Bedfordshire and Luton Joint Prescribing Committee

Treatment of Severe Active Crohn's disease in Adults (18 years and older) AFTER failure of conventional therapy (in line with NICE TAs and local guidance)

This algorithm is only applicable for use in patients who have failed to respond to, who are intolerant of, or have contraindications where deemed clinically inappropriate to the use of conventional therapies: aminosalicylates, corticosteroids and/or immunosuppressants (as per NICE NG 129)

*The choice of treatment should be made on an individual basis, taking into account individual patient factors such as therapeutic need, co-morbidities and adherence. If more than 1 treatment is suitable, the most appropriate and **least expensive** should be chosen (taking into account administration costs, dosage and price per dose). **Biosimilars** are cost-effective treatment options.*

Severe active Crohn's disease* - very poor general health and ≥1 symptoms e.g. weight loss, fever, severe abdominal pain and usually frequent (≥3) diarrhoeal stools daily. People may or may not develop new fistulae or have extra-intestinal manifestations of the disease. It normally but not exclusively corresponds to a Crohn's disease Activity Index (CDAI) score of ≥300 or Harvey Bradshaw score of 8 to 9 or above.

Active fistulising Crohn's disease ∞ - periods of disease activity (flare ups) and periods of inactivity (remission), and cycle between these two states. Symptoms during a flare up can include diarrhoea, abdominal pain or discomfort, fever, nausea, vomiting, tiredness and weight loss. The fistula may also drain pus or a foul-smelling discharge.

FIRST LINE TREATMENT OPTIONS: TNF inhibitors (TNFi) +/- immunosuppressant

Review at 12 months or treatment failure (including the need for surgery), whichever is sooner

●Adalimumab biosimilar# (TA 187) OR ● Infliximab biosimilar∞#* (TA 187)**

∞Infliximab is recommended within its licensed indication for treatment of **Active Fistulating Crohn's disease** that has not responded to conventional therapy (e.g. antibiotics drainage and immunosuppressants) or if there is conventional treatment intolerance/contraindications. Review within 12 months or at point of treatment failure (including need for surgery), whichever is sooner; IFR application is required for second line treatments and beyond.

SECOND LINE TREATMENT OPTION:

Review within 12 months or treatment failure (including the need for surgery), whichever is sooner

- **Infliximab biosimilar#∞*** (if adalimumab given first line)

Consider changing to an alternative treatment option if:

- the patient does not respond adequately to the first biologic (primary failure)
- the patient initially responds adequately but subsequently loses this response (secondary failure)
- the first biologic drug cannot be tolerated or is contraindicated.

THIRD LINE TREATMENT OPTIONS:

(second line if infliximab used first line)

Review within 12 months or treatment failure (including the need for surgery), whichever is sooner

●Ustekinumab #* (TA 456) OR ●Vedolizumab* (TA 352)

SUBSEQUENT BIOLOGIC TREATMENT OPTIONS:

Subsequent biologic use is NOT routinely commissioned, IFR submission for CCG panel consideration is required

ASSESS PATIENT'S RESPONSE:

Have they achieved an adequate response? Withdraw if adequate response is not maintained move to next stage in the pathway.

Remission achieved – HBI score ≤4, correlates with CDAI < 150 or 50% fistula drainage

Partial response – fall of HBI ≥3, correlates with CDAI > 150 but no remission

No symptomatic response – no clinical improvement, fall of HBI ≤ 2, no reduction in fistulae drainage

CONTINUATION OF TREATMENT:

Review within 12 months, and 12 monthly intervals thereafter. Continue treatment only if there is clear evidence of response as determined by clinical symptoms, biological markers and investigation, including endoscopy if necessary.

For patients in stable, clinical remission consider stopping treatment, resuming if there is a relapse. **Indications whereby TNFi clinically inappropriate:**

proven malignancy in the last 10 years, malignant melanoma at any point, bronchiectasis, pulmonary fibrosis, multiple sclerosis, SLE.

DOSE ESCALATION for infliximab, adalimumab or ustekinumab can be considered to recapture response in patients who have responded to conventional induction and treatment regimes and subsequently lost response and in patients whom are clinically symptomatic and require target to range - maximum duration: 6 months (submission of a prior approval proforma for CCG consideration is required).