Kent and Medway Policy Recommendation and Guidance Committee
Policy Recommendation

Policy:	**PR 2022-25: Dual biological therapy for inflammatory bowel disease (IBD) in adults**
Issue date:	**September 2022**

The Kent and Medway Policy Recommendation and Guidance Committee (PRGC) considered national guidance, the evidence base, baseline position, other ICB policies, the views of specialists and the potential impact of changing policy. All decisions were made with reference to the Ethical Framework. Taking these into account the PRGC recommends:

- Dual biological therapy is not routinely funded by Kent and Medway Integrated Care Board (ICB) to manage inflammatory bowel disease (IBD) in adults

This policy recommendation will be reviewed when new information becomes available that is likely to have a material effect on the current recommendation.

Kent and Medway Integrated Care Board (ICB) will always consider appropriate individual funding requests (IFRs) through its IFR process.

Supporting documents

Health Policy Support Unit (HPSU) (2022) *Dual biologic therapy for inflammatory bowel disease (IBD) – Scoping report*

Health Policy Support Unit (HPSU) (2022) *Cost impact of funding dual biologicals for inflammatory bowel disease (IBD) – Briefing note*

Equality Analysis Screening Tool – Dual biologic therapy for inflammatory bowel disease (IBD) (2022)

Key points

What is inflammatory bowel disease (IBD)?
IBD is an umbrella term used to describe disorders that cause chronic inflammation of the gastrointestinal tract. The most common forms of IBD are ulcerative colitis (UC) and Crohn's disease (CD). UC only affects the colon (large intestine). CD can affect any part of the digestive system, from the mouth to the anus. Symptoms of IBD include abdominal pain, cramps or swelling, recurring or bloody diarrhoea, weight loss and tiredness. People with IBD can go for long periods with few or no symptoms, followed by periods of active disease when symptoms flare up.

How is IBD managed?

- There is currently no cure for UC or CD. Treatment aims to relieve the symptoms and prevent them from returning, and includes specific diets, health behaviours, medicines and surgery.
- Biological therapy may be considered in patients with moderate-severe active IBD which has not responded to conventional therapy (such as aminosalicylates and immunosuppressants such as corticosteroids or azathioprine), or where conventional therapy is not tolerated. Biologicals are also effective at maintaining remission.
- There are 3 classes of biologicals used to treat IBD recommended by NICE technology appraisal guidance as mono biological therapy:
    - TNF-α antagonists (i.e., infliximab, adalimumab and golimumab[1])
    - Interleukin-12 (IL-12) and interleukin-23 (IL-23) antagonists (i.e., ustekinumab)
    - $\alpha_4\beta_7$ integrin antagonists (i.e., vedolizumab)
- A significant proportion of patients with IBD have a secondary loss of response to biological therapies or are primary non-responders.
- The combination of two classes of biologicals targeting different inflammatory pathways has the theoretical potential to improve therapeutic efficacy
- While surgery can be an effective treatment for some patients with refractory disease, perioperative risks exist, and (sequential) bowel resections may result in short bowel syndrome leading to intestinal failure and dependence on parenteral nutrition. In addition, for many patients, surgery is unsuitable or unacceptable – avoiding surgery is highly desirable.

What are the costs of biologicals for IBD?
The cost of different biological monotherapies varies considerably, from around £2.5k to around £13.5k in year 1; taking into account relevant patient access schemes. See the briefing note on the cost impact of funding dual biologicals for IBD for more information.
NHS Integrated Care Boards (ICBs) are responsible for the commissioning of biologicals for IBD in adults. NHS England are responsible for commissioning biologicals for IBD in children.

What does NICE guidance say?
NICE have not published guidance on the use of dual biologics for the treatment of IBD, but have published a number of technology appraisal guidance on biologicals and small molecules used as monotherapy for IBD that have been incorporated into clinical guidelines on the management of CD (NG129; 2019) and UC (NG130; 2019)[2].

What does other guidance say?

- In 2021, the South Regional Medicines Optimisation Committee (RMOC) released an advisory statement on the combination use of biologics, which concludes that there is currently insufficient evidence for RMOC to provide guidance. They note that no national or regional registries currently exist to monitor outcomes and safety.
- No professional society guidance on dual biologic therapy for IBD were identified.

What is the evidence base for dual biological therapy for IBD?
A literature search identified a recent systematic review of 30 studies (279 patients) evaluating dual biologic or small molecule therapy for IBD. Of these 30 studies, only 1 was a randomised controlled

[1] NICE recommend golimumab as an option for moderately to severely active UC if conventional therapy has failed or cannot be tolerated or is contraindicated. NICE have not developed technology appraisal guidance on golimumab for CD.
[2] NICE TA792 (2022) on filgotinib and NICE TA633 (2020) on ustekinumab have not yet been incorporated in NICE NG130 (2019).

trial (RCT), which evaluated a biological drug not approved for use in IBD in the UK; the remaining studies were case series or reports. The definitions of reported outcomes differed across the included studies and participants did not have available data for all outcomes. Consequently, the overall quality of the evidence on dual biological therapy in IBD is low and no specific recommendations regarding individual combinations of biologicals can be made, or outcomes predicted based on patient factors.

The median duration of treatment reported in studies was 24 (interquartile range [IQR], 13–32) weeks and the median follow-up period 32 (IQR, 24–52) weeks. The proportions of patients achieving clinical and endoscopic remission with dual biologic or small molecule therapy were 52% (110/ 211) and 33% (29/ 87), respectively. The proportions of patients achieving clinical and endoscopic response were 72% (99/ 138) and 58% (28/ 48), respectively. The proportion achieving corticosteroid-free remission was 48% (62/ 128) and the proportion requiring surgery was 10% (24/ 237). With respect to safety, pooled data demonstrated overall rates of adverse events, infections, and malignancy similar to historical rates of TNF antagonist monotherapy. However, the lack of high-quality evidence and longitudinal data beyond the median follow-up period of 32 weeks precludes drawing definitive conclusions.

No health economic studies assessing the cost-effectiveness of dual biologic therapy for IBD were identified.

What is the baseline position?

- There is currently no Kent and Medway-wide policy on dual biologic therapy for the treatment of IBD.
- Dual biological therapy is not currently used to treat Kent and Medway IBD patients.
- No individual funding requests (IFRs) for dual biologic therapy for the treatment of UC or CD in Kent and Medway have been received (up until February 2022).
- According to Blueteq data, in 2020/21, 7,154 treatments with biologics (as monotherapy) were delivered to patients in Kent and Medway with IBD, costing ~£6.77 million.
- The only formulary identified with a policy on dual biological therapy for IBD was South-East London which fund dual biologic therapy for severe, refractory CD in certain circumstances.

Change sheet

Reason for review:
Dual biological therapy for inflammatory bowel disease (IBD) was prioritised for policy development because of an increase in individual funding requests in neighbouring areas, lack of local policy on this topic and because local specialists have expressed a desire to use dual biologic therapy in selected patients.

Change from baseline:
None. Consistent with PR2022-25, dual biological therapy is not currently used to treat Kent and Medway IBD patients.

Rationale for PR2022-25:

- Published evidence on dual biological therapy for IBD is largely limited to observational studies. Although the efficacy of dual biologic therapy may be inferred based on their mechanisms of action, evidence to support this is lacking. The lack of long-term longitudinal data precludes drawing definitive conclusions on the long-term risks of infection or cancer. The evidence base is also too limited to support recommendations on particular combinations of biological therapies or to predict outcomes based on patient factors.
- No health economic studies assessing the cost-effectiveness of dual biologic therapy for IBD were identified.
- In the absence of a local policy on this topic currently, PR2022-25 establishes a consistent position on the provision of dual biological therapy for IBD across Kent and Medway.

Estimated cost impact of implementing PR2022-25:
Implementation of PR2022-25 is expected to be cost neutral.

The estimated cost avoided by not funding dual biologic therapy (restricted to the least expensive infliximab or adalimumab biosimilar plus either vedolizumab or ustekinumab) in 70 patients with refractory UC and CD in year 1, taking into account offset costs (excluding intestinal failure) is £480k to £799k. These estimates are based on a number of unverifiable assumptions and should therefore be treated with caution. See the briefing note on the cost impact of funding dual biologicals for IBD for more information.