NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Advanced Therapies - Crohn's Disease (CD)

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Approval Group:	Medicines Utilisation Subcommittee of ADTC

Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Treatment with advanced therapies should be initiated and reviewed by specialist clinicians with experience of these agents and of managing Crohn's disease. The British Society of Gastroenterology has established eligibility criteria for the use of these agents. This is the standard used in GGC and is accessible via www.bsg.org.uk. This document is designed to guide treatment decisions but these should be individualised where possible and made in line with SMC and GGC formulary restrictions.

Crohn's disease

Step 1: Assess severity and extent[a] (e.g. using Harvey Bradshaw Index (HBI)

Blood tests, stool cultures and faecal calprotectin (FCP)

Ensure appropriate endoscopy and imaging.

If severely active Crohn's disease, perianal abscess or significant systemic upset – Admit and follow Acute IBD Bundle

Step 2: Induction of remission as per ECCO e-guide:

www.e-guide.ecco-ibd.eu/

Consider clinical trials, budesonide and nutritional treatment

Step 3: Are there high-risk features?

Step 4: Assess response to induction therapy with HBI, bloods and FCP

Consider the need for maintenance therapy:

- Mild Crohn's disease with FCP <250microgram/g may not need maintenance treatment[a]
- Complete screening, counselling and vaccination according to NHSGGC protocols before treatment
- Consider early surgery especially in isolated ileal disease

Preferred 1st Line Therapy

Adalimumab or Infliximab (IV/SC) +/- immunomodulator[b,c]

***Ustekinumab**[d] or **Upadacitinib**[e,f]*

**Conditional use - consider 1st line in patients where other 1st line options are not clinically appropriate.*

Preferred 2nd Line Therapy

Anti-TNF Failure without immunogenicity:

Ustekinumab[d] or Upadacitinib[e,f]

Non-anti-TNF failure:

Adalimumab or Infliximab (IV/SC) +/- immunomodulator[b,c]

Other licensed options:

Vedolizumab[d]

Step 5: Assess response within 12-14 weeks.

Bloods, FCP, symptoms and therapeutic drug monitoring (TDM)[g].

Step 6: Ongoing drug monitoring and clinical care according to NHSGGC protocols and near patient testing (NPT) arrangements[h].

Step 7: Duration of therapy;

- Limit thiopurines to 5 years if possible
- Others review annually or if loss of efficacy / intolerance / side-effects
- Consider withdrawal or de-escalation of advanced therapies in those in complete clinical and endoscopic remission
- Monitor closely (e.g. using FCP) after any withdrawal and ensure prompt retreatment in the event of flare

NHS Greater Glasgow and Clyde

Consider clinical trials at every step in the treatment pathway.

Email: GastrointestinalTeam.Gcrf@ggc.scot.nhs.uk

or Call: 0141-232-7599

IBD Glasgow

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Prescribing Notes

a) Monitoring with faecal calprotectin is recommended for those not on treatment. If FCP is consistently above 250microgram/g the risks and benefits of starting treatment should be discussed with the patient.

b) There should be a low threshold for combination therapy with a thiopurine or methotrexate in those with fistulating disease, other high-risk features and especially when moving to a second anti-TNF drug following loss of response due to immunity. Co-prescription of an immunomodulator may be less important when subcutaneous (SC) anti-TNF agents are used.

c) Thiopurines should be used with caution in Epstein-Barr Virus (EBV) negative young males, history of lymphoma, skin cancer, cervical neoplasia and those >50 years.

d) Consider using Ustekinumab 1st line in the elderly/frail, those with a past history of cancer or significant co-morbidity that would make other first line options unsuitable. Vedolizumab may similarly be an appropriate 2nd line agent in some of these patients.

e) Consider using Upadacitinib 1st line in patients unsuitable for or unwilling to take prednisolone. JAK-inhibitors may interact with some drugs (e.g. Carbamazepine and Phenytoin) so check with IBD Pharmacist if any concerns.

f) The MHRA advice about the use of JAK-inhibitors with regard to venous thrombo-embolism, major adverse cardiovascular events and malignancies should be adhered to and discussed with patients. It should only be used in those over 65y, current or previous smoker and those with other risk factors for cardiovascular disease or malignancy if no other alternative exists.

g) Define treatment goals at the start of treatment which for most patients should be steroid free, clinical and biochemical remission. Non-response should precipitate treatment change and not procrastination.

h) The subsequent drug choice should take into account any initial response to existing treatment including symptoms and objective markers of response together with therapeutic drug monitoring where available. Primary non-response is often best addressed by moving treatment to a different class of drug.

High Risk or Complex IBD

1. Young patients (less than 40 years)
2. Fulminant disease
3. Previous surgery especially with early recurrence
4. Perianal or Fistulising disease
5. Unable to use steroids as a bridge to immunosuppression
6. Already on immunosuppression
7. Upper GI involvement
8. Diffuse stricturing small bowel disease

Factors to Consider When Making Treatment Choices

1. Route of administration
2. Speed of response
3. Potential immunogenicity and need for combination therapy
4. Family planning – consider avoiding Upadacitinib and Methotrexate in females planning pregnancy within 5y
5. Side effects including risk of cancer
6. Persistence of drug therapy
7. Availability of infusion facilities and TDM
8. Extra-intestinal manifestations and co-existing immune-mediated inflammatory diseases with the potential for dual benefit from some treatments
9. Overall Cost