BEDFORDSHIRE, LUTON AND MILTON KEYNES AREA PRESCRIBING COMMITTEE (APC)

Treatment of Moderate to Severe Ulcerative Colitis <u>after</u> failure of conventional therapy (Updated December 2023)

(Previous versions –Approved by the BLMK APC in July 2023, December 2022 and as an interim pathway in August 2022; Bedfordshire and Luton Joint Prescribing Committee, September 2020)

<u>General Prescribing notes</u>

- Clinicians should refer to the SmPCs for each individual drug for full prescribing information, noting ▼black triangle status where applicable. – **click here**
- **JAK inhibitors** –The MHRA have issued a drug safety update (DSU) bulletin (April 2023) detailing new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality with JAK inhibitors. See **MHRA advice** on measures to consider before considering prescribing a JAK inhibitor.
- Always prescribe by brand name
- Biosimilar biologics are preferred over the originator brand (cost effective)
- Switching from originator brand to a biosimilar should be carried out as per locally agreed switching protocols.
- Only 1 re-induction of Mirikizumab is supported.

Dose Escalation:-

- If at any point before 12 months of treatment has passed , and treatment has failed (including the need for surgery), consider TNF inhibitor drug and antibody levels to support a decision to dose escalate or switch.
- Consider dose escalation or interval reduction of adalimumab/ infliximab/ ustekinumab/ tofacitinib to recapture response.
- **Dose Escalation adalimumab / infliximab / tofacitinib/ ustekinumab**. When response to induction and maintenance treatment but then loss of response, an attempt to recapture response with temporary period of increased dose / shortened interval between doses may be made: **infliximab** - 1 dose of 10mg/kg or 3 doses of 5mg/kg given 4-6 weekly and then stretch back to 8 weekly; **adalimumab** – 40mg weekly for up to 8 weeks then stretch back to every other week; **tofacitinib** 10mg twice daily for 8 weeks then reduce back to 5mg twice daily (refer to <u>SPC</u> and <u>Drug Safety Updates</u> for restrictions for 10mg twice daily dose) ; **ustekinumab** 2 doses 8 weekly, then stretch back to 12 weekly.
- Consider trial of maintenance escalated dose for patients with clear objective evidence of response to escalated dose & loss of response on de-escalation to standard dose. Alternatively consider other treatment options as per the pathway. Reassess the patient after 6 months and then at least every 12 months to determine if ongoing escalated dose is still clinically appropriate. Patients without active disease in stable clinical remission should undergo a trial of de-escalation. Patients whose disease has relapsed after trial de-escalation may continue on escalated dose.
- NB. Infliximab dose escalation for UC is off label use.

The dose escalation outlined above is based on the Hertfordshire and West Essex ICB pathway which is acknowledged with thanks.

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

Bedfordshire, Luton and Milton Keynes Health and Care Partnership

Bedfordshire Luton and Milton Keynes ICS Local Commissioning Policy

Treatment of Moderate to Severe Ulcerative Colitis AFTER failure of conventional therapy

(December 2023 Update)

This algorithm is only applicable for use in patients who have failed to respond to, who are intolerant of, who have contraindications where it is deemed clinically inappropriate to use conventional therapies (aminosalicylate, corticosteroids or thiopurines) or ciclosporin (acute exacerbation of severely active disease only) as per NICE NG 130

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, **least expensive** should be chosen (taking into account administration costs, dosage and price per dose). Biosimilars# are cost-effective treatment options.

Moderate to severe active ulcerative colitis

First line treatment options

The most cost-effective, suitable treatment option should be chosen.

1. TNF inhibitors (TNFi) (TA 329)

- Adalimumab# Review at 8 weeks
- Infliximab# (S/C or IV) Review at 14 weeks
- Golimumab Review at 12-14 weeks

A switch from adalimumab to infliximab biosimilars or vice versa can be undertaken (with TDM) in line with BSG IBD Guidelines

2. JAK inhibitors (TA 547 , TA 792 and TA 856)

- Tofacitinib Review at 8-16 weeks
- Filgotinib Review at 10 weeks
- Upadacitinib Review at 8-16 weeks

3. α4β7 integrin inhibitor (TA 342)

- Vedolizumab (S/C or IV) Review at 10 weeks

First line treatment option only if TNFi is unsuitable (see note 1)

- **Interleukin inhibitor**
  Ustekinumab. **(TA 633)** Review at 16 weeks
  Mirikizumab. (TA 925) Review at 12-24 weeks.
- **Sphingosine 1-phosphate receptor modulator (TA 828)** – Ozanimod **(only if infliximab is not suitable)** Review at 10 weeks.

Acute exacerbation of severely active ulcerative colitis

Consider, in line with TA 163:
Infliximab (3 doses only).
Continued treatment indicated when criteria for moderately to severely active UC fulfilled after induction (a new funding request would be required).

Assess patient's response after 1st line treatment
If clinical response achieved (see **note 2**), follow maintenance advice (see **note 3**). Consider dose escalation (see page 1).
Treatment Failure - Withdraw and move to subsequent treatment line

Second line treatment options:

Filgotinib or Tofacitinib or Ustekinumab or Vedolizumab or Ozanimod or Upadacitinib or Mirikizumab

Consider changing to an alternative treatment option if:

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

Assess patient's response after 2nd line treatment option
If clinical response achieved (see **note 2**), follow maintenance advice (see **note 3**).
Treatment Failure - Withdraw and move to subsequent treatment line.

Two further treatment options with different modalities may be considered. TOTAL OF 4 OPTIONS (3 SWITCHES) PER PATIENT – this includes treatment failure and contra-indication/intolerance , but excludes an initial anti-TNF switch. Review as per 1st and 2nd line treatment options. Treatment requests beyond the end of the pathway, where clinical exceptionality can be demonstrated, can be considered via the Individual Funding Request (IFR) route.

Note 1– Patients unsuitable for TNFi
Proven malignancy – see ECCO Guidelines, malignant melanoma at any point, bronchiectasis, pulmonary fibrosis, multiple sclerosis, SLE, cardiac failure.

Note 2 – Adequate response
Improvement in clinical symptoms and progression towards mucosal healing.

Note 3 – Continuation of treatment
Give as a planned course of treatment until treatment fails (including the need for surgery) or until 12 months after starting treatment, whichever is shorter. 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.

Ratified by Bedfordshire, Luton and Milton Keynes Area Prescribing Committee December 2023