaemia
- ESR ≤ 30 mm/hr

This clinical definition corresponds to

- Mayo score ≥ 6
- Partial Mayo score ≥ 4

No

Yes

No

Has the adult responded inadequately or cannot tolerate or has medical contraindications to conventional therapies including:

- Corticosteroids **and**
- Immuno-modulators (e.g. 6-mercaptopurine, azathioprine)

Does the adult have an **acute exacerbation of severely active ulcerative colitis and is hospitalised?**

Acute exacerbation of severely active ulcerative colitis requires hospitalisation and urgent consideration for surgery and is defined by the following symptoms (Truelove & Witts)

- Bowel movements ≥ 6 plus at least one of the features of systemic upset (marked with *)
- Blood in stools – visible blood
- *Pyrexia (temperature greater than 37.8C)
- *Pulse > 90 bpm
- *Anaemia
- *ESR > 30 mm/hr

This clinical definition corresponds to:

- Mayo score ≥ 9
- Partial Mayo score ≥ 6

Yes

No

Optimise pre-high cost drug treatments.

See ULCERATIVE COLITIS:

- **Pathway 1: Inducing and maintaining remission (page 9)**
- **Pathway 2: Immuno-modulators (page 10)**

No

Yes

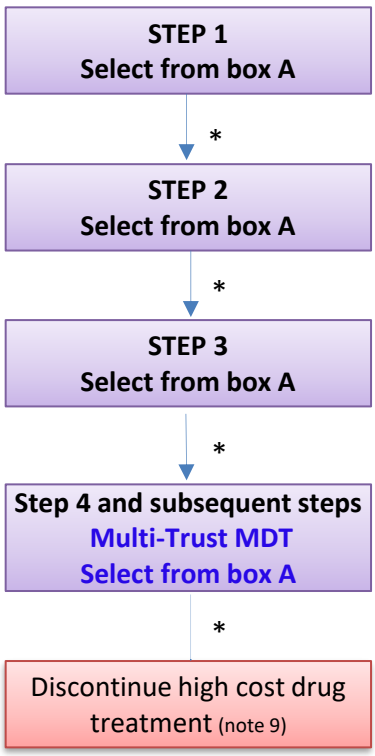
ULCERATIVE COLITIS - Pathway 3A: Adult with moderately to severely active ulcerative colitis (page 12)

ULCERATIVE COLITIS - Pathway 3B: Adult with acute exacerbation of ulcerative colitis (page 14)

Pathway 3A: Moderately to severely active ulcerative colitis managed in outpatients

If there is more than one NICE approved treatment available, NICE recommends a discussion between the responsible clinician and the patient about the advantages and disadvantages of each treatment (considering therapeutic need and likely adherence to treatment).
If more than one treatment option is suitable, the least expensive will be chosen (taking into account administration costs, dosage and price per dose) unless an order of preference is stated in the NICE TAs. Drugs are listed in order of cost (including relevant administration costs, using list price or nationally (NICE) / locally (LPP) agreed contract prices).

Choose **ONE** option per step before moving onto the next step due to primary or secondary treatment failure. Select different drug class (see page 15) in each step (note 1,2,8)



Box A: All listed drugs are available in all steps (note 1,2,8)	
Adalimumab biosimilar (TA329) (note 3) Etrasimod (TA956) Filgotinib (TA792)	£
Ustekinumab biosimilar (TA633) (only if TNF-inhibitor not suitable) Infliximab biosimilar SC/IV (TA329) (note 3) Ozanimod (TA828) (only if infliximab not suitable) Upadacitinib (TA856)	££
Tofacitinib (TA547) Golimumab (TA329) (if high BMI and > 80kg) Mirikizumab (TA925) (only if TNF-inhibitor not suitable or already tried)	£££
Risankizumab (TA998) (only if TNF-inhibitor not suitable or already tried) Vedolizumab SC/IV (TA342)	££££

***AFTER EACH STEP:** At any point **before 12 months** of treatment has passed, has treatment failed? (including the need for surgery) (note 3,4,5,7). IF

- **Yes** – Move to next step
- **No** – Maintain treatment and reassess **at 12 monthly intervals** after start of treatment (note 4,6) for evidence of on-going active disease.
  - **If evidence of on-going active disease**, maintain treatment and reassess at least every 12 months (note 3,4,5,6,7). If appropriate move to next step in treatment pathway if response is lost at any point during therapy.
  - **If no evidence of on-going active disease and patient is not in stable clinical remission**, maintain treatment and reassess at least every 12 months (note 3,4,5,6,7). If appropriate move to next step in treatment pathway if response is lost at any point during therapy.
  - **If no evidence of on-going active disease and patient is in stable clinical remission**, discuss the risks and benefits of continued treatment and whether a trial withdrawal is considered appropriate. If deemed appropriate, consider trial withdrawal and restart treatment if patient relapses after treatment is stopped

SWL IBD Pathway ULCERATIVE COLITIS - Pathway 3: High Cost Drugs

Version 5.2 (Reference: NICE[17] with local agreements)

Pathway 3A: Moderately to severely active ulcerative colitis managed in outpatients - Notes

Note 1- Adverse event or new contra-indication: Consider alternative from the same step (using the same or different drug class) (in steps 1, 2 and 3 only) if treatment is stopped due to an adverse event or new contra-indication **AND**:

- patient was responding to the drug **OR**
- response was not yet assessed i.e. before 8 (adalimumab), 14 (infliximab, golimumab), 16 (tofacitinib), 10 (vedolizumab) or 24 (risankizumab) weeks of initiating treatment.

Note 2- Contraindications and cautions: see page 15.

Note 3- Primary / secondary treatment failure with adalimumab or infliximab: An alternative TNF-alpha inhibitor may be chosen from the same step (in steps 1,2 and 3 only), if considered clinically appropriate. This is restricted to ONE switch within the TNF-alpha inhibitor class.

Note 4- Treatment response: At 8 weeks (adalimumab), 8 or 16 weeks (upadacitinib), 12 weeks (etrasimod), 14 weeks (infliximab, golimumab), 16 weeks (tofacitinib, ustekinumab), 10 weeks (vedolizumab, ozanimod), 10 or 22 weeks (filgotinib), 12 or 24 weeks (mirikizumab), 24 weeks (risankizumab), after the start of treatment and at least at 12 monthly intervals thereafter, reassess disease to determine if response is adequate to treatment and if ongoing treatment is still appropriate. Treatment should only be continued if there is clear evidence of response to biologic treatment defined by :

- a decrease in Full Mayo score by $\geq$ 3 points and ≥30% OR decrease in Partial Mayo score by $\geq$ 2 points and ≥25% AND
- a decrease in the rectal bleeding sub-score from baseline of ≥1 point OR the absolute rectal bleeding sub-score was 0 or 1.

Note 5- Dose escalation for patients with secondary treatment failure as follows:

- Adalimumab: 40mg every week for 3 months **or** 80mg every 2 weeks for 3 months
- Golimumab: 100mg every 4 weeks (<80kg)
- Infliximab: 5mg/kg / 4-6 weeks for 3 doses **or** 10mg/kg / 8 weeks for 3 doses (if low drug concentration <5mcg/ml) or antibodies to infliximab)
- Tofacitinib: 10mg twice daily for 4 months
- Ustekinumab: 90mg / 8 weeks for 4 months
- Vedolizumab: 300mg every 4 weeks for 3 months, ONLY if no alternative drug options are considered appropriate by the clinician and agreed through SWL multi-Trust MDT. Dose escalation is not commissioned if alternative drug options can be used.

For details and subsequent dose escalation requests see page 17.

Note 6- Disease reassessment: At 12 months after the start of treatment, reassess disease to determine whether ongoing treatment is clinically appropriate. Only continue if there is clear evidence of ongoing active disease determined by:

- Clinical symptoms **and**
- Biological markers **and**
- Investigation, including endoscopy if necessary.

Note 7- Drug levels and anti-drug antibodies: Consider where possible at clinician's discretion when considering switching drug within anti-TNF class or between classes.

Note 8- Immunomodulators: Optimise use before/ alongside biologics where possible.

Note 9- IFR: Requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process (see https://swlimo.southwestlondon.icb.nhs.uk/ for IFR policy and application form).

Clinicians and commissioners should refer to the relevant NICE TA and SPC for each drug for further information about their eligibility and prescription.

Pathway 3B: Acute exacerbation of severely active ulcerative colitis with hospitalisation

Acute exacerbation of severely active ulcerative colitis
Severely active ulcerative colitis requires hospitalisation and urgent consideration for surgery and is defined by the following symptoms (Truelove & Witts)

- Bowel movements ≥ 6 plus at least one of the features of systemic upset (marked with *)
- Blood in stools – visible blood
- *Pyrexia (temperature greater than 37.8C)
- *Pulse > 90 bpm
- *Anaemia
- *ESR > 30 mm/hr

This clinical definition corresponds to

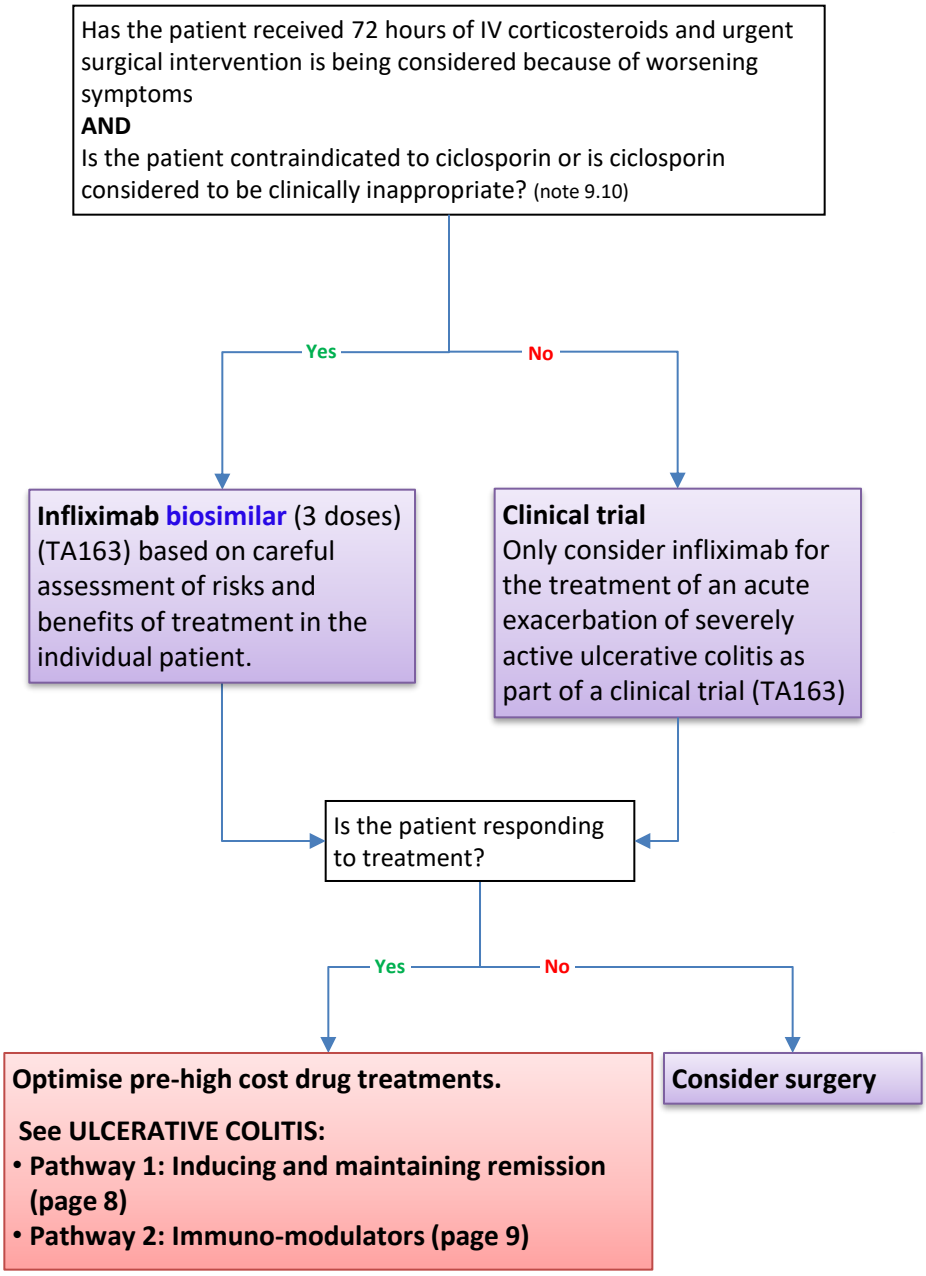
- Mayo score ≥ 9
- Partial Mayo score ≥ 6

Note 9- IFR: Requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process (see https://swlimo.southwestlondon.icb.nhs.uk/ for IFR policy and application form).

Note 10- Contraindications to ciclosporin IV:

- Hypersensitivity to the active substance or to any of the excipients listed in the Summary of Product Characteristics (SPC)
- Combination with products containing *hypericum perforatum*
- Combination with medicines that are substrates for the multidrug efflux transporter P-glycoprotein or the organic anion transporter proteins (OATP) and for which elevated plasma concentrations are associated with serious and/or life-threatening events, e.g. bosentan, dabigatran etexilate and aliskiren

NOTE: This information is not exhaustive. Please also consult the SPC for the respective drug prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk).



SWL IBD Pathway High Cost Drug Contraindications and cautions Version 5.2

NOTE: The information in tables 1 is not exhaustive. Please also consult the Summary of Product Characteristics (SPC) for full information (available via www.medicines.org.uk).

Table 1: Contraindications and cautions [18-23,26,28-32]

Drug Class	Drug Name	Contra-indications	Cautions
Tumour necrosis factor (TNF) alpha inhibitors	Adalimumab biosimilar SC Infliximab IV/ SC Golimumab SC	• Hypersensitivity to active substance or excipients • Active TB and other severe infections (sepsis, abcesses) and opportunistic infections • Moderate to severe heart failure (NYHA class III/IV)	• Infections (impaired lung function) • Hepatitis B reactivation • Demyelinating diseases • Malignancies – lymphomas • Non-melanoma skin cancer (history of prolonged immuno-modulator therapy, PUVA) • Mild heart failure (NYHA class I/II) • Autoimmune processes (Lupus) • Infusion-related reactions (infliximab only)
Interleukin (IL) 12/23 inhibitor Interleukin (IL) 23 inhibitor	Ustekinumab SC Risankizumab IV/SC Mirikizumab SC	• Hypersensitivity to active substance or excipients • Active, severe infections (e.g. TB)	• Chronic infections or history of recurrent infections • More susceptible to serious infections (e.g. TB) • Malignancies increased risk • Hepatic enzyme elevation (mirikizumab) Ustekinumab only: Non-melanoma skin cancer; Lupus-related conditions; >65 years
α4β7 integrin inhibitor	Vedolizumab IV/SC	• Hypersensitivity to active substance or excipients • Active severe infections such as TB, sepsis, CMV, listeriosis, and opportunistic infections such as PML	• No identified systemic immunosuppressive activity but effects on systemic immune system function in patients with IBD not known • The risk of malignancy is increased in patients with ulcerative colitis and Crohn's disease. Immuno-modulatory medicinal products may increase the risk of malignancy • Malignancies not listed as side-effect
JAK inhibitors	Tofacitinib PO Filgotinib PO Upadacitinib PO	• Hypersensitivity to active substance or excipients • Active TB, serious infections (e.g. sepsis) or opportunistic infections • Severe hepatic impairment (tofacitinib/upadacitinib) • Pregnancy and lactation • JAK inhibitors MHRA alert (see page 16)	• Serious infections and TB • Viral reactivation • DVT and PE • Malignancy and lymphoproliferative disorder • Non-melanoma skin cancer • Laboratory parameters (lymphocytes,neutrophils, haemoglobin,lipids)- see SPC for details • MACE • ≥ 65years Upadacitinib/tofacitinib: Liver enzymes; GI perforations; Hypersensitivity Tofacitinib only: Interstitial lung disease; RVT
Sphingosine 1-phosphate (S1P) receptor modulators	Ozanimod PO Etrasimod PO	• Hypersensitivity to active substance or excipients • Immunodeficient state • Patients with MI, unstable angina, stroke, TIA, decompensated HF requiring hospitalisation or NYHA Class III/IV heart failure in last 6 months. • Patients with history or presence of second or third degree AV block • Severe active infections (e.g. hepatitis / TB) • Active malignancies • Severe hepatic impairment • Pregnancy/women of childbearing potential not using effective contraception	• Bradyarrhythmia • Elevated AST • Increased risk of opportunistic infections (e.g PML) and malignancies • Live vaccines • Cutaneous neoplasms • Macular oedema • Posterior reversible encephalopathy syndrome (PRES) • Hypertension • Severe respiratory disease, pulmonary fibrosis, COPD • Women of childbearing potential

SWL IBD Pathway High Cost Drug
JAK inhibitors and MHRA safety warnings Version 5.2

SWL pathway relaxations for existing patients on JAK inhibitors who require a switch to an alternative drug due to MHRA safety warnings

Background

Janus Kinase (JAK) inhibitors include tofacitinib (Xeljanz®), upadacitinib (Rinvoq® ▼), and filgotinib (Jyseleca® ▼) which are locally commissioned and NICE approved for use in ulcerative colitis and Crohn's disease.

On 26 April 2023 the Medicines and Healthcare products Regulatory Agency (MHRA) issued updated safety advice to reduce risk of major adverse cardiovascular events, malignancy, venous thromboembolism (VTE), serious infections and increased mortality for all JAK inhibitors, in line with measures previously introduced for tofacitinib (Xeljanz®) in 2021, as follows:

JAK inhibitors **should not** be used in the following patients unless there are no suitable treatment alternatives:
- age 65 years of age and older
- current or past smokers
- other risk factors for cardiovascular disease or malignancy

- JAK inhibitors should be used with caution in patients with risk factors for VTE other than those listed above
- Where applicable, use lower doses in patients with risk factors (refer to Summary of Product Characteristics of each medicine for further detail)
- Carry out periodic skin examinations in all patients on JAK inhibitor medicines to check for signs of skin malignancy
- Inform patients of these risks and key signs and symptoms that could warrant urgent medical attention (i.e. new growths on skin or changes to moles (including itching, shape and discharge, which may not be as obvious on darker skin tones))
- Report suspected adverse drug reactions associated with JAK inhibitors via the Yellow Card scheme

SWL agreement
Patients on JAK inhibitors may be switched to an alternative treatment option within the same treatment step in SWL pathways if the request to switch is in response to new MHRA safety advice for one of the following reasons:
- age is 65 years or older
- current or past long-time smoker
- other risk factors for cardiovascular disease or malignancy
- risk factors for VTE other than those listed above

This does not apply to patients with primary or secondary treatment failure. These patients should move to the next step in treatment pathways as per usual practice.

SWL IBD Pathway High Cost Drugs
Dose escalation strategy

Version 5.2 (References: 18, 19, 20, 21, 22, 23 with local agreements)

SWL dose escalation agreement for patients with secondary treatment failure:

(1) 1st course of temporary dose escalation as per table below [Blueteq application required for vedolizumab]
(2) De-escalate to standard dose after 1st temporary escalation course
(3) 2nd course of temporary dose escalation if relapse occurs after > 1 month as per table below [Blueteq application required for vedolizumab]
(4) De-escalate to standard dose after 2nd temporary escalation course
(5) Continuous (up to 1 year) dose escalation if rapid relapse occurs (< 1 month) or if relapse occurs after 2nd temporary course
(6) After 1 year, de-escalate to standard dose (if in remission) unless there is evidence for active residual disease and agreement following Trust MDT discussion. Participants must include gastroenterologists, colorectal surgeon, clinical nurse specialist, dietician, pharmacist, pathologist and radiologist with special interest in gastroenterology as per IBD standards, standard A1 and A2[25])*

* **Not applicable to vedolizumab**

NOTE: Immunomodulators should be optimised alongside biologics where possible especially in patients who are not achieving remission/require dose escalation

Drug	Crohn's disease	Ulcerative colitis
Adalimumab [18]	40mg every week for 3 months **or** 80mg every 2 weeks for 3 months	40mg every week for 3 months **or** 80mg every 2 weeks for 3 months
Infliximab [19]	5mg/kg every 6 weeks for 3 doses **or** 5mg/kg every 4 weeks for 3 doses **or** 10mg/kg every 8 weeks for 3 doses	If low drug concentrations (<5micrograms/ml) or antibodies to infliximab: 5mg/kg every 6 weeks for 3 doses **or** 5mg/kg every 4 weeks for 3 doses **or** 10mg/kg every 8 weeks for 3 doses (all dose escalation unlicensed; SWL local agreement)
Golimumab [20]		100mg every 4 weeks in patients <80kg (routinely commissioned)
Ustekinumab [21]	90mg every 8 weeks for 4 months	90mg every 8 weeks for 4 months
Vedolizumab [22] (Use Blueteq dose escalation form)	300mg every 4 weeks for 3 months if no alternative drug options are considered appropriate by the clinician and agreed through SWL multi-Trust MDT. Dose escalation is not commissioned if alternative drug options can be used.	300mg every 4 weeks for 3 months if no alternative drug options are considered appropriate by the clinician and agreed through SWL multi-Trust MDT. Dose escalation is not commissioned if alternative drug options can be used.
Tofacitinib [23]		10mg twice daily for 4 months

SWL IBD Pathway - References

Version 5.2

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SWL IBD Pathway – Version control

Version 5.2

Version number	Amendments made	Date of approval
0		26 May 2011
1.0	Include approved recommendations from South West London Biologics Care Pathway Review for Inflammatory Bowel Disease (IBD) (8 Feb 2017): • Local agreement (Crohn's disease) – allow use of alternative TNF-alpha inhibitor (adalimumab or infliximab) if appropriate (step 2) • Local agreement (ulcerative colitis) – allow use of alternative TNF-alpha inhibitor (adalimumab, infliximab or golimumab (if high BMI and >100kg)) if appropriate (step 2)	27 Feb 2017
2.0	Include approved recommendations from SWL IBD network meeting (28 Jun 2017): • Preferred drug choices • Add existing agreements on dose escalation • Add contraindications and information on cancer risk • Improved pathway presentation • Crohn's disease: ➢Ustekinumab (NICE TA 456) in step 1 (only if anti-TNF contraindicated/not tolerated (local agreement)) and in step 3 ➢New local agreement: vedolizumab step 4 ➢Add dose escalation with ustekinumab in line with license and NICE TA	01 Nov 2017
2.1	Amend note 1 to clarify that a discussion between the responsible clinician and the patient should take place about the advantages and disadvantages of each treatment (considering therapeutic need and likely adherence to treatment) and if more than one treatment option is suitable, the least expensive will be chosen (taking into account administration costs, dosage and price per dose) unless an order of preference is stated in the TAs.	11 Jan 2018
3.0	Include approved recommendations from SWL IBD network meeting (12 Jul 2018): • Change presentation to clarify that step 2 is an optional step and not mandated (local agreement) • Include note 7- reference to IFR process • Crohn's disease: ➢Change pathway presentation to clarify that TNF-alpha inhibitors are not currently commissioned after ustekinumab or vedolizumab •Ulcerative colitis: ➢Change pathway presentation to clarify that TNF-alpha inhibitors are not currently commissioned after use of vedolizumab	08 Oct 2018
4.0	Include approved recommendations from SWL IBD network meeting (28 Feb 2019): • Integration of pathways into one SWL IBD pathway including: ➢Presenting with symptoms ➢Inducing and maintaining remission ➢Name change from "Drug pathway" to "High cost drug pathway" • Crohn's disease: ➢Remove the following statement for vedolizumab: "if unable to use SC alternative" ➢Include note 4 instead of "optional step 2" ➢Add adalimumab and infliximab biosimilar as 1st choice options in all steps ➢In the final step, add ustekinumab as an option • Ulcerative colitis: ➢Include tofacitinib in step 1, 2 and 3 ➢Include all treatment option in step 1,2 and 3 ➢Include note 4 instead of "optional step 2" ➢New dose escalation policy	04 Oct 2019
4.1	Include recommendations from St George's NHS Foundation Trust- Infliximab dose escalation (unlicensed) for Ulcerative Colitis (Dec 2019) following approval through SWL Trust Governance processes: Include infliximab dose escalation (5mg/kg every 6 weeks for 3 doses **or** 5mg/kg every 4 weeks for 3 doses **or** 10mg/kg every 8 weeks for 3 doses (unlicensed; SWL local agreement) in pathway 3A, note 6 and page 15 (dose escalation strategy) if low drug concentrations (<5 micrograms/ml) or antibodies to infliximab	26 Mar 2020

SWL IBD Pathway – Version Control

Version 5.2

4.2	Add Ustekinumab (NICE TA633) to Ulcerative Colitis pathway: • Insert ustekinumab- 3rd choice option to step 1, 2 and 3 • Move vedolizumab from 3rd to 4th choice option. • Include ustekinumab dose escalation (90mg / 8 weeks for 4 months)	9 Sept 2020
4.2	• Add Filgotinib (NICE TA792) to Ulcerative Colitis Pathway	20 July 2022
4.2	• Add Ozanimod (NICE TA828) to Ulcerative Colitis Pathway	21 Dec 2022
4.2	• Add Upadacitinib (NICE TA856) to Ulcerative Colitis Pathway	15 Mar 2023
4.2	• Add Upadacitinib (NICE TA905) to Crohn's Disease Pathway	19 July 2023
4.2	• Add Risankizumab (NICE TA888) to Crohn's Disease Pathway	20 Sept 2023
4.2.1	• Add Mirikizumab (NICE TA925) to Ulcerative Colitis Pathway	12 Dec 2023
4.2.2	• Add Etrasimod (NICE TA956) to Ulcerative Colitis Pathway	10 Apr 2024
5.0	Pathway updated as follows: • Adalimumab biosimilar 1st choice and infliximab biosimilar 2nd choice • Include "Consider" trial withdrawal… as per NICE TA187, 456 and 352, which equally applies to all drugs including ustekinumab and tofacitinib • Include SC infliximab, SC vedolizumab and filgotinib (TA792) • Include SWL multi-Trust MDT process for 4th and 5th line treatment and 3 month vedolizumab dose escalation requests • Add JAK inhibitors and MHRA safety warnings • Update contraindications and cautions table • Reflect interleukin (IL) inhibitors as having different mechanism of action • Include addendums within pathway • Include new contraindication to note 1 for pathway 3A • Update dose escalation strategy to reflect Blueteq dose escalation forms required only for infliximab and vedolizumab (not adalimumab, tofacitinib and ustekinumab) • Add Risankizumab (NICE TA998) to Ulcerative Colitis Pathway • Improved pathway format	18 Sept 2024
5.1	• Update cost order of drugs for Crohn's disease pathway (page 6, Box A and Box B) and Ulcerative Colitis Pathway (page 12, Box A) to reflect availability of ustekinumab biosimilars. • References (page 18) updated.	29 Jan 2025
5.2	• Remove requirement to complete any infliximab dose escalation Blueteq forms. However, infliximab dose escalation should still be undertaken in line with the SWL IBD dose escalation strategy.	21 May 2025
Date of next review: Jan 2027 (or earlier if indicated)		