South West London Inflammatory Bowel Disease Pathway

Developed and agreed by the SWL IBD Medicines Optimisation Clinical Network

Version 4.2.3 (09/09/2020)

Based on recommendations made by the
SWL IBD Medicines Optimisation network meeting held on 28/02/2019
and subsequent amendment ratified at SWL Medicines Optimisation Group on 26/03/2020

Contents:

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

(References: 1, 2, 3, 4 with local agreements) (09/09/2020)

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 8)**

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 ugi-egh@nhs.net
Epsom and St. Helier Hospital (St. Helier site)	IBD helpline: 07831 120969	02082962000 (ext:2340)	ugi-sth@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	stgh-tr.ibdadviceline@nhs.net
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

(Reference: NICE Guideline NG129[5]) (09/09/2020)

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

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

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

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

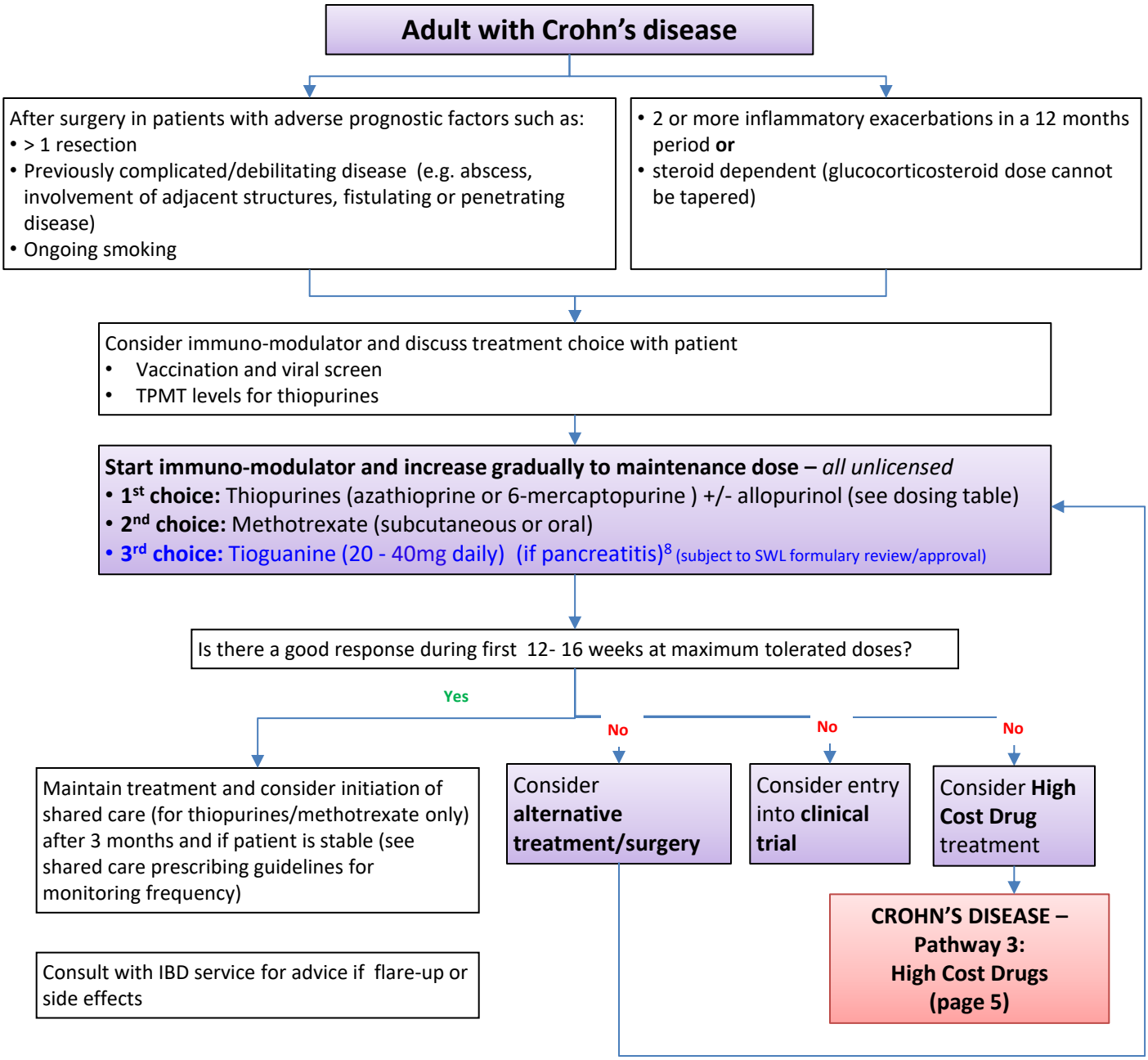
Do not offer: conventional glucocorticosteroids or budesonide

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

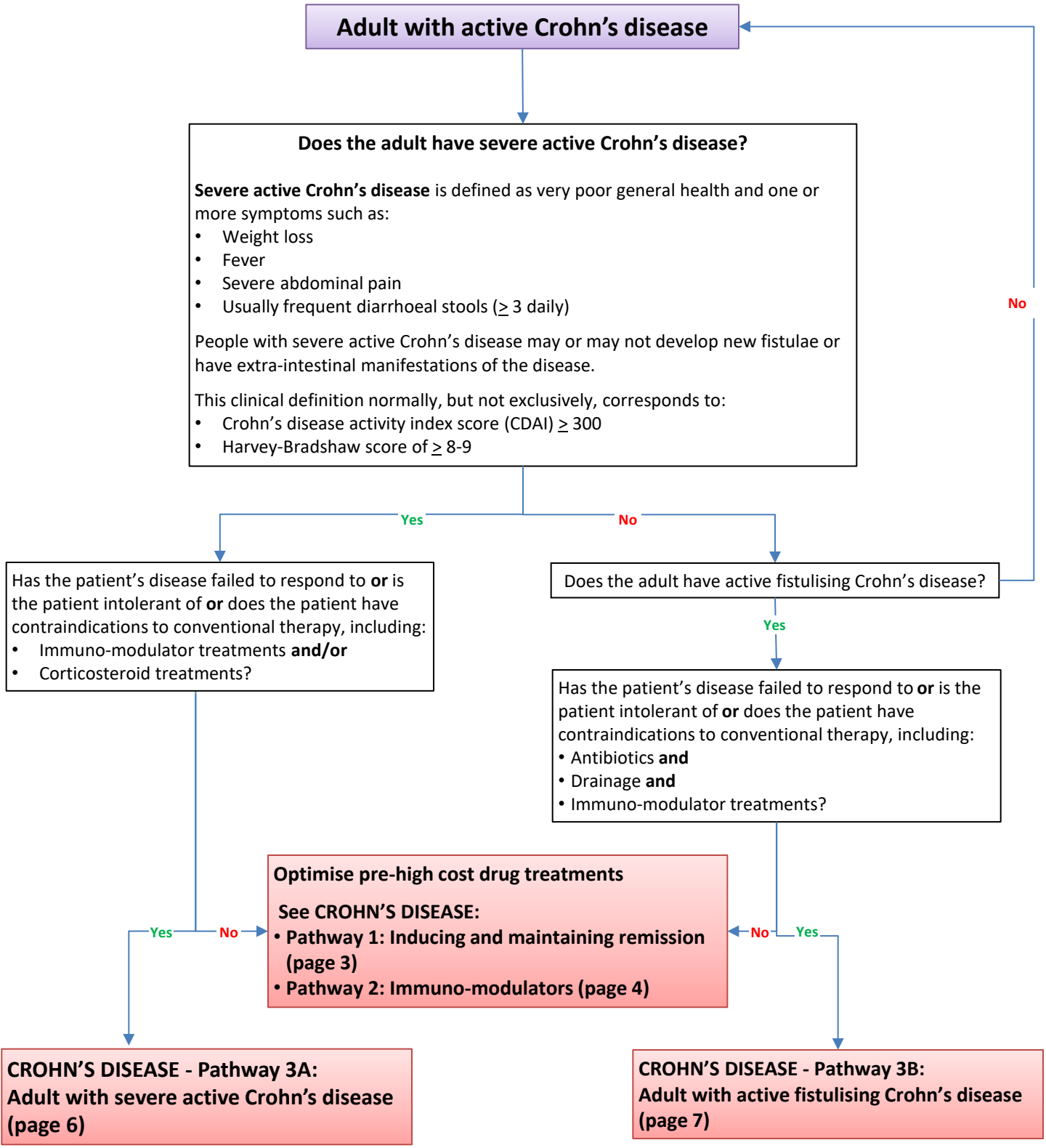
(References: 5, 8, 9, 10, 11, 12, 13 with local agreements) (09/09/2020)



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

(Reference: NICE[14] with local agreements) (09/09/2020)



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

(Reference: NICE[14] with local agreements) (09/09/2020)

Pathway 3A: Severe active Crohn's Disease

Step 1: Use least expensive drug as a planned course of treatment (note 1,2)

1st choice: Adalimumab (TA187) (note 4) **or**
Infliximab biosimilar (TA187) (note 4) **or**
2nd choice: Ustekinumab (TA456)

If both TNF-alpha inhibitors contra-indicated or not tolerated (note 3)
1st choice: Ustekinumab (TA456) **or**
2nd choice: Vedolizumab (TA352)

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery)? (note 4,5,6)

Yes

Step 2: **1st choice:** Adalimumab (note 4) **or**
Infliximab biosimilar (note 4) **or**
2nd choice: Ustekinumab (TA456) **or**
3rd choice: Vedolizumab (TA352)

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery)? (note 4,5,6)

No

Yes

Step 3: **1st choice:** Adalimumab (note 4) **or**
Infliximab biosimilar (note 4) **or**
2nd choice: Ustekinumab **or**
3rd choice: Vedolizumab

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery)? (note 4,5,6)

No

Yes

Discontinue high cost drug treatment (note 8)

No

At 12 months after the start of treatment, reassess the disease (note 7). Is there evidence of ongoing active disease?

Yes

No

Is the patient in stable clinical remission?

No

Yes

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

No

Yes

Trial withdrawal from drug used. Restart treatment if patient relapses after treatment is stopped

Maintain treatment & reassess patient at least every 12 months (note 5,6)
If appropriate move to **next step** in treatment pathway if response is lost at any point during therapy

Note 1: Choose **ONE** drug per step (note that step 2 is optional) before moving onto the next step due to primary or secondary treatment failure.
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 TAs.
The SWL drug choices in this algorithm are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices).

Note 2: Consider alternative drug from the same step if treatment had to be stopped due to an adverse event in patients who:
- had responded to CCG approved drug **OR**
- treatment response was not yet assessed i.e. before 12 weeks (adalimumab), 6 weeks (infliximab), 14 weeks (vedolizumab), 16 weeks (ustekinumab).

Note 3: For contraindications, cautions and information on malignancies see page 13

Note 4: If treatment failure with adalimumab or infliximab, an alternative TNF-alpha inhibitor may be chosen from the same step, if considered clinically appropriate. This is restricted to ONE switch within the TNF-alpha inhibitor class only.

Note 5: Treatment response
At 12 weeks (adalimumab), 6 weeks (infliximab), 14 weeks (vedolizumab), 16 weeks (ustekinumab) after the start of treatment, people should have their disease reassessed to determine whether patients are responding adequately 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 ≥ 3 points or CDAI by ≥ 70 points.

Note 6: Temporary dose escalation is commissioned 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. Dose escalation is not commissioned if alternative drug options can be used.

For details and subsequent dose escalation requests see page 14.

Note 7: 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

Note 8: Funding requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process to the relevant commissioning organisation (see www.swlmcg.nhs.uk for IFR policy and application form)

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

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

(Reference: NICE [14] with local agreements) (09/09/2020)

Pathway 3B: Active fistulising Crohn's Disease

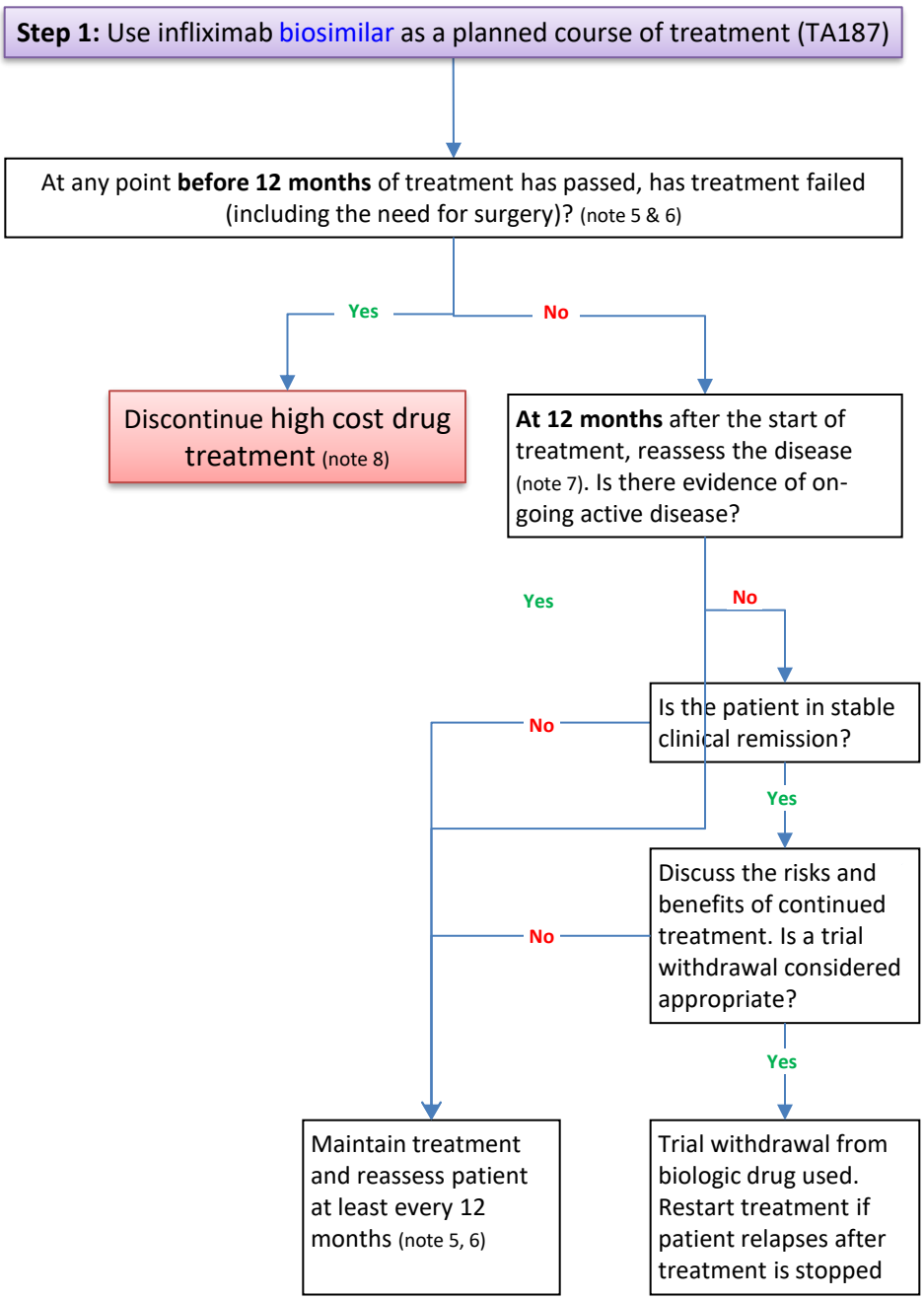
Note 5: Treatment response
At 6 weeks (infliximab) after the start of treatment, people should have their disease reassessed to determine whether patients are responding adequately to treatment and if ongoing treatment is still appropriate. Treatment should only be continued if there is clear evidence of response to biologic treatment defined by a decrease in Harvey-Bradshaw Index by ≥ 3 points or CDAI by ≥ 70 points.

Note 6: Temporary dose escalation is allowed for:
- 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 14.

Note 7: 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

Note 8: Funding requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process to the relevant commissioning organisation (see www.swlmcg.nhs.uk for IFR policy and application form)



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

(Reference: NICE Guideline NG130 [15] with local agreements) (09/09/2020)

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 9)

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 10)

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

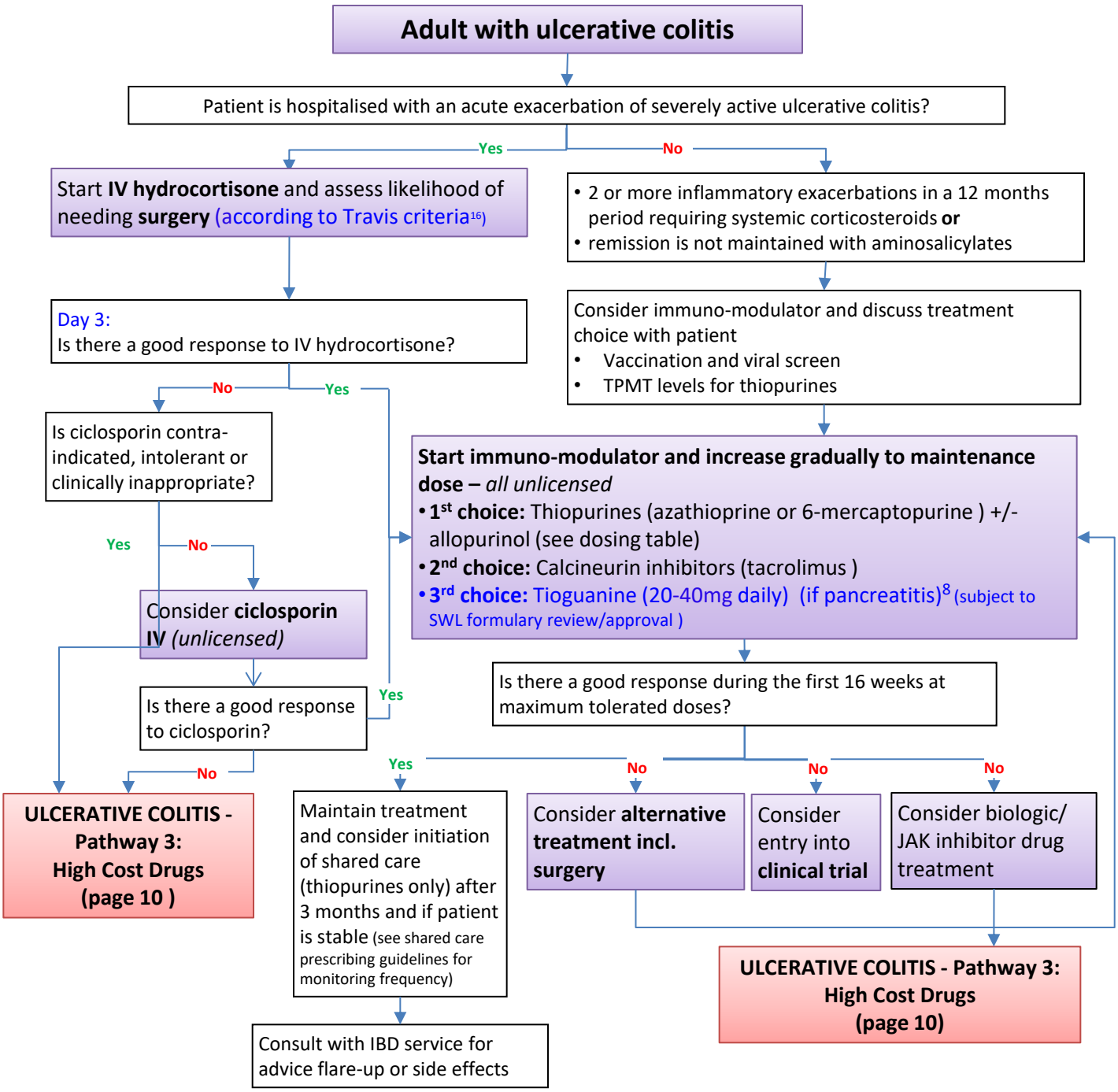
Acute severe ulcerative colitis (single episode)

ULCERATIVE COLITIS - Pathway 2: Immuno-modulators (page 9)

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

(References: 8, 9, 10, 11, 12, 15, 16 with local agreements) (09/09/2020)



Dosing table [ref 8, 9, 10, 11, 12]	TPMT normal activity (wild type)	TPMT intermediate activity (heterozygous)	TPMT low to no activity (homozygous)
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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

(Reference: NICE[17] with local agreements) (09/09/2020)

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 8)**
- **Pathway 2: Immuno-modulators (page 9)**

No

Yes

ULCERATIVE COLITIS - Pathway 3A: Adult with moderately to severely active ulcerative colitis (page 11)

ULCERATIVE COLITIS - Pathway 3B: Adult with acute exacerbation of ulcerative colitis (page 12)

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

(Reference: NICE[17] with local agreements) (09/09/2020)

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

Note 1: Choose **ONE** drug per step (note that step 2 is optional) before moving onto the next step due to primary or secondary treatment failure.
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 TAs.
The SWL drug choices in this algorithm are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices)

Note 2: Consider alternative drug from the same step if treatment had to be stopped due to an adverse event in patients who:
- had responded to CCG approved drug **OR**
- treatment response was not yet assessed i.e. 8 weeks (adalimumab), 14 weeks (infliximab, golimumab), 16 weeks (tofacitinib), 10 weeks (vedolizumab).

Note 3: For contraindications, cautions and information on malignancies see page 13

Note 4: If treatment failure with adalimumab or infliximab, an alternative TNF-alpha inhibitor may be chosen from the same step, if considered clinically appropriate. This is restricted to ONE switch within the TNF-alpha inhibitor class only.

Note 5: Treatment response
At 8 weeks (adalimumab), 14 weeks (infliximab, golimumab), 16 weeks (tofacitinib, ustekinumab), 10 weeks (vedolizumab) after the start of treatment, people should have their disease reassessed to determine whether patients are responding adequately 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 ≥ 3 points and at least 30% OR decrease in Partial Mayo score by ≥ 2 points and at least 25% AND
- a decrease in the rectal bleeding sub-score from baseline of at least 1 point OR the absolute rectal bleeding sub-score was 0 or 1

Step 1: Use least expensive drug as a planned course of treatment (note 1,2,3)
1st choice: Adalimumab (TA329) (note 4) **or**
Infliximab biosimilar (note 4) (TA329) **or**
Tofacitinib (TA547) **or**
2nd choice: Golimumab (TA329) (if high BMI and > 100kg) **or**
3rd choice: Ustekinumab (TA633)
4th choice: Vedolizumab (TA342)

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery) (note 4,5,6)

No

Yes

Step 2: (note 1,2,3,4)
1st choice: Adalimumab **or**
Infliximab biosimilar **or**
2nd choice: Golimumab
(if high BMI and > 100 kg) **or**
Tofacitinib (TA547) **or**
3rd choice: Ustekinumab (TA633)
4th choice: Vedolizumab (TA342)

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery)? (note 4,5,6)

No

Yes

Step 3: (note 1,2,3,4)
1st choice: Adalimumab **or**
Infliximab biosimilar **or**
2nd choice: Golimumab
(if high BMI and > 100 kg) **or**
Tofacitinib (TA547) **or**
3rd choice: Ustekinumab (TA633)
4th choice: Vedolizumab (TA342)

At any point **before 12 months** of treatment has passed, has treatment failed (including the need for surgery)? (note 4,5,6)

No

Yes

Discontinue high cost drug treatment (note 8)

At 12 months after the start of treatment, reassess the disease (note 7)
Is there evidence of on-going active disease?

Yes

No

Maintain treatment and reassess patient at least every 12 months (note 4,5,6)

If appropriate move to **next step** in treatment pathway if response is lost at any point during therapy

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 drug used. Restart treatment if patient relapses after treatment is stopped

Note 6: Dose escalation is commissioned 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. Dose escalation is not commissioned if alternative drug options can be used.

For details and subsequent dose escalation requests see page 14.

Note 7: 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

Note 8: Funding requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process to the relevant commissioning organisation (see www.swlmcg.nhs.uk for IFR policy and application form)

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

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

(reference: NICE [17] with local agreements) (09/09/2020)

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

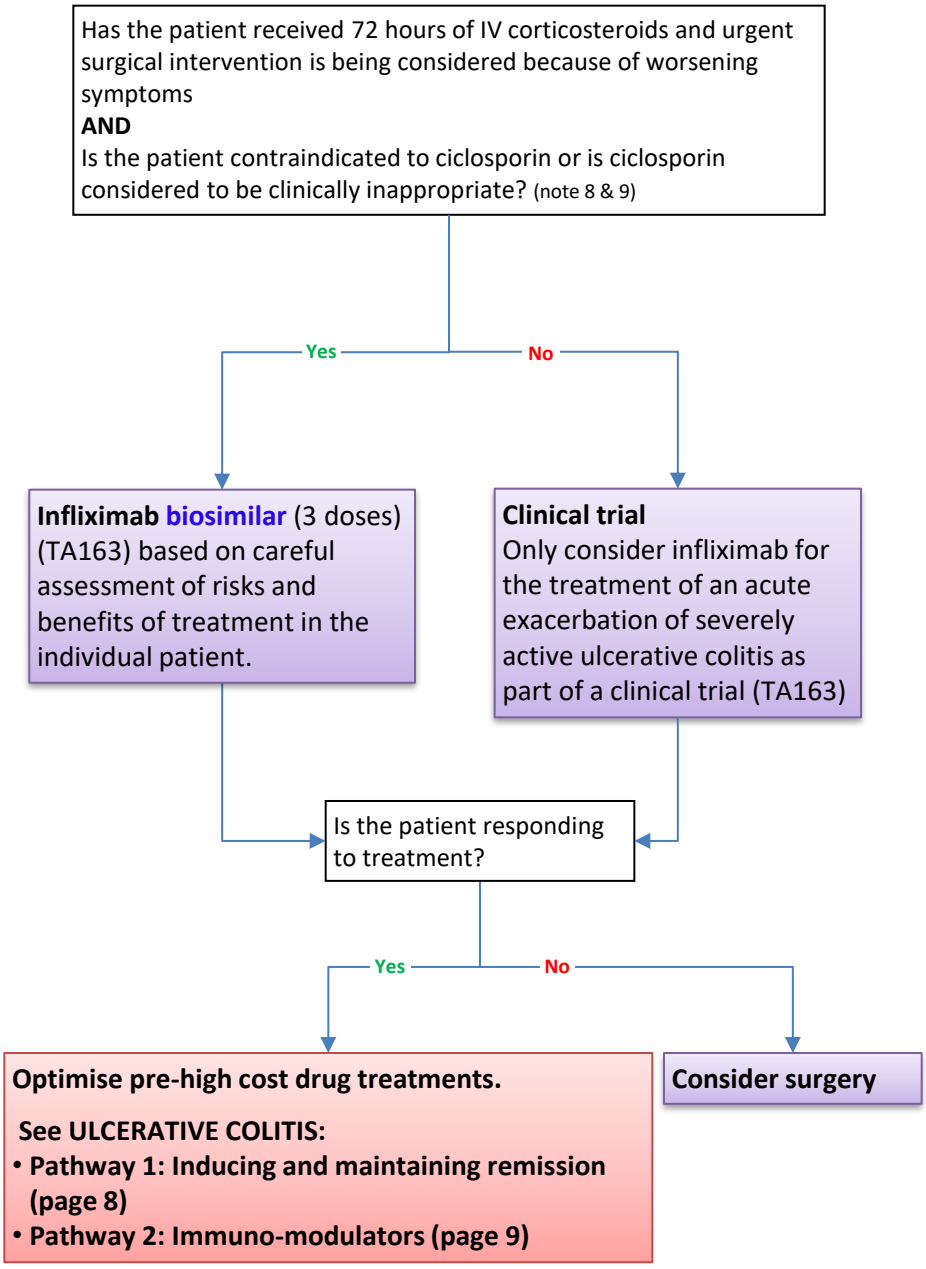
- Mayo score ≥ 9
- Partial Mayo score ≥ 6

Note 8: Funding requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process to the relevant commissioning organisation (see www.swlmcg.nhs.uk for IFR policy and application form)

Note 9: 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, cautions and information about malignancies (09/09/2020)

NOTE: The information in tables 1 and 2 is not exhaustive. Please also consult the Summary of Product Characteristics (SPC) for the respective drugs 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).

Table 1: Contraindications

TNF-alpha inhibitors [18,19,20]	Ustekinumab [21]	Vedolizumab [22]	Tofacitinib [23]
• 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)	• Hypersensitivity to active substance or excipients • Clinically important, active infection (eg active TB)	• Hypersensitivity to active substance or excipients • Active severe infections such as TB, sepsis, CMV, listeriosis, and opportunistic infections such as PML	• Hypersensitivity to active substance or excipients • Active TB, serious infections (e.g. sepsis) or opportunistic infections • Severe hepatic impairment • Pregnancy and lactation

Table 2: Cautions

TNF-alpha inhibitors [18,19,20]	Ustekinumab [21]	Vedolizumab [22]	Tofacitinib [23]
• 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)	• Chronic infections or history of recurrent infections • Malignancies – no studies • Non-melanoma skin cancer (> 60 years of age, history of prolonged immuno-modulator therapy, PUVA)	• 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	• Serious infections • TB • Viral reactivation • Malignancy and lymphoproliferative disorder • Non-melanoma skin cancer • Interstitial lung disease • GI perforations • Liver enzymes • Hypersensitivity • Laboratory parameters (lymphocytes,neutrophils, haemoglobin,lipids)- see SPC for details

Table 3: immuno-modulator therapies to use or avoid in IBD patients with a history of cancer [24]

Type of cancer	Avoid	Use with caution	Can be used
Lymphoma	Thiopurines	Anti-TNF, methotrexate, steroids	
Acute myeloid leukaemia and severe myelodysplastic disorders	Thiopurines	Anti-TNF	Methotrexate, steroids
Melanoma	Anti-TNF	Thiopurines, steroids	Methotrexate
Non-melanoma skin cancer	Thiopurines	Anti-TNF, steroids	Methotrexate
Urinary tract cancer	Thiopurines	Anti-TNF	Methotrexate, steroids
Other tumours		Thiopurines, anti-TNF	Methotrexate, steroids

Table 4: Risk of cancer occurrence [24]

Risk	Organ/type of cancer	
Low [< 10%]	Incidental asymptomatic renal tumour Lymphomas Testicle	Uterine cervix Thyroid
Intermediate [11-25%]	Uterine body Colon	Prostate Breast
High [>25%]	Bladder Sarcoma Melanoma and non-melanoma skin cancer	Myeloma Symptomatic renal carcinoma

SWL IBD Pathway High Cost Drugs
Dose escalation strategy

(References: 18, 19, 20, 21, 22, 23 with local agreements) (09/09/2020)

SWL dose escalation agreement for patients with secondary treatment failure:

(1) 1st course of temporary dose escalation as per table below [Blueteq application#]
(2) De-escalation 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#]
(4) De-escalation 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 [Blueteq application#] *
(6) After 1 year de-escalation to standard dose (if in remission) or provide evidence for active residual disease and agreement following multi-Trust MDT discussion (requires submission of notes of multi-Trust MDT discussion and agreement. 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

\# Golimumab dose escalation from 50mg to 100mg every 4 weeks in patients under 80kg is routinely commissioned and does not require a dose escalation Blueteq application

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 (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]	300mg every 4 weeks for 3 months if no alternative drug options are considered appropriate by the clinician. 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. Dose escalation is not commissioned if alternative drug options can be used.
Tofacitinib [23]		10mg twice daily for 4 months

SWL IBD Pathway - References

(09/09/2020)

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SWL IBD Pathway – Version control

(09/09/2020)

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 14 (dose escalation strategy) if low drug concentrations (<5 micrograms/ml) or antibodies to infliximab	26 Mar 2020

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
4.2.1	• 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
4.2.3	• Add Risankizumab (NICE TA958) to Ulcerative Colitis pathway	18 Sept 2024
Date of next review: September 2022 (or earlier if indicated)		

ADDENDUM 1

(Approved by SWL Integrated Medicines Optimisation Committee on 20 July 2022)

NICE published TA792 (June 2022) - Filgotinib for treating moderately to severely active ulcerative colitis. This addendum aims to inform clinicians that filgotinib is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* filgotinib is commissioned as follows:

Ulcerative Colitis - Pathway 3A

- Step 1 – 1st choice option
- Step 2 – 1st choice option
- Step 3 – 1st choice option

* The SWL drug choices in the "SWL Inflammatory Bowel Disease Pathway – Ulcerative Colitis" are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices).

ADDENDUM 2

(Approved by SWL Integrated Medicines Optimisation Committee on 21st December 2022)

NICE published TA828 (Oct 2022) – Ozanimod for treating moderately to severely active ulcerative colitis. This addendum aims to inform clinicians that ozanimod is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* ozanimod is commissioned as follows:

Ulcerative Colitis - Pathway 3A

- Step 1 – 2nd choice option (only if infliximab is not suitable)
- Step 2 – 2nd choice option (infliximab is not suitable or already tried)
- Step 3 – 2nd choice option (infliximab is not suitable or already tried)

ADDENDUM 3

(Approved by SWL Integrated Medicines Optimisation Committee on 15 March 2023)

NICE published TA856 (Jan 2023) - Upadacitinib for treating moderately to severely active ulcerative colitis. This addendum aims to inform clinicians that Upadacitinib is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* Upadacitinib is commissioned as follows:

Ulcerative Colitis - Pathway 3A

- Step 1 – 2nd choice option
- Step 2 – 2nd choice option
- Step 3 – 2nd choice option

* The SWL drug choices in the "SWL Inflammatory Bowel Disease Pathway – Ulcerative Colitis" are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices).

ADDENDUM 4

(Approved by SWL Integrated Medicines Optimisation Committee on 19 July 2023)

NICE published TA905 (June 2023) – Upadacitinib for previously treated moderately to severely active Crohn's disease

This addendum aims to inform clinicians that Upadacitinib is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* Upadacitinib is commissioned as follows:

Crohn's Disease - Pathway 3A

- Step 1 –1st choice only if TNF alpha inhibitors are contra-indicated or not tolerated
- Step 2 – 2nd choice option
- Step 3 – 2nd choice option

* The SWL drug choices in the "SWL Inflammatory Bowel Disease Pathway – Crohn's disease" are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices).

ADDENDUM 5

(Approved by SWL Integrated Medicines Optimisation Committee on 20 September 2023)

NICE published TA888 (May 2023) - Risankizumab for previously treated moderately to severely active Crohn's disease

This addendum aims to inform clinicians that once risankizumab on-body device is granted approval from MHRA, it is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* Risankizumab is commissioned as follows:

Crohn's Disease - Pathway 3A

- Step 1 – 2nd choice option (only if TNF alpha inhibitors not suitable)
- Step 2 – 3rd choice option
- Step 3 – 3rd choice option

* The SWL drug choices in the "SWL Inflammatory Bowel Disease Pathway – Crohn's disease" are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices).

ADDENDUM 6

(Approved by SWL Integrated Medicines Optimisation Committee on 24 November 2023)

NICE published TA925 (Oct 2023) - Mirikizumab for treating moderately to severely active ulcerative colitis. This addendum aims to inform clinicians that Mirikizumab is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* Mirikizumab is commissioned as follows:

Ulcerative Colitis - Pathway 3A

- Step 1 – 2nd choice if anti-TNFs are unsuitable
- Step 2 – 2nd choice if anti-TNFs already tried or not suitable
- Step 3 – 2nd choice if anti-TNFs already tried or not suitable

* The SWL drug choices in the "SWL Inflammatory Bowel Disease Pathway – Ulcerative Colitis" are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices)

ADDENDUM 7

(Approved by SWL Integrated Medicines Optimisation Committee on 09 April 2024)

NICE published TA956 (Mar 2024) - Etrasimod for treating moderately to severely active ulcerative colitis. This addendum aims to inform clinicians that Etrasimod is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* Etrasimod is commissioned as follows:

Ulcerative Colitis - Pathway 3A

- Step 1 – 1st choice option
- Step 2 – 1st choice option
- Step 3 – 1st choice option

* The SWL drug choices in the "SWL Inflammatory Bowel Disease Pathway – Ulcerative Colitis" are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices)

ADDENDUM 8

(Approved by SWL Integrated Medicines Optimisation Committee on 18 September 2024)

NICE published TA998 (Aug 2024) – Risankizumab for treating moderately to severely active ulcerative colitis. This addendum aims to inform clinicians that risankizumab is available as a treatment option in line with NICE recommendations and local agreements. Based on its relative cost* risankizumab is commissioned as follows:

Ulcerative Colitis - Pathway 3A

- Step 1 – 4th choice option
- Step 2 – 4th choice option
- Step 3 – 4th choice option

* The SWL drug choices in the "SWL Inflammatory Bowel Disease Pathway – Ulcerative Colitis" are based on cost (using list price or nationally (NICE) / locally (LPP) agreed contract prices)