Kent and Medway Policy Recommendation and Guidance Committee

Policy Recommendation

Policy:	**PR 2024-10: Dose escalation of subcutaneous infliximab for inflammatory bowel disease (IBD)**
Issue date:	**May 2024**

The Kent and Medway Policy Recommendation and Guidance Committee (PRGC) considered NICE guidance, the evidence base, baseline position, other Integrated Care Board (ICB) policies, the views of clinical specialists, equality and equity issues, and the potential impact of a new policy.

All decisions were made with reference to the Kent and Medway ICB principles for clinical decision-making. Taking these into account, the PRGC recommends:

- Dose escalation of infliximab (to 240mg every 2 weeks), via subcutaneous (SC) injection is only funded as a treatment option for patients with IBD if initial response to SC infliximab 120mg every 2 weeks is lost in the maintenance phase*.
- Dose escalation should only be undertaken after consideration of anti-TNF trough levels and the presence of anti-TNF antibodies, as set out in the Kent and Medway IBD high-cost drug pathway.

** Definition of loss of response for ulcerative colitis (UC): the need for initiation of a new treatment for active UC or a ≥1-point increase from the lowest rectal bleeding subscore with an actual value of >1 point, with either a ≥2-point increase from the lowest partial Mayo score, with an actual value of ≥4 points, or a ≥1-point increase from the lowest score in endoscopic subscore with an actual value of >1 point. Definition of a loss of response for Crohn's disease (CD): the need for initiation of a new treatment for active CD or a ≥70-point increase from the lowest CDAI score with a total score ≥220.*

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

South, Central and West (SCW) Clinical Effectiveness team (2024) *Dose escalation of subcutaneous infliximab for inflammatory bowel disease (IBD) – Report for Kent and Medway ICB*

Equality Analysis Screening Tool – Dose escalation of subcutaneous infliximab for inflammatory bowel disease (IBD) (2024)

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). 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. Both UC and CD are thought to be immune-mediated conditions caused by environmental triggers in genetically susceptible people.

How is IBD managed?
IBD treatment aims to relieve symptoms and to prevent them from returning. Treatment options include consuming specific diets, lifestyle changes, medicines, and surgery.

Biological therapy (such as infliximab) may be considered in patients with moderate-severe active IBD which has not responded to conventional drug therapy (such as aminosalicylates, corticosteroids and immunosuppressants), or where conventional therapy is not tolerated.

While surgery can be an effective treatment for some patients with refractory disease, it is associated with perioperative risks and other complications. In addition, for many patients, surgery is unsuitable or unacceptable – avoiding surgery is highly desirable.

What is infliximab?
Infliximab is a monoclonal antibody that inhibits the activity of tumour necrosis factor alpha (TNFα), a pro-inflammatory mediator.

Infliximab (Remicade) has been licensed in the UK for the treatment of UC and CD for many years. Infliximab (Remicade) is administered by intravenous (IV) infusion. There exist a number of infliximab biosimilars for intravenous infusion (i.e., Flixabi, Inflectra, Remsima, Zessly). There is also a subcutaneous (SC) version of Remsima, which is the only infliximab product licensed in the UK for subcutaneous administration[1].

In contrast to intravenous infliximab, which is dosed according to weight, subcutaneous infliximab is administered according to a flat-fixed dosing schedule (after initial loading intravenous dosing according to weight). According to the license for the SC formulation of Remsima (infliximab), the recommended maintenance dose is 120mg once every 2 weeks in adults with IBD.

As with all biologics and small molecule drugs (such as Janus kinase inhibitors and sphingosine-1-phosphate receptor modulators) used for treating CD and UC, subcutaneous infliximab would be prescribed and started in secondary care gastroenterology clinics. Unlike intravenous infliximab, which is usually given in secondary care, subcutaneous infliximab can be self-administered at home if the person, family member or carer has been given the appropriate training.

What does NICE guidance say?
NICE have not issued technology appraisal (TA) guidance specifically on the use of subcutaneous infliximab for CD or UC. However, NICE have issued a number of TAs recommending intravenous infliximab for the treatment of CD and UC in certain circumstances, i.e., TA163 (2008), TA187 (2010), TA329 (2015).

What does the evidence say?
The evidence base to support the use of dose escalated SC infliximab (i.e., 240mg every 2 weeks) is limited. In 2 small observation studies, most participants receiving SC infliximab 120 mg every 2 weeks who experienced disease recurrence reported a clinical benefit when escalated to SC infliximab 240mg every 2 weeks. Similarly, results from post-hoc analyses (available as abstract only) of 2 unpublished randomised controlled trials suggest that dose escalation of SC infliximab from 120mg to 240mg every 2 weeks may be effective in restoring efficacy in some patients. No new safety concerns were found after dose escalation. No studies evaluating the cost-effectiveness of SC infliximab at a dose of 240mg every 2 weeks for IBD were identified.

[1] Remsima for subcutaneous injection received a marketing authorisation for managing rheumatoid arthritis in 2019 and received a license extension for Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis, and psoriasis in 2020.

What is the cost of infliximab?

Infliximab is a high-cost drug excluded from the NHS Payment Scheme.

A confidential local discount is in place for infliximab.

What is the baseline position in Kent and Medway?

- Dose escalation of subcutaneous infliximab for IBD is not included as an option on Kent and Medway formularies or the Kent and Medway IBD high-cost drug pathway. Local specialists have confirmed that their patients do not currently receive SC infliximab 240mg every 2 weeks for IBD.
- 187 patients were approved for use of infliximab (including biosimilars) in 2023/24; 72 for IV infliximab and 115 for SC infliximab.
- Total expenditure on infliximab for IBD in 2023/24 was £819k; £609k on IV infliximab and £209k on SC infliximab, although expenditure data for 2023/24 from Dartford, Gravesham and Swanley is currently incomplete.

Change sheet

Reason for review:

- Local specialists have requested the option to use an escalated maintenance dose of subcutaneous (SC) infliximab for inflammatory bowel disease (IBD), off-label.
    - According to the license for the SC formulation of Remsima (infliximab), the recommended maintenance dose is 120 mg once every 2 weeks in adults with IBD for all weights, without dose escalation[2].
    - Local specialists have requested to use SC infliximab at a maintenance dose of 240 mg once every 2 weeks, in a small number of carefully selected adults with IBD.
- NICE have not developed guidance on the use of SC infliximab for IBD.
- Infliximab is a high-cost drug excluded from the NHS Payment Scheme. Consequently, it is important to ensure appropriate commissioning, financial, and governance arrangements are in place to support consideration of its use.

Change from baseline:

Dose escalation of SC infliximab for IBD is not currently used to treat Kent and Medway IBD patients. Implementing PR2024-10, would mean dose escalation of SC infliximab for IBD would be funded in certain specified circumstances.

Rationale for PR 2024-10:

Low quality evidence suggests that dose escalation of SC infliximab from 120mg to 240mg every 2 weeks may be effective in restoring efficacy in some patients with IBD. Local specialists support the eligibility criteria set out in PR2024-10, noting that dose escalation of SC infliximab may potentially avoid the use of more expensive alternative treatments, and/or requirement for intravenous infusion in secondary care, which is less convenient for patients.

Estimated impact of implementing PR 2024-10:

If dose escalation of SC infliximab (i.e., 240mg every 2 weeks) for IBD is not available, patients are likely to revert to IV infliximab or be switched to an alternative treatment instead. The cost impact of SC infliximab 240mg every 2 weeks is therefore dependent on the cost of the treatment that would otherwise be used. The cost of these alternative treatments varies considerably; some are more expensive, and some are less expensive than SC infliximab 240mg every 2 weeks. The cost of switching to the cheapest as well as most expensive alternative treatment has been calculated, creating a range of estimates.

The cost impact to Kent and Medway ICB of funding SC infliximab 240mg every 2 weeks for IBD (according to PR2024-10), is estimated to range between a cost pressure of £66k and a cost saving of £339k in year 1.

If it is assumed that half of the patients potentially eligible for SC infliximab 240mg every 2 weeks (according to PR2024-10), instead switch to the most expensive alternative biological available and the other half instead switch to the least expensive alternative available, the cost impact of funding SC infliximab 240mg every 2 weeks for IBD is estimated to be a saving of £136k in year 1.

Note, these estimates should be treated with caution as they were calculated using a number of unverifiable assumptions. See the accompanying report for more information.

[2] Remsima SC is the only infliximab product licensed in the UK for subcutaneous administration.