Infliximab Dose Escalation Policy for IBD

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

Introduction

This policy has been developed to support the decision making process associated with the allocation of resources for commissioning. In creating this policy BSW CCG has reviewed this treatment and the clinical conditions for which it is prescribed. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

Background

Infliximab was approved by NICE for adults with severe active Crohn's disease in May 2010[1] and for adults with moderately to severely active Ulcerative Colitis in February 2015[2]. The licensed maintenance dose for these indications is 5mg/kg 8 weekly[3]. However it is current practice that some patients are treated with doses that are outside of the license in order to maximise treatment response. Therapeutic options for patients with Inflammatory Bowel Disease (IBD) are limited and so optimising drug therapy is essential to ensure patients get the maximum value from treatments. Patients without further drug options are likely to be left with a high symptom burden and require frequent hospital admissions and/or surgery.

Proposal

In order to ensure that our patients across BSW CCG are dealt with in an equitable manner, this policy aims to provide clarity to acute provider trusts on how to deal with patients where dose escalation is being considered. Proposed commissioned dose escalation for infliximab in IBD:

- 5mg/kg 6 weekly (off label)
- 10mg/kg 8weekly (off label)
- 10mg/kg 6 weekly (off label)
- Criteria based access using blueteq.

We have identified that a proportion of infliximab treated patients experience a return in their IBD symptoms before their next dose at the licensed interval of 8 weekly. We propose that for a small number of patients increasing the dose to 10mg/kg 8 weekly, or reducing the frequency of administration to 5mg/kg 6 weekly would be beneficial. For an even smaller number of patients where a further dose escalation is required, we propose the option to increase the dose and reduce the frequency to 10mg/kg 6 weekly. The patients eligible for this escalation of infliximab would be carefully selected based on assessment of their clinical symptoms, drug and antibody levels. As these dose escalations are outside of license, where one of these dose escalations are utilised, both the patient and consultant would need to aware of and agree to the use of an off-license dosing schedule.

The annual cost of 1 year of infliximab treatment for a 70kg patient at 5mg/kg 8weekly is £3954.51. When escalated to 5mg/kg 6 weekly the average annual cost of treatment increases to £5084.37, and at 10mg/kg 8 weekly to £5446.41. However these suggested dose escalations are already being utilised and this change in policy would seek to align us with the current practice of our clinicians. The associated IBD Therapeutic Drug Monitoring Pathway demonstrates the criteria based access that clinicians have agreed to. The aim is to minimise the variation in dose escalation and assessment taking place and unify practice across BSW.

Evidence

This review has been generated due to the wide usage of infliximab dose escalation within IBD and increasing anecdotal evidence from clinicians. NICE TA187 and TA329 does not address dose escalation in their guidance[1,2] and the manufacturers (Merck Sharp & Dohme Limited), state that the safety and efficacy of infliximab other than every 8 weeks has not been established[3]. The British Society of Gastroenterology consensus guidelines do not address dose escalation of infliximab, however do reference studies for UC and Crohn's in which doses of 5mg/kg and 10mg/kg are utilised (ACT1, ACT2+ ACCENT1). [4] The most recent study and pivotal study in this area is by Kennedy et al. 2019[5].

Kennedy et al. PANTS. Lancet 2019 – A prospective observational UK-wide study, 955 anti-TNF-naive patients with active Crohn's disease were treated with infliximab and evaluated for 12 months or until drug withdrawal. Findings indicate that Anti-TNF treatment failure is common and is predicted by low drug concentrations and development of anti-drug antibodies. Interpretation suggests it might be possible to improve patient outcomes by utilising direct monitoring and dose optimisation to achieve effective drug concentrations. Alongside mitigation of anti-drug antibodies, such strategies would allow these drugs to be used more effectively, in a safer, more cost effective manner.

Monitoring

To ensure that these patients are appropriate for initiating dose escalation drug levels and antibody levels will be taken as per the IBD Therapeutic Drug Monitoring Pathway. To determine if dose escalation has been successful, these levels will be repeated immediately before the fourth dose escalated dose is given. If successful then it is expected that the ongoing need for dose escalation will continue to be reviewed at the patient's annual review. If the patient is well maintained and asymptomatic, de-escalation of treatment should be considered by the clinician. Where the dose escalation has not improved the patient's condition guidance has been provided on when to consider discontinuing/ switching therapy. Further dose escalation beyond 5mg/kg 6 weekly, 10mg/kg 8 weekly or 10mg/kg 6 weekly is not commissioned and requires an Individual Funding Request. BSW CCG will require secondary care service providers to embrace the policy and monitoring pathway and advise patient's accordingly. Adherence to this policy will be demonstrated by clinicians via Blueteq criteria based access. BSW CCG will monitor blueteq, alongside standard contractual process monitoring on an ongoing basis.

References

[1] Infliximab and adalimumab for the treatment of Crohn's disease NICE TA187, May 2010. https://www.nice.org.uk/guidance/ta187

[2] Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy NICE TA329, February 2015. https://www.nice.org.uk/guidance/ta329

[3] Summary of product characteristics. Remicade 100 mg powder for concentrate for solution for infusion (infliximab); date of revision of text 23 October 2020. Merck Sharp & Dohme Limited. https://www.medicines.org.uk/emc/medicine/3236

[4] Lamb et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. BMJ Gut 2019; 0:1-106.

[5] Kennedy et al. Predictors of anti-TNF treatment failure in anti-TNF-naive patients with active luminal Crohn's disease: a prospective, multicentre, cohort study. The Lancet May 2019; 4:5-P341-353