South East London Inflammatory Bowel Disease treatment pathways - March 2022

Developed by: The Inflammatory Bowel Disease sub-group of the South East London Integrated Medicines Optimisation Committee

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Approved: March 2022  Review date: March 2023 or sooner if evidence/practice changes

This pathway is correct at the time of publication. NICE Technology Appraisals (TAs) relating to Crohn’s disease or ulcerative colitis in adults which are published after the approval date of this guideline will be commissioned 3 months (one month for fast track TAs) from publication and in line with the TA recommendations.

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IBD pathway 1: Presenting with symptoms

- **Patient presenting with lower GI symptoms suggestive of IBD**
  - **Known IBD?**
    - **YES**
      - **Bloods abnormal and/or FCALP >150**
        - **YES**
          - Refer urgently for flexible sigmoidoscopy (one-stop clinic if exists)
        - **NO**
          - Refer for ‘new IBD’ OPA via hotline (to be seen <2/52)
    - **NO**
      - **Pt under ‘active’ FU in 2º care?**
        - **YES**
          - **Bloody diarrhoea?**
            - **YES**
              - Refer for ‘new IBD’ OPA via hotline (to be seen <2/52)
            - **NO**
              - **FBC, ESR, Calprotectin, Coeliac screen, TFTs, (stool MCS)**
                - **Bloods normal and FCALP 50-150**
                  - **YES**
                    - FCALP rising >150?
                      - **YES**
                        - Refer urgently for flexible sigmoidoscopy (one-stop clinic if exists)
                      - **NO**
                        - Repeat FCALP in 4 weeks from first test; Consider IBS advice in meantime (with proviso of re-test)
                - **NO**
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        - **NO**
          - **Bloods normal and FCALP 50-150**
            - **YES**
              - FCALP rising >150?
                - **YES**
                  - Refer urgently for flexible sigmoidoscopy (one-stop clinic if exists)
                - **NO**
                  - Equivocal FCALP results can be monitored over a longer period every 4-6w
            - **NO**
              - **Repeat FCALP in 4 weeks from first test; Consider IBS advice in meantime (with proviso of re-test)**
  - **NO**
    - **Known IBD?**
      - **YES**
        - **Bloods abnormal and/or FCALP >150**
          - **YES**
            - Refer urgently for flexible sigmoidoscopy (one-stop clinic if exists)
          - **NO**
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              - **NO**
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**IBD pathway 2: ULCERATIVE COLITIS**

**Mesalazine (5asa) pathway**

**Patient with known UC**
- with flare of symptoms
- Taking mesalazine only
- On maximum dose
  - (4.8g Octasa™/Mezavant ™, 3g Salofalk™, 4g Pentasa ™)
- On zero or maintenance dose
  - (2.4g Octasa™/Mezavant ™, 1.5g Salofalk™, 2g Pentasa ™)

**Severity of this flare?**
- **MILD**
  - BO 1-3x per day +/- blood
  - No systemic symptoms
  - On rectal 5asa therapy alone (enema or supps)
- **MODERATE**
  - BO 4-6x per day with blood
  - No systemic symptoms
  - Increase to maximum dose 5asa; Consider adding rectal therapy
- **SEVERE**
  - BO >6 per day with blood
  - Fever, tachycardia, hypotension

**Consider minimising tablet burden with high strength formulations if not already**
- Add oral 5asa at maximum dose and strength
- On maximum dose (4.8g Octasa™/Mezavant ™ 3g Salofalk™, 4g Pentasa ™)

**2/52 review if Rx changed. Symptoms controlled?**
- YES
  - Continue maximal therapy for 8/52 then reduce to maintenance unless evidence of disease activity
  - Advice from IBD helpline and/or refer for urgent OPA via helpline(<2/52)
- NO
  - Any steroids in last 12 months?
    - NO
      - Call Gastro SpR on-call Admit via Medical team Seen by IBD Cons within 48h
    - YES
      - Prescribe prednisolone 40mg OD reducing by 5mg per week to zero with Ca+vitD suppl OD

**≥ 2 flares in last 6/12?**
- NO

**MAY NEED DISEASE-MODIFYING THERAPY**
- EG. AZATHIOPRINE

**≥ 2 flares in last 6/12?**
- YES

**Contact Secondary care at any stage in this pathway**

**Mesalazine – choice of oral preparation**
- The 1st line oral mesalazine preparation is Octasa™ MR. Nb: Oral Asacol™ MR is not included in the SEL Joint Medicines Formulary and should usually be switched to Octasa™ MR. Other oral preparations should not be considered interchangeable and should not normally be switched in primary care.

**Rectal (‘topical’) therapies can be sole treatment**
- * Enema added for ‘left-sided’
- * Suppository for ‘proctitis’
- * Enema can be added if ‘pancolitis’

**Yearly faecal calprotectin tests are useful for monitoring disease activity. Faecal calprotectin > 250 should prompt discussion with secondary care.**
IBD pathway 3: IMMUNOSUPPRESSANT progression to BIOLOGIC THERAPY

**INITIAL AZA MONITORING**
- FBC, LFTs at week 0, 2, 4, 8 and 12
- Three-monthly thereafter

**VACCINATION AND VIRAL SCREEN**
Should be performed at this stage

**Methotrexate (MTX) can be considered if Crohn’s**
**SUITABLE FOR ENTRY INTO CLINICAL TRIAL?**

**HIGH RISK OR COMPLEX IBD**
- Young patients (<40 years); Fulminant disease
- Previous surgery for Crohn’s disease / early recurrence
- Fistulising/penetrating Crohn’s disease at presentation
- Unable to use steroids as bridge to immunosuppression
- Already on immunosuppression (and adequate dosing)

**VACCINATION AND VIRAL SCREEN**
Should be performed at this stage

**Mercaptopurine may be used in AZA intolerant cases. Tioguanine is a 3rd line option. See SEL IMOC recommendation 074**

**INITIAL AZA MONITORING**
- FBC, LFTs at week 0, 2, 4, 8 and 12
- Three-monthly thereafter

**TGN level at least at 12/52**
Recheck if failing therapy

**Optimised AZA monotherapy**

**Response at 12-16 weeks?**

**SUITABLE FOR ENTRY INTO CLINICAL TRIAL?**

**Virtual / telephone/ nurse-led F2F follow-up**

**Offer of shared care**

**Secondary care**
- In-hospital response?
  - YES
  - NO

**Colectomy**

**Biologic Pathway (#4a (UC) or #4b (CD))**

**Start point 1**
- Patient requiring therapy despite pathway 2
  - Start AZA based on TPMT result
  - High risk IBD?
    - YES
    - “Acute severe” UC
    - Chronic active CD
    - “Chronic active” UC
    - Methotrexate (MTX) can be considered if Crohn’s
  - NO
    - Optimised AZA monotherapy

**Response at 12 weeks?**

**Start point 2**
- Hospitalised patient
  - “Acute severe” UC
  - High risk IBD?
    - YES
    - “Acute severe” UC
    - Chronic active CD
    - “Chronic active” UC
    - Methotrexate (MTX) can be considered if Crohn’s
  - NO
    - Optimised AZA monotherapy

**Shared care can only start after 3/12 and only if patient stable**

**Ciclo should not be started if already on AZA**

**PROBIOTICS are not recommended for treatment of IBD, except for pouchitis, when use should be directed by secondary care. Probiotics are not available on NHS prescription and patients will normally need to purchase these themselves.**
Colectomy should be considered for all patients with ASUC, but is usually indicated for those failing at least one rescue therapy (IFX or CsA).

Remission for acute severe UC defined by Mayo <2 when steroid-free.

Dose optimisation or drug-switching must be discussed in IBD MDM; Consider surgery. Consider if a clinical trial would be suitable at each point of the pathway prior to switching drug. Consider topical therapy if appropriate. If patients are optimised, respond, de-escalated and relapse in the future, this section 're-sets'. Where patients are dose escalated they will be subject to regular review so that de-escalation of dose can be considered.

Remission for biologic cessation is defined as asymptomatic and biochemical and/or endoscopic and/or radiologic evidence of healing.

Dose escalation is supported in line with the medicine’s product licence, as per the Summary of Product Characteristics.

As part of the medicines reconciliation process, it is important that GP practices accurately record hospital prescribed and supplied medicines for their patients on their practice system but do not inadvertently issue a prescription for them. This includes biologic medicines and advanced medicines used in IBD. Local guidance on reconciling hospital only medicines in GP practice electronic record systems can be found at: https://selondonccg.nhs.uk/download/12197/
IBD pathway 4b: BIOLOGIC THERAPY for Crohn’s disease

**Consider Clinical Trial**

Commissioning is not sought for experimental therapy

- **1st line**
  - **ADALIMUMAB**
  - **INFLIXIMAB**

- **2nd or 3rd line**
  - **USTEKINUMAB**
  - **VEDOLIZUMAB**

**Further considerations for Severe Crohn’s disease**

- There is local agreement that anti-TNF therapy (intravenous infliximab/adalimumab) can be escalated above standard escalated doses within the agreed criteria to achieve therapeutic levels if this is thought more clinically appropriate than switching to other agents (e.g. in perianal CD, extensive stricturing disease). The agreed escalated dosing’s are:
  - Intravenous infliximab: 10mg/kg every four/six weeks
  - Adalimumab 80mg weekly
- Dual biologic therapy (intravenous infliximab/adalimumab + vedolizumab/ustekinumab) may be considered within the locally agreed criteria for refractory Crohn’s disease where combined mechanisms of action may be more effective

**Choice should take into account cost (including service related) and informed patient preference, unless clinically inappropriate**

**Switching of stable patients is clinically inappropriate**

- The most appropriate and cost-effective biologic will be selected according to NICE guidance for CD
- Expect 20% of local population of CD in this arm
- The proportion of patients will be higher in tertiary care (population outside LSLBGB)

**Response at 12-16 weeks?**

- **YES**
  - Continue scheduled Rx Virtual / telephone/ nurse-led F2F follow-up
  - Remission at 12 months?
    - **YES**
      - Consider stopping or de-escalating biologic therapy
    - **NO**
      - Remission for biologic cessation is defined as asymptomatic and biochemical and/or endoscopic and/or radiologic evidence of healing

- **NO**
  - Possible to dose-optimise based on drug/Ab level/clinical response?
    - **YES**
      - Dose escalation is supported in line with the medicine’s product licence, as per the Summary of Product Characteristics
    - **NO**
      - Possible to dose-optimise based on drug/Ab level/CR?

**Secondary care**

As part of the medicines reconciliation process, it is important that GP practices accurately record hospital prescribed and supplied medicines for their patients on their practice system but do not inadvertently issue a prescription for them. This includes biologic medicines and advanced medicines used in IBD. Local guidance on reconciling hospital only medicines in GP practice electronic record systems can be found at: https://selondonccg.nhs.uk/download/12197/
Pathway 5: Iron deficiency treatment pathway for patients with Inflammatory Bowel Disease (IBD)

Confirmed iron deficiency
- Ferritin < 20 g/L or
- Iron saturations < 15%
- For active disease, ferritin < 100 g/L
- Iron saturations < 15%
- Hb < 70 g/L

Hb

Hb < 70 g/L
- Iron infusion urgently +/- blood transfusion
  - Repeat Hb (not ferritin or iron studies) in 2 weeks

Hb 70-100 g/L
- Iron infusion (or blood transfusion in selected patient group)
  - Repeat Hb (not ferritin or iron studies) in 8 weeks

Hb > 100 g/L

Commence one of the following oral iron supplements:
- Ferrous fumarate 210 mg OD
- Ferrous sulphate 200 mg OD
- Ferrous gluconate start at 300 mg OD for 12 weeks

Repeat Hb, ferritin, iron studies, CRP in 12 weeks

If intolerant trial of sodium feredetate start at 5 ml OD

If intolerant commence ferric maltol 30 mg BD first prescription from Gastro specialist

If intolerant organise iron infusion

Primary Care to take over prescribing

Advice to patients to improve adherence to oral iron treatment
- Adverse effects usually settle down with time.
- Iron preparations can be taken after food to reduce gastro-intestinal side-effects.
- Reduce dose frequency to alternate days
- Oral iron should be taken 2 hours apart from other medication
- Further information can be found within the SEL IMOC formulary recommendation

An additional check of Hb after 2-4 weeks of iron supplement treatment can be carried out to assess clinical response and adherence. If Hb in normal range and iron stores replenished, consider discontinuing treatment after 12 weeks, and check 3 monthly for recurrence of anaemia for first year, then 6 monthly. Note that reduced doses of oral iron are recommended in patients with IBD (no more than 100 mg elemental iron per day).
# Inflammatory Bowel Disease Pathway Cost profiling sheet for Advanced Therapies

<table>
<thead>
<tr>
<th>Option</th>
<th>Drug (listed by increasing price, including infusion tariff in cost comparison)</th>
<th>Dosing</th>
<th>Cost tier</th>
<th>Mode of Action</th>
<th>Route/Form</th>
<th>Licensing</th>
<th>Intravenous (requiring day case admission)</th>
<th>Notes</th>
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<td>Adalimumab biosimilar</td>
<td>standard/escalated</td>
<td>£</td>
<td>TNF inhibitor</td>
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<td>✓</td>
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</table>

Subcut = subcutaneous administration, IV = intravenous administration

Updated: January 2022
Next update: October 2022 or sooner if deemed necessary
Inflammatory Bowel Disease Pathway Cost profiling sheet for Advanced Therapies

Cost calculations are based on annual cost of maintenance treatment for a 70kg patient (induction doses are not included in cost comparison). There is a reference price in place for adalimumab at the time of publication of this document.

Due to patient convenience and additional costs of administration it is always preferable to use a subcutaneous option.

The choice of best value biologic will be dependent upon a number of factors (for example contraindications to therapy, co-morbidities and other patient factors). Where more than one agent is suitable for the patient, the agent with the lowest acquisition cost (taking into account method of administration) will be chosen.