South West London
Inflammatory Bowel Disease
Pathway
Developed and agreed by the SWL IBD Medicines Optimisation Clinical Network

Version 4.1 (26/03/2020)

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

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Patient presenting with lower GI symptoms suggestive of IBD

Is the patient known to have IBD?

Yes

No

Go to:
• CROHN’S DISEASE – Pathway 1: Inducing and maintaining remission (page 3)
• ULCERATIVE COLITIS – Pathway 1: Inducing and maintaining remission (page 8)

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)

Yes

No

Suspected cancer

Suspected acute severe IBD

Follow SWL cancer referral pathway

Discuss with IBD team

Treat as IBS (note: equivocal FCP can be monitored over a longer period every 4 – 6 weeks)

Bloods abnormal and/or FCP > 150

Bloods normal and FCP 50 - 150

Bloods normal and FCP < 50

Repeat FCP in 4 weeks from first test
Consider IBS in meantime

New IBD referral (to be seen within 4 weeks)

Yes

No

FCP rising > 150

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

IBD contact details for healthcare professionals:

<table>
<thead>
<tr>
<th>IBD professionals:</th>
<th>Tel:</th>
<th>Switchboard:</th>
<th>E-Mail:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epsom and St. Helier Hospital (Epsom site)</td>
<td>IBD helpline: 01372 735363</td>
<td>02082962000 (ext:5129)</td>
<td><a href="mailto:esth.cnsrgastroegh@nhs.net">esth.cnsrgastroegh@nhs.net</a></td>
</tr>
<tr>
<td></td>
<td>Secretary: 01372 735129</td>
<td></td>
<td><a href="mailto:ugi-egh@nhs.net">ugi-egh@nhs.net</a></td>
</tr>
<tr>
<td>Epsom and St. Helier Hospital (St. Helier site)</td>
<td>IBD helpline: 07831 120969</td>
<td>02082962000 (ext:2340)</td>
<td><a href="mailto:ugi-sth@nhs.net">ugi-sth@nhs.net</a></td>
</tr>
<tr>
<td>Kingston Hospital</td>
<td>IBD helpline: 020 8934 2760</td>
<td>020 8546 7711</td>
<td><a href="mailto:khtf.ibdadviceline@nhs.net">khtf.ibdadviceline@nhs.net</a></td>
</tr>
<tr>
<td>St. George’s Hospital</td>
<td>IBD helpline: 020 8725 2996</td>
<td>020 8672 1255</td>
<td><a href="mailto:stgh-tr.ibdadviceline@nhs.net">stgh-tr.ibdadviceline@nhs.net</a></td>
</tr>
<tr>
<td>Croydon University Hospital</td>
<td>IBD helpline: 020 8401 3000</td>
<td>020 8401 3000 (ext:4484)</td>
<td><a href="mailto:ch-tr.ibdcoh@nhs.net">ch-tr.ibdcoh@nhs.net</a></td>
</tr>
</tbody>
</table>
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

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)

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
  • Abdominal 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)

CROHN’S DISEASE – Pathway 3: High Cost Drugs (page 5)
**Adult with Crohn’s disease**

- 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)* *(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)

- **No**
  - Consider **alternative treatment/surgery**
  - Consider entry into **clinical trial**
  - **Consider High Cost Drug treatment**

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

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### Dosing table

<table>
<thead>
<tr>
<th></th>
<th>TPMT normal activity (wild type)</th>
<th>TPMT intermediate activity (heterozygous)</th>
<th>TPMT low to no activity (homozygous)</th>
</tr>
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<tbody>
<tr>
<td><strong>Azathioprine (AZA)</strong></td>
<td>100% dose [2.0 - 2.5 mg/kg]</td>
<td>50% dose [1.0 - 1.25 mg/kg]</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Low dose azathioprine + allopurinol</strong> <em>(100mg daily)</em></td>
<td>Initially 25% monotherapy dose [0.5 - 0.625mg/kg]</td>
<td>Initially 25% monotherapy dose [0.25 - 0.313mg/kg]</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>6-mercaptopurine</strong> <em>(half of AZA dose)</em></td>
<td>100% dose [1.0 - 1.5 mg/kg]</td>
<td>50% dose [0.5 - 0.75mg/kg]</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Low dose 6-mercaptopurine + allopurinol</strong> <em>(100mg daily)</em></td>
<td>Initially 25% monotherapy dose [0.25 - 0.375mg/kg]</td>
<td>Initially 25% monotherapy dose [0.125 - 0.188mg/kg]</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
Severe active Crohn’s disease is defined as very poor general health and one or more symptoms such as:

- Weight loss
- Fever
- Severe abdominal pain
- Usually frequent diarrhoeal stools (> 3 daily)

People with severe active Crohn’s disease may or may not develop new fistulae or have extra-intestinal manifestations of the disease.

This clinical definition normally, but not exclusively, corresponds to:

- Crohn’s disease activity index score (CDAI) > 300
- Harvey-Bradshaw score of ≥ 8-9

**CROHN’S DISEASE - Pathway 3A:**
Adult with severe active Crohn’s disease (page 6)

**CROHN’S DISEASE - Pathway 3B:**
Adult with active fistulising Crohn’s disease (page 7)
**SWL IBD Pathway CROHN’S DISEASE - Pathway 3: High Cost Drugs**

(Reference: NICE with local agreements) (26/03/2020)

**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)

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**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

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**Step 2:**

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

No → **At 12 months** after the start of treatment, reassess the disease (note 7). Is there evidence of ongoing active disease?

Yes → Is the patient in stable clinical remission?

No → Discuss the risks and benefits of continued treatment. Is a trial withdrawal considered appropriate?

Yes → 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

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**Step 3:**

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

No → **Discontinue high cost drug treatment** (note 8)

Yes → 1st choice: Adalimumab (note 4) or Infliximab biosimilar (note 4) or

2nd choice: Ustekinumab or

3rd choice: Vedolizumab

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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
- Biological markers
- 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.
**Pathway 3B: Active fistulising Crohn’s Disease**

**Step 1:** Use infliximab biosimilar as a planned course of treatment (TA187)

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

- **Discontinue high cost drug treatment (note 8)**
- **At 12 months** after the start of treatment, reassess the disease (note 7). Is there evidence of ongoing active disease?
  - **Yes**
    - Is the patient in stable clinical remission?
      - **Yes**
        - Discuss the risks and benefits of continued treatment. Is a trial withdrawal considered appropriate?
        - **Yes**
          - Trial withdrawal from biologic drug used. Restart treatment if patient relapses after treatment is stopped
        - **No**
          - Maintain treatment and reassess patient at least every 12 months (note 5, 6)
      - **No**
        - Maintain treatment and reassess patient at least every 12 months (note 5, 6)
  - **No**
    - Continue treatment.

**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
  - Biological markers
  - 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 CROHN’S DISEASE - Pathway 3: High Cost Drugs**
(Reference: NICE 14 with local agreements (26/03/2020))
**Proctosigmoiditis or left-sided ulcerative colitis:**
- Topical aminosalicylate
  - If remission not achieved within 4 weeks:
    - Add oral aminosalicylate
  - 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 topical 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)

**MAINTAINING REMISSION**

**For patients with a mild to moderate first presentation or inflammatory exacerbation**

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

**Monitoring:**
**Adults:** Offer colonoscopic surveillance according to NICE CG118. Assess the risk of fragility fractures according to NICE CG146.
Adult with ulcerative colitis

Patient is hospitalised with an acute exacerbation of severely active ulcerative colitis?

Yes

Start IV hydrocortisone and assess likelihood of needing surgery (according to Travis criteria\(^\text{14}\))

No

• 2 or more inflammatory exacerbations in a 12 months period requiring systemic corticosteroids or • remission is not maintained with aminosalicylates

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

• 1\(^{\text{st}}\) choice: Thiopurines (azathioprine or 6-mercaptopurine ) +/- allopurinol (see dosing table)
• 2\(^{\text{nd}}\) choice: Calcineurin inhibitors (tacrolimus )
• 3\(^{\text{rd}}\) choice: Tioguanine (20-40mg daily) (if pancreatitis)\(^\text{8}\) (subject to SWL formulary review/approval )

Is ciclosporin contra-indicated, intolerant or clinically inappropriate?

Yes

Is there a good response to ciclosporin?

No

Consider ciclosporin IV (unlicensed)

Yes

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

No

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

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

ULCERATIVE COLITIS - Pathway 3: High Cost Drugs (page 10 )

consider alternative treatment incl. surgery

Is there a good response to ciclosporin?

Yes

No

Consider biologic/ JAK inhibitor drug treatment

No

ULCERATIVE COLITIS - Pathway 3: High Cost Drugs (page 10 )

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<tr>
<th>Dosing table [ref 8, 9, 10, 11, 12]</th>
<th>TPMT normal activity (wild type)</th>
<th>TPMT intermediate activity (heterozygous)</th>
<th>TPMT low to no activity (homozygous)</th>
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</thead>
<tbody>
<tr>
<td>Azathioprine (AZA)</td>
<td>100% dose [2.0 - 2.5 mg/kg](^\text{8,9,11})</td>
<td>50% dose (^\text{8,9,11}) [1.0 - 1.25 mg/kg]</td>
<td>Not recommended (^\text{12})</td>
</tr>
<tr>
<td>Low dose azathioprine + allopurinol (100mg daily)</td>
<td>Initially 25% (^\text{8,12}) of monotherapy dose [0.50 - 0.625mg/kg]</td>
<td>Initially 25% (^\text{8,12}) of monotherapy dose [0.25 - 0.313mg/kg]</td>
<td>Not recommended (^\text{12})</td>
</tr>
<tr>
<td>6-mercaptopurine (half of AZA dose)</td>
<td>100% dose [1.0 - 1.5 mg/kg](^\text{8,9,11})</td>
<td>50% dose (^\text{11}) [0.5 - 0.75mg/kg]</td>
<td>Not recommended (^\text{12})</td>
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<tr>
<td>Low dose 6-mercaptopurine + allopurinol (100mg daily)</td>
<td>Initially 25% (^\text{8,12}) of monotherapy dose [0.25 - 0.375mg/kg]</td>
<td>Initially 25% (^\text{8,12}) of monotherapy dose [0.125 - 0.188mg/kg]</td>
<td>Not recommended (^\text{12})</td>
</tr>
</tbody>
</table>
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 37.8°C)
- Normal pulse rate (≤ 90 bpm)
- Absence of anemia
- ESR < 30 mm/hr

This clinical definition corresponds to
- Mayo score ≥ 6
- Partial Mayo score ≥ 4

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 37.8°C)
- *Pulse > 90 bpm
- *Anaemia
- *ESR > 30 mm/hr

This clinical definition corresponds to:
- Mayo score ≥ 9
- Partial Mayo score ≥ 6

**Optimise pre-high cost drug treatments.**

See **ULCERATIVE COLITIS**:
- Pathway 1: Inducing and maintaining remission (page 8)
- Pathway 2: Immuno-modulators (page 9)

**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)
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), 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

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
• 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 treatment options can be used.
• Tofacitinib: 10mg twice daily for 4 months
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
• Biological markers
• 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)

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 Tofacitinib (TA547) or
3rd 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)

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: Vedolizumab (TA342)

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

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: Vedolizumab (TA342)

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

Discontinue high cost drug treatment (note 8)

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

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

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

Is the patient in stable clinical remission?

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

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

Clinicians and commissioners should refer to the relevant technology appraisal and SPC for each drug for further information about their eligibility and prescription.
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 37.8°C)
• *Pulse > 90 bpm
• *Anaemia
• *ESR > 30 mm/hr

This clinical definition corresponds to
• Mayo score > 9
• Partial Mayo score > 6

Clinical trial

Infliximab biosimilar (3 doses) (TA163) based on careful assessment of risks and benefits of treatment in the individual patient.

Clinical trial

Only consider infliximab for the treatment of an acute exacerbation of severely active ulcerative colitis as part of a clinical trial (TA163)

Optimise pre-high cost drug treatments.

See ULCERATIVE COLITIS:
• Pathway 1: Inducing and maintaining remission (page 8)
• Pathway 2: Immuno-modulators (page 9)
## SWL IBD Pathway High Cost Drug

**Contraindications, cautions and information about malignancies (26/03/2020)**

**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](http://www.medicines.org.uk)).

### Table 1: Contraindications

<table>
<thead>
<tr>
<th>TNF-alpha inhibitors 18,19,20</th>
<th>Ustekinumab 21</th>
<th>Vedolizumab 22</th>
<th>Tofacitinib 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hypersensitivity to active substance or excipients &lt;br&gt; • Active TB and other severe infections (sepsis, abscesses) and opportunistic infections &lt;br&gt; • Moderate to severe heart failure (NYHA class III/IV)</td>
<td>• Hypersensitivity to active substance or excipients &lt;br&gt; • Clinically important, active infection (eg active TB)</td>
<td>• Hypersensitivity to active substance or excipients &lt;br&gt; • Active severe infections such as TB, sepsis, CMV, listeriosis, and opportunistic infections such as PML</td>
<td>• Hypersensitivity to active substance or excipients &lt;br&gt; • Active TB, serious infections (e.g. sepsis) or opportunistic infections &lt;br&gt; • Severe hepatic impairment &lt;br&gt; • Pregnancy and lactation</td>
</tr>
</tbody>
</table>

### Table 2: Cautions

<table>
<thead>
<tr>
<th>TNF-alpha inhibitors 18,19,20</th>
<th>Ustekinumab 21</th>
<th>Vedolizumab 22</th>
<th>Tofacitinib 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Infections (impaired lung function) &lt;br&gt; • Hepatitis B reactivation &lt;br&gt; • Demyelinating diseases &lt;br&gt; • Malignancies – lymphomas &lt;br&gt; • Non-melanoma skin cancer (history of prolonged immuno-modulator therapy, PUVA) &lt;br&gt; • Mild heart failure (NYHA class I/II) &lt;br&gt; • Autoimmune processes (Lupus)</td>
<td>• Chronic infections or history of recurrent infections &lt;br&gt; • Malignancies – no studies &lt;br&gt; • Non-melanoma skin cancer (&gt; 60 years of age, history of prolonged immuno-modulator therapy, PUVA)</td>
<td>• No identified systemic immunosuppressive activity but effects on systemic immune system function in patients with IBD not known &lt;br&gt; • 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 &lt;br&gt; • Malignancies not listed as side-effect</td>
<td>• Serious infections &lt;br&gt; • TB &lt;br&gt; • Viral reactivation &lt;br&gt; • Malignancy and lymphoproliferative disorder &lt;br&gt; • Non-melanoma skin cancer &lt;br&gt; • Interstitial lung disease &lt;br&gt; • GI perforations &lt;br&gt; • Liver enzymes &lt;br&gt; • Hypersensitivity &lt;br&gt; • Laboratory parameters (lymphocytes, neutrophils, haemoglobin, lipids)- see SPC for details</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Avoid</th>
<th>Use with caution</th>
<th>Can be used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma</td>
<td>Thiopurines</td>
<td>Anti-TNF, methotrexate, steroids</td>
<td>Methotrexate, steroids</td>
</tr>
<tr>
<td>Acute myeloid leukaemia and severe myelodysplastic disorders</td>
<td>Thiopurines</td>
<td>Anti-TNF</td>
<td>Methotrexate, steroids</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Anti-TNF</td>
<td>Thiopurines, steroids</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Non-melanoma skin cancer</td>
<td>Thiopurines</td>
<td>Anti-TNF, steroids</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Urinary tract cancer</td>
<td>Thiopurines</td>
<td>Anti-TNF</td>
<td>Methotrexate, steroids</td>
</tr>
<tr>
<td>Other tumours</td>
<td>Thiopurines, anti-TNF</td>
<td>Methotrexate, steroids</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4: Risk of cancer occurrence 24

<table>
<thead>
<tr>
<th>Risk</th>
<th>Organ/type of cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low &lt; 10%</td>
<td>Incidental asymptomatic renal tumour &lt;br&gt; Lymphomas &lt;br&gt; Testicle</td>
</tr>
<tr>
<td>Intermediate [11-25%]</td>
<td>Uterine body &lt;br&gt; Colon</td>
</tr>
<tr>
<td>High &gt;25%</td>
<td>Bladder &lt;br&gt; Sarcoma &lt;br&gt; Melanoma and non-melanoma skin cancer</td>
</tr>
</tbody>
</table>

24 Melanoma and non-melanoma skin cancer (history of prolonged immuno-modulator therapy, PUVA)
**SWL IBD Pathway High Cost Drugs**

*Dose escalation strategy*

(References: 18, 19, 20, 21, 22, 23 with local agreements) (26/03/2020)

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### 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)[#]

* 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

---

<table>
<thead>
<tr>
<th>Drug</th>
<th>Crohn’s disease</th>
<th>Ulcerative colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adalimumab</strong></td>
<td>40mg every week for 3 months or 80mg every 2 weeks for 3 months</td>
<td>40mg every week for 3 months or 80mg every 2 weeks for 3 months</td>
</tr>
</tbody>
</table>
| **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 | If low drug concentrations (<5 micrograms/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** |                                                                                | 100mg every 4 weeks in patients <80kg (routinely commissioned)                    |
| **Ustekinumab**| 90mg every 8 weeks for 4 months                                                |                                                                                  |
| **Vedolizumab**| 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**| 10mg twice daily for 4 months                                                  |                                                                                  |
References:
1. NICE DG 11 – Faecal calprotectin diagnostic tests for inflammatory bowel disease (Oct 2013)
2. Inflammatory Bowel Disease Toolkit. RCGP (see: https://www.rcgp.org.uk/clinical-and-research/resources/toolkits/inflammatory-bowel-disease-toolkit.aspx)
3. SEL APC. Primary & Secondary Care Inflammatory Bowel Disease Pathway (Feb 2018).
17. NICE Ulcerative Colitis pathway (see: https://pathways.nice.org.uk/pathways/ulcerative-colitis)
<table>
<thead>
<tr>
<th>Version number</th>
<th>Amendments made</th>
<th>Date of approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
<td>26 May 2011</td>
</tr>
</tbody>
</table>
| 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  
• Ulcerative colitis:  
  ➢ Change pathway presentation to clarify that TNF-alpha inhibitors are not currently commissioned after ustekinumab or vedolizumab  | 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      |

Date of next review: September 2022 (or earlier if indicated)