NHS
North East London
Barts Health NHS Trust
Homerton Healthcare NHS Foundation Trust
Barking, Havering and Redbridge University Hospital NHS Foundation Trust

North East London

Treatment Pathway for Inflammatory Bowel Disease in adults

Contents:

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Document version history	
Date / Version	**Comments / Changes**
September 2023 v1.2	Addition of Risankizumab to Crohn's pathway Addition of Upadacitinib to Crohn's and UC pathways

With thanks and acknowledgement to South East London ICS, their IBD pathway was adapted in the production of this pathway.

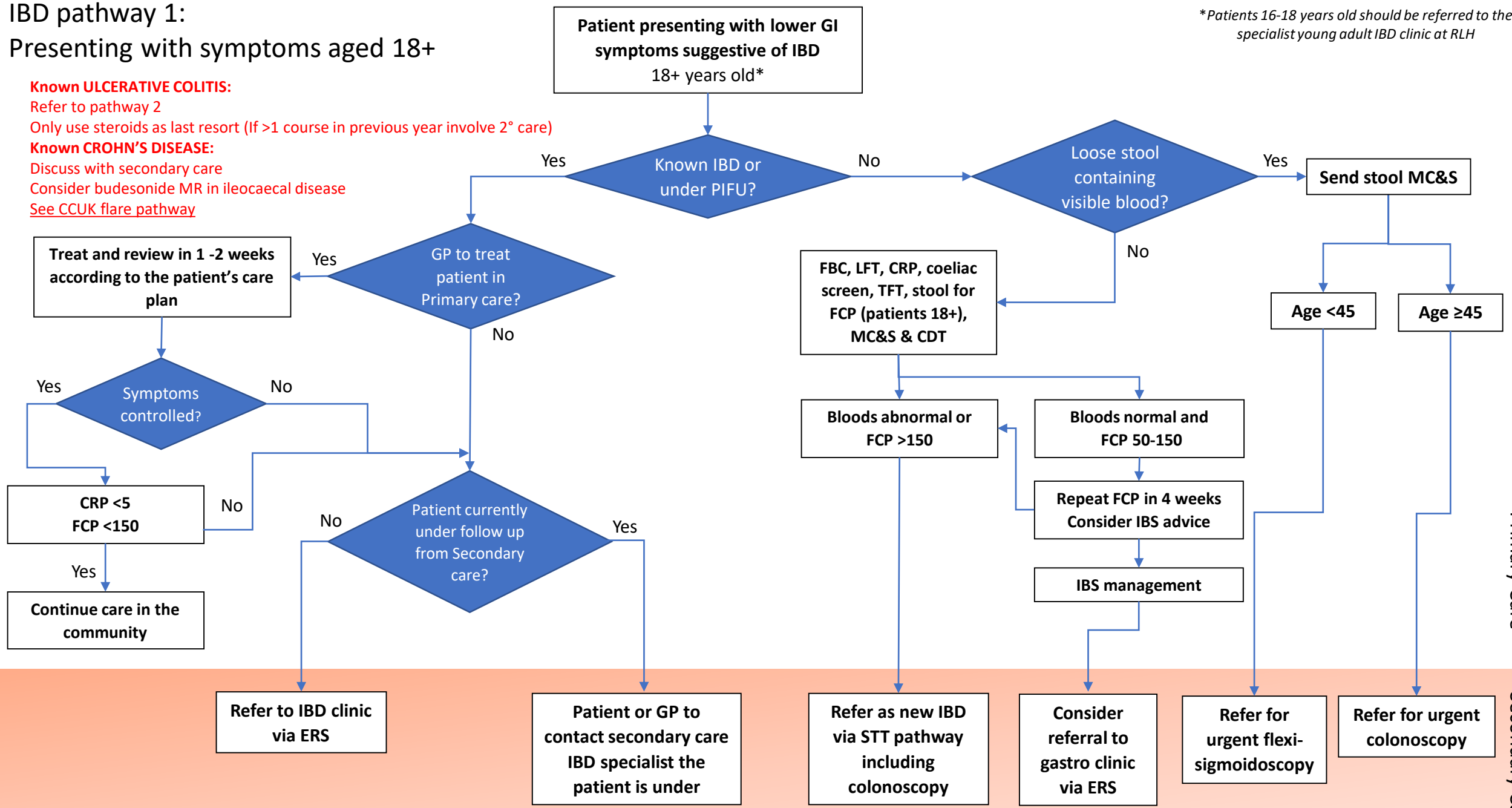
NB: *This pathway is correct at the time of publication. Any NICE Technology Appraisals which are published after this date in relation to IBD (adults) will be commissioned in line with the TA implementation recommendations.*

IBD pathway 1:
Presenting with symptoms aged 18+

**Patients 16-18 years old should be referred to the specialist young adult IBD clinic at RLH*

Known ULCERATIVE COLITIS:
Refer to pathway 2
Only use steroids as last resort (If >1 course in previous year involve 2° care)

Known CROHN'S DISEASE:
Discuss with secondary care
Consider budesonide MR in ileocaecal disease
See CCUK flare pathway



See page 9 for relevant IBD helpline contact details

IBD pathway 2:
Ulcerative colitis – 5ASA pathway

Patient presenting with known UC with flare
Taking no medication or 5ASA only

Check & encourage adherence
Bloods and stool MC&S & CDT
Consider FCP if non bloody

>1 flare in last 6 months?

Yes

No

Assess severity of flare

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

Moderate
BO 4-6x/day + blood
No systemic symptoms

Severe
BO >6x/day + blood
Fever, tachycardia, low BP

On rectal therapy alone?

On zero or maintainance oral dose?
(2.4g Asacol/Mezavant/Octasa, 2g Pentasa)*

On maximum dose?
(4.8g Asacol/ Mezavant/Octasa, 4g Pentasa +/- rectal therapy)*

**Check local formulary for brand and formulation of mesalazine that can be prescribed.*

Add oral 5ASA at maximum dose

Increase to maximum dose 5ASA; consider adding rectal therapy

Consider adding budesonide MMX (Cortiment) 9mg OD for 8 weeks

Start Prednisolone 40mg OD reducing by 5mg/week plus calcium + vitamin D supplement

Review in 2 weeks. Symptoms controlled?

Yes

No

Continue maximal 5ASA therapy for 8 weeks and arrange routine IBD OPD

Any steroids in last 12 months?

No

Yes

Contact IBD helpline or refer to "Known IBD clinic" via ERS

Enters Pathway 3

Call Gastro ST Doctors at local referral centre
Admit via medical team
IBD consultant input within 24h

Patient presenting with known Crohn's with flare
- **Discuss with secondary care**
- Budesonide ER (Entocort/Budeonofalk) 9mg OD 4 weeks can be used for mild ileocaecal disease
- See CCUK flare pathway:

Rectal therapy:
- Suppository for proctitis
- Enema for left sided UC

Enema *can* be added for pancolitis

Primary Care

Secondary Care

See page 9 for relevant IBD helpline contact details

IBD pathway 3
Immunosuppressant to advanced therapy pathway

Symptoms defined by Truelove and Witt criteria, which also corresponds to full Mayo ≥ 9. partial Mayo ≥ 7

Patient requiring therapy despite Pathway 2 (5ASA) with UC & CD as OPD

Pre-screening performed at this stage:
TB elispot/QFT + CXR, HBsAg, HBcAb, HCV IgG, HIV Ab, EBV IgG, CMV IgG, VZV IgG and TPMT
Vaccinate if required

Hospitalised patient

Crohn's Disease

Acute Severe Ulcerative Colitis

Start immunomodulator therapy
Thiopurine (in UC/CD) based on TPMT
Methotrexate (CD only)

Response to IV steroids?
Yes
No

Thiopurine first line is azathioprine

Consider mercaptopurine [*unlicensed*] if azathioprine intolerant

Consider methotrexate in CD as first line, in particularly if EBV IgG not detected

Thiopurine intolerant/ CI/ inappropriate?
Yes
No

Methotrexate intolerant/CI/ inappropriate?
Yes
No

***Rescue* therapy according to local protocol**

Advanced therapy Pathway (4)

Immunomodulator drug monitoring:
Follow local shared care guideline

Optimise thiopurine monotherapy

Consider clinical trial

Response at 8- 12 weeks?
Yes
No

If thiopurine used first in CD, consider methotrexate

Immunomodulator drug monitoring:
Continue shared care with GP

Outpatient IBD clinic
Nurse/Pharmacist led clinic/virtual follow-up

IBD pathway 4: Advanced therapy pathway

Patient requiring therapy despite Pathway 3

Ulcerative Colitis

Clinical Trial?

Moderate/ severe Crohn's Disease +/- fistula
See boxes 2 and 3

Hospitalised with acute severe UC
Symptoms defined by Truelove and Witt criteria, which also corresponds to full Mayo ≥ 9. partial Mayo ≥ 7

Rescue therapy according to local protocol (including failed IV hydrocortisone 72 hours)

No — Clinical Response by day 7? — Yes

Chronic moderate/ severe active UC
See box 1

See Box 4 for further notes
Adalimumab[1,3] (TA329)
Infliximab[1,2,3] (TA329)
Golimumab (TA329)
Tofacitinib* (TA547)
Filgotinib* (TA792)
Upadacitinib* (TA856)
Vedolizumab[2] (TA342)
Ozanimod (TA828) **[If IFX not suitable]**
Ustekinumab (TA633) **[If anti-TNF not suitable]**

If more than 1 suitable, the least expensive treatment should be chosen.
Follow NICE guidance:
Consider cost, efficacy, route of administration, patient preference.
**consider PRAC recommendations for JAKi (here)*

If on Ada/IFX, consider combination therapy with immunomodulator for immunogenicity prevention (Pathway 3)

See box 4 for further notes
Adalimumab[1,5] (TA187)
Infliximab[1,2,5,6] (TA187)
Ustekinumab (TA456)
Upadacitinib* (TA905) **[If anti-TNF not suitable]**
Risankizumab (TA888) **[If anti-TNF not suitable]**
Vedolizumab[2,4] (TA352) **[If anti-TNF not suitable]**

Initial response at 12 – 16 weeks? (see box 5 overleaf)

Switch therapy
(TDM based decision)
Surgery/ Clinical trial

Adequate response
See box 6 for post-initation dosing

Partial response

No response

Colectomy?

On ciclosporin

If ciclosporin CI/ clinically inappropriate

On infliximab x 3 doses (TA 163)

Start thiopurine (Pathway 3)

Yes — Thiopurine naïve? — No

If on IFX or Vedo IV – consider switch to SC

Trial dose optimisation
(see box 7)
+/- TDM/Ab levels

Response in 16 weeks?

No

Adequate response

Outpatient IBD clinic
Nurse led clinic/virtual follow-up

Where patient is dose escalated, review regularly at 6-12 monthly intervals

Stable clinical remission?

Yes

Consider trial withdrawal or dose de-escalate
If disease relapses, consider restart biologic/ dose escalation

No

Maintain treatment

Reassess patient every 12 months. Consider 6-12 months reviews for patients on escalated dosing

Follow pathway for secondary loss of response

Evidence of active disease (see box 8)?

Yes

No

Annual therapy review

No — Secondary loss of response? — Yes

Trial dose optimisation
(see box 7)
+/- TDM/Ab levels

Not appropriate or already on escalated dose

IBD pathway 4: Advanced therapies pathway (notes)

Box 1. Ulcerative colitis- access criteria and definition of disease

Patients would need to have had:

- Inadequate response/ intolerance/ contraindication to optimised conventional therapy taken for an adequate period, including:
  - Corticosteroids **and/or**
  - Azathioprine/ 6-mercaptopurine
- Moderate to severe active UC, **normally corresponds to a Mayo score ≥ 6, partial Mayo score ≥5 or SCCAI ≥ 6**

If an alternative disease severity scoring system is used, evidence of correlation with disease severity (e.g. endoscopy or radiology results, faecal calprotectin) and response criteria needs to be provided by the clinician.

Box 2. Crohn's Disease access criteria and definition of disease

Patients would need to have had:

- Inadequate response/ intolerance/ contraindication to optimised conventional therapy taken for an adequate period, including:
  - Immunosuppressants (e.g. azathioprine/6-mercaptopurine/methotrexate) **and/or**
  - Corticosteroids
- Moderate to severe active CD, **normally corresponds to a Crohn's disease activity index (CDAI) score ≥ 220 or Harvey-Bradshaw (HBI) score ≥6**

If an alternative disease severity scoring system is used, evidence of correlation with disease severity (e.g. colonoscopy, stoma output, faecal calprotectin) and response criteria needs to be provided by the clinician.

Box 3: Fistulising Crohn's disease- treatment options

Infliximab is the only treatment option (NICE TA 187), provided that the disease has not responded to conventional therapy (including antibiotics, drainage and immunosuppressive treatments), or who are intolerant of or have contraindications to conventional therapy. From clinical practice, it is very rare that patients would present with pure fistulising disease without meeting the moderate/ severe Crohn's criteria

Box 4: Choice of therapy

[1]Biosimilars available. Use best value brand.
[2]Subcutaneous = clinically approved and commissioned locally. Not evaluated by NICE TAs
[3]Consider combination therapy with immunomodulator for immunogenicity prevention (Pathway 3)
[4]Only if anti-TNF failed/ not tolerated/ contraindicated as per NICE TAs
[5]Moderate disease not included in the economic analysis for NICE TA187 but clinically approved and commissioned locally (pending)
[6]Infliximab is first choice in perianal disease

Box 5: Definition of response

Adequate response (UC):

Complete Mayo:

- decrease in full Mayo score from baseline by ≥3 points and ≥30%, AND
- decrease in rectal bleeding sub-score from baseline by ≥1 point, OR absolute rectal bleeding sub-score of 0 or 1.

Partial Mayo (where further endoscopy not considered necessary/appropriate):

- decrease in partial Mayo score from baseline of ≥2 points and ≥25% AND
- decrease in rectal bleeding sub-score from baseline of ≥1 point OR absolute rectal bleeding sub-score of 0 or 1.

Adequate response (CD) - decrease in HBI ≥3 points or CDAI ≥70 points

- **Partial response-** any improvement in HBI/CDAI/Mayo/partial Mayo that does not meet adequate response criteria
- **No response –** worsening/ no change of HBI/CDAI/ Mayo/partial Mayo

If alternative disease severity scoring system used, evidence of treatment response (e.g. endoscopy or radiology results, faecal calprotectin) to be provided.

Box 6: Ustekinumab and Upadacitinib dosing post-initiation*:*

- Ustekinumab can be administered every 8 weeks or 12 weeks according to SPC post-initiation provided **adequate response is demonstrated. If patient is not in remission by week 14, use 8 weekly dosing.**
- The recommended Upadacitinib maintenance dose is 15mg or 30mg once daily based on individual presentation, see the SPC for further information. The **lowest effective dose** should be used whenever possible, whilst considering the patient's risk factors.

Box 7: Trial dose escalation, review for clinical response at 12 - 16 weeks

Note only infliximab and adalimumab dose escalation is allowed **if partial response during induction period**
Infliximab: 10mg/kg 8 weekly OR 5mg/kg 4 weekly OR 5mg/kg 6 weekly
Adalimumab 40mg weekly
Tofacitinib 10mg twice daily (consider VTE risk)
Ustekinumab 90mg 8 weekly
Upadacitinib in UC 45 mg once daily for 8 weeks. Patients who do not achieve adequate response by week 8, 45 mg once daily may be continued for an additional 8 weeks.
Vedolizumab 300mg 4 weekly. (Use of vedolizumab TDM for dose adjustments is unvalidated at time of writing)

Box 8: Disease reassessment at 12 months

Treatment should only be continued if there is evidence of ongoing adequate response and active disease, or it is considered clinical inappropriate to withdraw therapy. Ongoing active disease may be determined by:

- Clinical symptoms and
- Biological markers and
- Investigations, including endoscopy, imaging if necessary.

Clinical Remission:

UC: Normally defined as complete Mayo ≤2 with no subscore >1, partial Mayo ≤1 or SCCAI ≤2
CD: Normally defined as HBI ≤ 4 or CDAI ≤ 150

Appendix 1. Drug factors to consider (including modes of action)

The table below provides an approximate drug cost for each biologic based upon first year of therapy, with the loading dose schedule taken into consideration. The cost will vary depending upon commercial arrangements and access to short-term free of charge supplies, which has not been taken into consideration for this guidance.

Mode of action	Drug name	Indicated for	TA (other indications)	Reviewed within	Drug cost
Anti-TNFα	Adalimumab (subcutaneous injection)	<u>TA187 – Crohn's disease</u> Severe active Crohn's: which has not responded/ intolerant/ contraindication to conventional therapy (immunosuppressive and/or corticosteroid treatments)	TA199 – Psoriatic arthritis TA195 – Rheumatoid arthritis TA373 – JIA TA375 – Rheumatoid arthritis TA383 – Ankylosing spondylitis and non-radiographic axial spondylitis TA392 – Hidradenitis suppurativa TA715 – Rheumatoid arthritis	12 weeks	£
		<u>TA329 – Ulcerative colitis</u> Moderate to severe active ulcerative colitis: which has not responded/ intolerant/ contraindication to conventional therapy including corticosteroids and mercaptopurine/ azathioprine.		2-8 weeks	
	Golimumab (subcutaneous injection)	<u>TA329 – Ulcerative colitis</u> Moderate to severe active ulcerative colitis: which has not responded/ intolerant/ contraindication to conventional therapy including corticosteroids and mercaptopurine/ azathioprine.	TA220 – Psoriatic arthritis TA225 – Rheumatoid arthritis TA375 – Rheumatoid arthritis TA383 – Ankylosing spondylitis and non-radiographic axial spondylitis TA497 – Ankylosing spondylitis	12-14 weeks	££
	Infliximab (biosimilar) (subcutaneous injection or intravenous injection)	<u>TA163 – Ulcerative colitis (acute)</u> Acute exacerbations of ulcerative colitis: which has not responded/ intolerant/ contraindication to conventional therapy including corticosteroids and mercaptopurine/ azathioprine. <u>TA329 – Ulcerative colitis</u> Moderate to severe active ulcerative colitis: which has not responded/ intolerant/ contraindication to conventional therapy including corticosteroids and mercaptopurine/ azathioprine.	TA195 – Rheumatoid arthritis TA199 – Psoriatic arthritis TA375 – Rheumatoid arthritis TA383 – Ankylosing spondylitis and non-radiographic axial spondylitis TA715 – Rheumatoid arthritis	3 doses (acute ulcerative colitis) 14 weeks (ulcerative colitis)	£
		<u>TA187 – Crohn's disease</u> Severe active Crohn's: which has not responded/ intolerant/ contraindication to conventional therapy (immunosuppressive and/or corticosteroid treatments) Active fistulising Crohn's disease which has not responded/ intolerant/ contraindication to conventional therapy (including antibiotics, drainage and immunosuppressive treatments).		2 doses (Crohn's disease) 3 doses (fistulising Crohn's disease)	

Mode of action	Drug name	Indicated for	TA (other indications)	Reviewed within	Drug cost
JAK inhibitors	Tofacitinib (oral)	TA547 – Ulcerative colitis Moderately to severely active ulcerative colitis when conventional therapy of biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment.	TA735 – JIA TA480 – Rheumatoid arthritis TA543 – Psoriatic arthritis	16 weeks	**ff**
	Filgotinib (oral)	TA792 – Ulcerative colitis Moderately to severely active ulcerative colitis: which has not responded/ intolerant/ contraindication to conventional or biological treatment.	TA676 – Rheumatoid arthritis	10 weeks	**f**
	Upadacitinib (oral)	TA856 – Ulcerative colitis Moderately to severely active ulcerative colitis: which has not responded/ intolerant/contraindication to conventional or biological treatment.	TA829 – Ankylosing spondylitis TA665 – Severe Rheumatoid arthritis TA744 – Moderate Rheumatoid arthritis TA861 – Non-radiographic axial Spondyloarthritis TA768 - Psoriatic arthritis TA814 – Atopic dermatitis	8 weeks (UC) *[which may be followed by a further 8 weeks for inadequate responders]* 12 weeks (Crohn's)	**ff** 15mg dose
		TA905 – Crohn's disease Moderately to severely active Crohn's disease when a previous biological agent cannot be tolerated/ has responded inadequately to/ lost response or a TNF alpha- inhibitor is contraindicated.			**fff** 30mg dose
IL-12 and IL-23 inhibitor	Ustekinumab (subcutaneous injection)	TA456 – Crohn's disease Moderately to severely active Crohn's disease when conventional therapy or a TNF-alpha inhibitor cannot be tolerated, or the disease has responded inadequately or lost response to treatment.	TA180 – Psoriasis TA340 – Psoriatic arthritis	16 weeks	**fff**
		TA633 – Ulcerative colitis Moderately to severely active ulcerative colitis when a TNF-alpha inhibitor cannot be tolerated, or the disease has responded inadequately, lost response to treatment or is not suitable.			
IL-23 inhibitor	Risankizumab (subcutaneous injection) *	TA905 – Crohn's disease Moderately to severely active Crohn's disease when a previous biological agent cannot be tolerated/ has responded inadequately to/ lost response or a TNF alpha- inhibitor is contraindicated.	TA596 – Psoriasis TA803 – Psoriatic arthritis	12 weeks	**fff**

* Patients may inject Risankizumab after training in subcutaneous injection technique with the on body injector

Mode of action	Drug name	Indicated for	TA (other indications)	Reviewed within	Drug cost
IL-23 inhibitor	Vedolizumab (subcutaneous injection or intravenous injection)	TA352 – Crohn's disease Moderately to severely active Crohn's disease when a TNF-alpha inhibitor cannot be tolerated, or the disease has responded inadequately, lost response to treatment or is contraindicated. To be provided with the discount agreed in the patient access scheme.		14 weeks	££ SC
		TA342 – Ulcerative colitis Moderately to severely active ulcerative colitis when conventional therapy or a TNF-alpha inhibitor cannot be tolerated, or the disease has responded inadequately or lost response to treatment.To be provided with the discount agreed in the patient access scheme.		10 weeks	£££ IV
Sphingosine 1-phosphate (S1P) receptor modulator	Ozanimod (oral)	TA828 – Ulcerative colitis Moderately to severely active ulcerative colitis when conventional treatment cannot be tolerated or is not working well enough and infliximab is not suitable, or biological treatment cannot be tolerated or is not working well enough and the company provides it according to the commercial arrangement.	TA706 – Relapsing-remitting multiple sclerosis	10 weeks	£££

Pathway 1

Abbreviation	Name
CDT	Clostridium difficile test
GI	Gastrointestinal
IBD	Inflammatory bowel disease
MC&S	Microscopy, culture and sensitivity
FCP	Faecal calprotectin
FBC	Full blood count
LFT	Liver function test
CRP	C-reactive protein
TFT	Thyroid function test
IBS	Irritable bowel syndrome
ERS	Electronic referral system
STT	Straight to test
PIFU	Patient Initiated Follow-Up

Pathway 2

Abbreviation	Name
BO	Bowels open
BP	Blood pressure
5ASA	Aminosalicylates
OD	Once daily
OPD	Out-patient department

Pathway 3

Abbreviation	Name
HBsAg	Hepatitis B surface antigen
HBcAb	Hepatitis B core antibody
HCV IgG	Hepatitis C virus antibody
TB elispot/QFT	Tuberculosis elisportor quantiferon test
HIV Ab	Human immunodeficiency virus antibody
EBV IgG	Epstein-Barr virus antibody
CMV IgG	Cytomegalovirus antibody
VZV IgG	Varicella zoster virus antibody
TPMT	Thiopurine S-methyltransferase
IV	Intravenous
CI	Contraindicated
MTX	Methotrexate

Pathway 4

Abbreviation	Name
Ada	Adalimumab
IFX	Infliximab
Vedo	Vedolizumab
SC	Subcutaneous
TDM	Therapeutic drug monitoring
Ab	Antibody
IBD	Inflammatory bowel disease

IBD contact details

Barts Health NHS Trust
Royal London and Mile End hospitals:
Adult service Tel: 020 3594 3700 email: bhnt.ibdhelpline@nhs.net
Paediatric service Tel: 020 3594 0402 email: bartshealth.pibd.helpline@nhs.net

Whipps Cross hospital
Tel: 0208 539 5522 ext 4210 email: bartshealth.wxhibdhelpline@nhs.net

Newham hospital
Tel: 07761405192

Homerton Healthcare NHS Foundation Trust
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