South East London Inflammatory Bowel Disease treatment pathways - October 2023

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

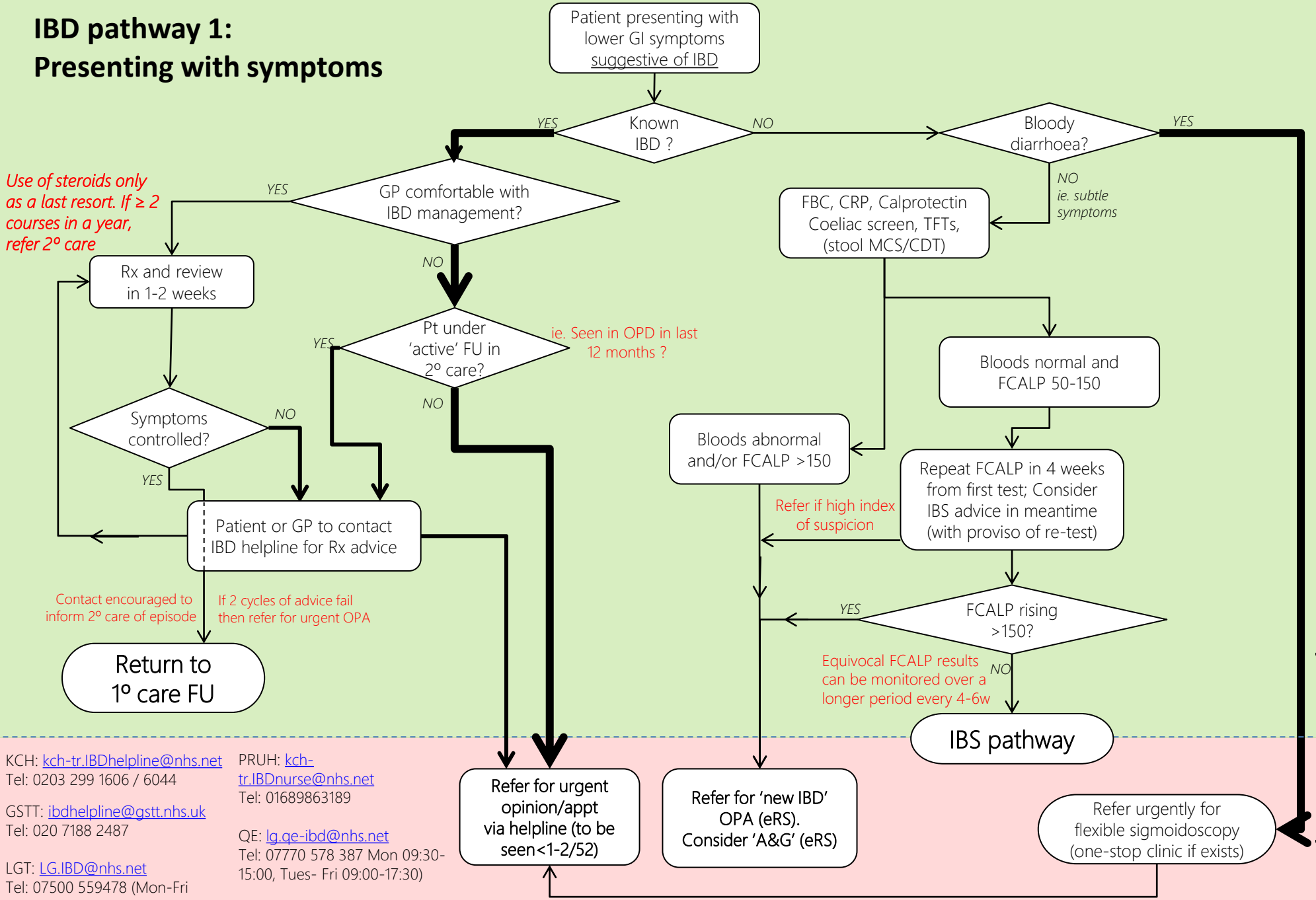
Contents:

Approved: October 2023 **Review date:** October 2024 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.

South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: NHS South East London (covering the boroughs of Bexley, Bromley, Greenwich, Lambeth, Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts/Lewisham & Greenwich NHS Trust.

IBD pathway 1:
Presenting with symptoms



KCH: kch-tr.IBDhelpline@nhs.net
Tel: 0203 299 1606 / 6044

GSTT: ibdhelpline@gstt.nhs.uk
Tel: 020 7188 2487

LGT: LG.IBD@nhs.net
Tel: 07500 559478 (Mon-Fri 08:00-16:00)

PRUH: kch-tr.IBDnurse@nhs.net
Tel: 01689863189

QE: lg.qe-ibd@nhs.net
Tel: 07770 578 387 Mon 09:30-15:00, Tues- Fri 09:00-17:30)

IBD pathway 2: ULCERATIVE COLITIS
Mesalazine (5asa) pathway

Patient with known UC with flare of symptoms Taking mesalazine only

CHECK / ENCOURAGE ADHERENCE
- Typically 55% are adherent -

http://www.nice.org.uk/guidance/cg76/chapter/key-principles

Newly diagnosed patient

Patients with Crohn's disease experiencing flare-ups should be discussed with secondary care. Entocort (Budesonide MR) 9mg od for 4-6/52 may be used for mild or moderate Crohn's if ileocaecal location (may be started in primary care).

Exclusive enteral nutrition (EEN) may be prescribed as an alternative to corticosteroids under the guidance of the patient's gastroenterologist or specialist dietitian

MAY NEED DISEASE-MODIFYING THERAPY EG. AZATHIOPRINE

YES ≥ 2 flares in last 6/12? NO Severity of this flare?

CONTACT SECONDARY CARE AT ANY STAGE IN THIS PATHWAY

Yearly faecal calprotectin tests are useful for monitoring disease activity. Faecal calprotectin > 250 should prompt discussion with secondary care.

Consider minimising tablet burden with high strength formulations if not already

MILD
BO 1-3x per day +/- blood
No systemic symptoms

MODERATE
BO 4-6x per day with blood
No systemic symptoms

SEVERE
BO >6 per day with blood
Fever, tachycardia, hypotension

On rectal 5asa therapy alone (enema or supps)

On zero or maintenance dose (2.4g Octasa™/Mezavant ™ 1.5g Salofalk ™, 2g Pentasa ™)

On maximum dose (4.8g Octasa ™ /Mezavant ™ 3g Salofalk ™, 4g Pentasa ™)

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****.*

Add oral 5asa at maximum dose and strength

Increase to maximum dose 5asa; Consider adding rectal therapy

Consider adding Clipper (beclometasone) 5mg OD for max 4 weeks

Rectal ('topical') therapies can be sole treatment

- *Mesalazine enema added for 'left-sided' or pancolitis*
- *Mesalazine suppository for 'proctitis'*
- *Steroid supps/enemas 2nd line – choose most cost-effective*

Prescribe prednisolone 40mg OD reducing by 5mg per week to zero with Ca+vitD suppl OD

YES 2/52 review if Rx changed. Symptoms controlled? NO

Continue maximal therapy for 8/52 then reduce to maintenance unless evidence of disease activity

Any steroids in last 12 months? NO

WILL NEED DISEASE-MODIFYING THERAPY EG. AZATHIOPRINE YES

Advice from IBD helpine and/or refer for urgent OPA via helpline(<2/52)

Call Gastro SpR on-call
Admit via Medical team
Seen by IBD Cons within 48h

Primary or secondary care

Secondary care

IBD pathway 3: IMMUNOSUPPRESSANT progression to BIOLOGIC THERAPY

Ciclo should not be started if already on AZA

Start point 1

Patient requiring therapy despite pathway 2

Start point 2

Hospitalised patient

Start INFLIXIMAB or CICLOSPORIN. for patients who have not previously failed thiopurine therapy (add AZA if naïve)

VACCINATION AND VIRAL SCREEN
Should be performed at this stage

Start AZA based on TPMT result

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

"Acute severe" UC

In-hospital response? YES / NO

NO — High risk IBD? — YES

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

Colectomy

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

Methotrexate (MTX) can be considered if Crohn's

Response at 12-16 weeks? YES / NO

Chronic active CD

"Chronic active" UC

SUITABLE FOR ENTRY INTO CLINICAL TRIAL ? NO

Response at 12 weeks? YES / NO

Virtual / telephone/ nurse-led F2F follow-up

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

Offer of shared care

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)

Secondary care

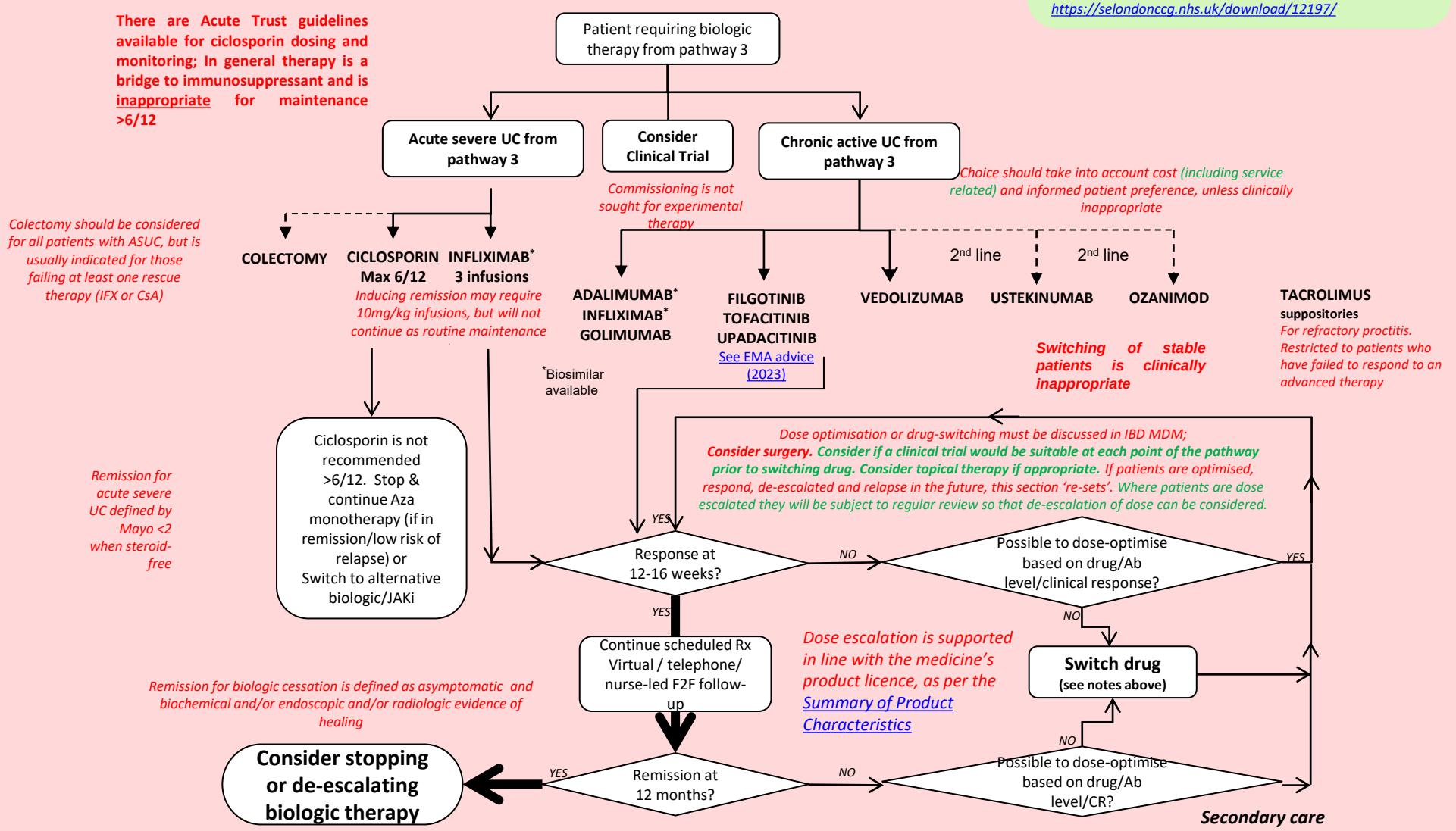
PROBIOTICS are not recommended for treatment of IBD, except for pouchitis, when use should be directed by secondary care. Probiotics are not available on NHS prescription and patients will normally need to purchase these themselves.

Primary care

IBD pathway 4a: BIOLOGIC THERAPY for UC

*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/*

There are Acute Trust guidelines available for ciclosporin dosing and monitoring; In general therapy is a bridge to immunosuppressant and is inappropriate for maintenance >6/12



IBD pathway 4b: BIOLOGIC THERAPY for Crohn's disease

*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/*

Patient requiring biologic therapy from pathway 3

Consider Clinical Trial

Commissioning is not sought for experimental therapy

- *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)*

	1st line	1st line	2nd line	2nd line
*Biosimilar available	**ADALIMUMAB*** **INFLIXIMAB***	**USTEKINUMAB**	**UPADACITINIB**	**RIZANKIZUMAB**	**VEDOLIZUMAB**

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

Switching of stable patients is clinically inappropriate

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*
- *There is local agreement that an additional single re-induction IV dose of ustekinumab (based on weight) may be administered in patients with CD on subcutaneous ustekinumab where there is a secondary loss of response to subcutaneous ustekinumab treatment to help re-capture a response to therapy.*

*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.** 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.***

YES

Response at 12-16 weeks?

NO

Possible to dose-optimise based on drug/Ab level/clinical response?

YES

NO

YES

Continue scheduled Rx Virtual / telephone/ nurse-led F2F follow-up

Switch drug **(see notes above)**

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

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

Consider stopping or de-escalating biologic therapy

YES

Remission at 12 months?

NO

NO

Possible to dose-optimise based on drug/Ab level/CR?

Secondary care

Pathway 5: Iron deficiency treatment pathway for patients with Inflammatory Bowel Disease (IBD)

Key:

- Management in Primary care
- Management in Secondary care

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

Hb

Hb <70g/L

Iron infusion urgently +/- blood transfusion

Repeat Hb (not ferritin or iron studies) in 2 weeks

Hb 70-100g/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 210mg OD
ferrous sulphate 200mg OD
ferrous gluconate start at 300mg OD
Sodium feredetate 5ml OD
for 12 weeks

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

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

Primary Care to take over prescribing

If intolerant organise iron infusion

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 100mg elemental iron per day).

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

Patients requiring repeat iron supplementation who have not tolerated standard oral iron supplements can start ferric maltol directly

Inflammatory Bowel Disease Pathway Cost profiling sheet for Advanced Therapies

Option	Drug (listed by increasing price, including infusion tariff in cost comparison)	Dosing	Cost tier	Mode of Action	Route/Form	Licensing		Intravenous (requiring day case admission)	Notes
						CD	UC		
1	Adalimumab biosimilar	standard/escalated	£	TNF inhibitor	subcut syringe/pen	☑	☑	X	
2	Filgotinib	standard	£	JAK inhibitor	oral tablets	X	☑	x	
3	Adalimumab originator	standard	£	TNF inhibitor	subcut syringe/pen	☑	☑	X	
4	Infliximab biosimilar	standard	£	TNF inhibitor	subcut syringe/pen	☑	☑	☑	
5	Upadacitinib	standard (15mg)	££	JAK inhibitor	oral tablets	☑	☑	X	Excludes induction course of 45mg daily*
6	Infliximab biosimilar	standard	££	TNF inhibitor	IV vial for infusion	☑	☑	☑	
7	Tofacitinib	standard	££	JAK inhibitor	oral tablets	X	☑	X	
8	Ozanimod	standard	££	S1P modulator	oral capsules	X	☑	X	
9	Adalimumab originator	escalated	££	TNF inhibitor	subcut syringe/pen	☑	☑	X	
10	Infliximab biosimilar	escalated	££	TNF inhibitor	IV vial for infusion	☑	☑	☑	
11	Upadacitinib	standard (30mg)	££	JAK inhibitor	oral tablets	☑	☑	X	Excludes induction course of 45mg daily*
12	Ustekinumab	standard	£££	IL-23 & IL-12 inhibitor	subcut syringe	☑	☑	☑	
13	Vedolizumab	standard	£££	α4β7 integrin inhibitor	subcut syringe/pen	☑	☑	☑	
14	Tofacitinib	escalated	£££	JAK inhibitor	oral tablets	X	☑	X	negligible difference between 14 and 15
15	Golimumab	standard/escalated	£££	TNF inhibitor	subcut syringe/pen	X	☑	X	
16	Ustekinumab	escalated	££££	IL-23 & IL-12 inhibitor	subcut syringe	☑	☑	☑	
17	Vedolizumab	standard	££££	α4β7 integrin inhibitor	IV vial for infusion	☑	☑	☑	
18	Vedolizumab	escalated	£££££	α4β7 integrin inhibitor	IV vial for infusion	☑	☑	☑	

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Inflammatory Bowel Disease Pathway Cost profiling sheet for Advanced Therapies

Subcut = subcutaneous administration, IV = intravenous administration

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.

*Inclusion of 45mg induction between 8-16 weeks does not change the position within the cost profile

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