Record of the Rheumatology Subcommittee of PTAC Meeting held on 13 October 2020

Present from the Rheumatology Subcommittee:

Marius Rademaker (Chair)
Andrew Harrison
Alan Fraser (PTAC member)
Keith Colvine
Michael Corkill
Priscilla Campbell-Stokes
Will Taylor
Janet Hayward
Lisa Stamp (PTAC member)

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1. Summary of outcome

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 The Rheumatology Subcommittee reviewed a PHARMAC generated paper on the potential impact of an adalimumab brand change for patients treated for rheumatology conditions.

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 rheumatology indications, 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 several different rheumatology indications. The Subcommittee noted approximately 60% of patients who receive adalimumab do so for the management of a rheumatological condition including rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, and Adult-Onset Still's disease.

2.4 The Subcommittee noted the different funded biologic treatments available for these conditions in New Zealand, noting etanercept and infliximab are also tumour necrosis

factor (TNF) inhibitor treatments, and tocilizumab and rituximab which have differing mechanisms of action; however, the Subcommittee noted that, of these drugs, only TNF inhibitor treatments are currently funded and indicated for management of ankylosing spondylitis and psoriatic arthritis.

2.5 The Subcommittee considered that a large proportion of patients who show initial response to adalimumab treatment maintain this response for several years. The Subcommittee considered the time on treatment for Adult-Onset Still's disease is likely shorter than other rheumatological conditions due to faster onset of loss of response; however the Subcommittee also noted the lower patient numbers in this group, which limited guidance on expected duration on treatment.

2.6 The Subcommittee considered that approximately 50% of patients may experience either inadequate response or loss of response in the first six to twelve months of adalimumab treatment, resulting in switching to an alternative biologic treatment.

2.7 The Subcommittee considered the timing of loss of response to adalimumab treatment for patients was highly variable. The Subcommittee considered that patients experiencing loss of response to adalimumab were either switched to an alternative biologic agent, or a disease modifying antirheumatic agent (DMARD) or immunomodulator was added to their treatment regime, dependent on the degree of disease severity.

2.8 The Subcommittee considered the available evidence indicated no difference in efficacy of adalimumab to the adalimumab biosimilar formulations approved by the FDA/EMA, with similar rates of treatment related adverse events. Members considered the rate of primary lack of response, and secondary loss of response was likely to be equivalent between adalimumab and a biosimilar adalimumab.

2.9 The Subcommittee noted that, depending on the outcome, a competitive process for adalimumab could result in the first transition for many patients to a biosimilar. Members noted that, due to the presence of patents in New Zealand, rheumatoid arthritis patients were not switched to biosimilar rituximab when this was first introduced. Members noted the importance of clear and effective communication with prescribers regarding any switch and considered that evidence-based information and guidance would be helpful to encourage both clinician and patient confidence in a switch to a biosimilar.

2.10 The Subcommittee considered that, whilst adalimumab treatment is typically initiated at a secondary care level by rheumatologists, ongoing treatment monitoring including application for Special Authority renewals was often managed within primary care. Members considered that General Practitioners (GP's), pharmacists, and nurse practitioners would therefore play a significant role in supporting and switching patients, and considered it was important that appropriate counselling and practical education support regarding use of an adalimumab biosimilar was available to assist in the navigation of any change.

2.11 Members considered that whilst the available evidence suggests there is no difference in efficacy or safety of the biosimilar adalimumab formulations approved by the FDA/EMA to the reference product, there are likely to be patients who experience anxiety regarding switching to a biosimilar adalimumab. Members discussed the impact of prescriber-patient interactions on a patient's perception and confidence regarding a switch and considered clear communication of the evidence to support use of biosimilars as well as adequate information, education and reassurance for healthcare professionals and patients would be required.

2.12 The Subcommittee considered there may be some patients who experience loss of treatment response following switch to a biosimilar adalimumab, but this would not necessarily be related to the switch, but likely a loss of treatment effect. However, the Subcommittee acknowledged the risk that patients experiencing a disease flare following switch to a biosimilar adalimumab may attribute this to the change, particularly patients with a history of prior disease stability. The Subcommittee considered clear communication and reassurance that a biosimilar adalimumab is equally efficacious would be required to help reduce this perception of loss of disease control following a switch and manage concerns regarding any change.

2.13 The Subcommittee considered that the majority of rheumatology patients would be able to be successfully switched to a biosimilar adalimumab. The Subcommittee considered that a mechanism was needed for PHARMAC to consider patients who were unable to switch and the justification for this, and to consider who had tried and experience loss of disease response following a switch, noting that based on the available evidence, the number of patients this was likely to apply to should be low.

2.14 Members noted switching and use of biosimilar's was becoming increasingly common internationally due to evidence of biosimilar equivalence and noted that a rituximab biosimilar had recently been introduced into New Zealand without significant concern. Members considered that the primary difference in these markets is the familiarity of patients with the branding and device of the reference adalimumab and therefore support relating to the change in appearance, or changes in use of the device, would be required.

2.15 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. Members considered the desire to return to reference adalimumab treatment could vary dependent on the indication and based on what alternative treatments were available. Members considered there may be difficulty for some clinicians in objectively identifying loss of treatment response in patients reporting subjective changes in disease control.

2.16 The Subcommittee noted that widened access, both to new indications and widened access to enable greater flexibility of dosing and extended Special Authority renewal durations as a result of any procurement activity, would likely make any brand change more acceptable.

2.17 The Subcommittee noted the range of different formulations of adalimumab available, including citrate-free formulations. The Subcommittee considered there were patients who experience pain associated with the subcutaneous injection of adalimumab; however, noted that overall, the benefit of treatment generally outweighed any short-term injection related pain. The Subcommittee considered termination of treatment with adalimumab due to injection related pain is rare and noted that the exact cause of pain associated with adalimumab was unknown and likely multifactorial. Members considered that pain associated with injection was a particular issue for paediatric patients and required active management. The Subcommittee considered that whilst there may be some benefit of a citrate free product, this should not be at a cost to the Pharmaceutical Budget.

2.18 The Subcommittee noted that the majority of patients administer adalimumab treatment themselves, with the exception of paediatrics who typically have treatment administered by a parent or caregiver. The Subcommittee noted there was a range of

device and training considerations and considered that easy use of any adalimumab device was an important consideration, particularly sizing of a device, gauge of needle, and ease of administration for patients with limited dexterity. Members noted some patient preference for the pre-filled syringe formulations of adalimumab due to the ability to control the rate of drug delivery.

2.19 The Subcommittee noted the AbbVie funded support available for patients when initiating treatment with Humira and considered this was well accessed by patients. Members considered this support was valuable in assisting patients leaning how to self-inject, particularly in remote regions where access to available healthcare professionals is limited and noted that this service extended to include a mechanism for disposal of syringes and sharps. The Subcommittee considered education on the use of a new adalimumab device would be important but did not envision that patients would struggle substantively with changes in devices required for self-injection.

2.20 The Subcommittee considered that a seven-month transition period in the event of a brand change was reasonable; however considered it was important that any logistics (and technology) relating to the management of two brands of adalimumab in the market simultaneously were clear and well communicated. The Subcommittee considered this could be achieved through different Special Authority access as long as this enabled easy and practical prescribing of the required brand to prevent additional work for prescribers and prevented inadvertent switching of patients before they had discussed the switch with their clinician.

2.21 The Subcommittee noted following evidence relating to biosimilar usage in rheumatology indications. Members noted the results of a nationwide mandatory switch from originator to biosimilar etanercept in Denmark (Glintborg, B et al. Ann Rheum Dis. 2019: 78(2); 192-200.) showing the impact of patient-related factors such as anxiety and perception regarding nocebo effects on treatment retention and outcomes. The following publications were reviewed:

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

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

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

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

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

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

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

2.21.8 Cohen, S et al. Ann Rheum Dis. 2017; 76(10): 1679-1687.

2.21.9 Hodge J. et al. Arthritis Rheumatol. 2017;69 [abstract 2879].

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

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