Record of the Gastrointestinal Subcommittee of PTAC Meeting held on 14 October 2020

Present from the Gastrointestinal Subcommittee:

Jonathan Bishop
Alan Fraser (PTAC member)
Russel Walmsley

Apologies
Simon Wynn Thomas (Chair, PTAC member)
Murray Barclay
Sandy Dawson
Michael Schultz
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Table of contents

Summary of outcome 1
Adalimumab 1

Summary of outcome

1. The Subcommittee discussed the impact the possible introduction of a biosimilar adalimumab would have, in the event of a Request for Proposals (RFP) for adalimumab.

2. Adalimumab

Application

2.1 Members of the Gastrointestinal Subcommittee (hereafter collectively referred to as the Subcommittee) reviewed a PHARMAC generated paper on the potential impact of an adalimumab brand change for patients treated for Crohn's disease.

Discussion

2.2 The Subcommittee noted the purpose of the discussion was to seek advice on implementation considerations in advance of a possible competitive process for the supply of adalimumab in New Zealand. The Subcommittee noted that advice was sought specifically regarding the management of patients treated with adalimumab for Crohn's disease, in the event that a biosimilar adalimumab became the sole subsidised adalimumab for all funded indications.

2.3 The Subcommittee noted adalimumab has been listed on the Pharmaceutical Schedule since 2009, subject to Special Authority restrictions, including funding for fistulising Crohn's disease, and Crohn's disease affecting both adult and children. The

Subcommittee noted approximately one third of patients currently receive adalimumab for management of Crohn's disease.

2.4 The Subcommittee noted the evidence provided to guide their discussion and considered this was a reasonable representation of the evidence available to support biosimilar usage within Crohn's disease. The following publications were reviewed:

2.4.1 Blauvelt, A et al. Br J Dermatol. 2018; 179(3) 623-631.

2.4.2 Weinblatt, ME et al. Arthritis and Rheumatology. 2018; 70(6); 832-840.

2.4.3 Cohen, SB et al. Ann Rheum Dis. 2018; 77: 914-921.

2.4.4 Lukas, M et al. Journal of Crohns and Colitis. 2020; 14(7); 915-919.

2.4.5 Jorgensen, KK et al. Lancet. 2017: 389; 2304-2316.

2.4.6 Bellinvia, S et al. BioDrugs. 2019; 33:241-253.

2.4.7 Barbier, L et al, Clinical pharmacology and therapeutics. 2020; 0(0),

2.4.8 Kang. et al. Inflammatory Bowel Diseases 2018;24:607-16.

2.4.9 de Ridder, L et al. Journal of Paediatric Gastroenterology and Nutrition.

2.4.10 Renton, WD et al. Pediatric Rheumatology 2019; 17(67).

2.4.11 Hemmington, A et al. Pharmacoepidemiol Drug SAf. 2017; 25(5):570-577.

2.5 The Subcommittee noted infliximab is another tumour necrosis factor inhibitor (TNF inhibitor) funded for patients for Crohn's disease; however, unlike adalimumab which is a subcutaneous injection and able to be administered in the community, infliximab is delivered by intravenous injection in hospital. The Subcommittee noted that adalimumab is used as the first line biologic treatment in the majority of adults with Crohn's disease, however, is used as a second line biologic following infliximab use for most children with Crohn's disease and/or patients presenting with perianal fistulising Crohn's disease.

2.6 The Subcommittee considered time on treatment typically spanned several years for patients who demonstrate an initial response to treatment. The Subcommittee noted that approximately 10-20% of adults experience secondary loss of response to adalimumab treatment annually. Members considered the annual rate of loss of response was difficult to predict in the paediatric setting due to the low patient numbers in this group, but the medical literature would suggest an annual rate of loss of response to be 8-15%.

2.7 The Subcommittee noted loss of response to treatment, or lack of response to treatment has differing effects relative to when adalimumab was used in the treatment pathway. The Subcommittee noted that the initial step in evaluating a loss of response to treatment or lack of treatment response was to confirm symptoms of active disease and determine whether the patient was experiencing primary failure evidenced by therapeutic drug levels or having difficulty with adherence. The Subcommittee considered, in the event of low therapeutic drug levels or secondary loss of response, alternative treatments are limited due to inability to increase the dose of adalimumab

for this patient group. Members considered that patients using adalimumab as a first line biologic who experience a loss of response to treatment or a lack of treatment response, would likely be switched to infliximab treatment and for patients using adalimumab as a last line biologic therapy, there are no or very limited remaining pharmacological options available.

2.8 The Subcommittee considered the rate of primary lack of response, and secondary loss of response was likely to be equivalent between adalimumab and a biosimilar adalimumab; however, noted that, unlike conditions where patient feedback on loss of response is far quicker (such as for rheumatology indications), it can take several months before disease relapse is able to be identified for Crohn's patients which can result in significant relapses and difficulty managing the resultant symptoms.

2.9 The Subcommittee noted that, depending on the outcome, a competitive process for adalimumab could result in the first transition for Crohn's patients to a biosimilar. Members noted a key consideration regarding this would be management of both patient and clinician anxiety regarding the switch to a biosimilar, particularly in patients using adalimumab as a last-line therapy. The Subcommittee considered that clinicians' confidence in the evidence supporting biosimilar use and switching of patients to a biosimilar would have an impact on a patients' perception of any change. It was considered that clear and effective communication with prescribers regarding a switch including relevant evidence-based information would be helpful. Members noted the familiarity of patients with the branding and device of the reference adalimumab and considered that support relating to the change in appearance, or changes in use of the device, would be required.

2.10 The Subcommittee considered that there is a risk of patients experiencing loss of treatment response in the time following switch to a biosimilar adalimumab, but due to the nature of these treatments, considered that this would likely occur for patients regardless of whether there was a switch to a biosimilar or not. The Subcommittee did not identify any specific patient groups who would be most at risk of adverse outcomes following switch to a biosimilar adalimumab and acknowledged that available evidence indicates comparable efficacy.

2.11 The Subcommittee noted Principal Supply Status (PSS) was a possible management tool for the majority of indications for which adalimumab was used for, which would enable some patients to remain on, or switch back to, their originator treatment. The Subcommittee considered that, due to the lack of alternative biologic treatment options and impact of loss of disease control, there may be a number of high risk Crohn's patients who could be considered unsuitable to switch to a biosimilar and considered a strategy for management of these patients was required.

2.12 The Subcommittee noted that widened access, both to new indications and widened access to enable greater flexibility of dosing, would likely assist in both patient and clinician acceptance of any change to the funded brand of adalimumab.

2.13 The Subcommittee considered there were patients who experience pain associated with the subcutaneous injection of adalimumab; however, considered it was difficult to differentiate between pain relating to procedural anxiety compared to the constituents of an adalimumab formulation (e.g. presence of citrate, injection volume and needle size). The Subcommittee considered that the majority of patients were able to manage injection related pain and considered pain to be a barrier to starting treatment rather than a barrier for continuation of treatment; however, noted that pain relating to injection remained a primary non-medical reason for ceasing treatment. Members noted that, particularly for paediatric patients, the requirement for fortnightly

subcutaneous injections meant many patients preferred infliximab treatment compared to adalimumab.

2.14 The Subcommittee noted that there are a range of device and training considerations relevant to the use and administration of adalimumab treatment; however, considered there was a degree of patient preference as to which formulation was preferred. Members noted that the majority of patients self-administered treatment, with the exception of paediatrics who typically had treatment administered by a parent or caregiver.

2.15 The Subcommittee noted the support provided by the supplier available for patients when initiating on Humira treatment and considered this was well accessed by patients. The Subcommittee noted that whilst initial discussions regarding initiation of biologic treatment were held by Specialists and/or inflammatory bowel disease (IBD) nurses, further ongoing support was available and valuable for patients.

2.16 The Subcommittee considered that a seven-month transition period in the event of a brand change was reasonable and noted that most patients were reviewed by their IBD service quarterly.

2.17 The Subcommittee recommended that, in the event of a brand change, it would be important to ensure the logistics (and technology) relating to the management of two brands in the market simultaneously were clear and Special Authority access enabled easy and practical prescribing of the required brand to prevent additional work for prescribers and prevent accidental dispensing of a new brand before a patient has engaged with their clinician.