Record of the Dermatology and Ophthalmology Subcommittees of PTAC Combined Meeting held on 8 October 2020

Present from the Dermatology and Ophthalmology Subcommittees:

Dermatology:
Lisa Stamp (Chair, PTAC member)
Melissa Copland
Paul Jarrett
Diana Purvis
Marius Rademaker (PTAC member)

Apologies
Julie Betts
Martin Denby
Sharad Paul

Ophthalmology:
Stephen Munn (Chair, PTAC member)
Joanne Sims
Samuel Whittaker
Marius Rademaker (PTAC member)

Apologies
Peter Grimmer
Malcolm McKellar
David Squirrell

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Summary of outcome

1. The Dermatology Subcommittee and the Ophthalmology Subcommittee (hereafter collectively referred to as the combined Subcommittees) discussed the impact a 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 Dermatology Subcommittee and the Ophthalmology Subcommittee (hereafter collectively referred to as the combined Subcommittees) jointly reviewed a paper from

PHARMAC staff on the potential impact of an adalimumab brand change for patients treated for dermatology and/or ophthalmology indications.

Discussion

2.2 The combined Subcommittees 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 combined Subcommittees noted that advice was sought specifically regarding the management of patients treated with adalimumab for dermatology and ophthalmology indications in the event that a biosimilar adalimumab became the sole subsidised adalimumab for all funded indications.

2.3 The combined Subcommittees noted adalimumab has been listed on the Pharmaceutical Schedule since 2009, subject to Special Authority restrictions, including funding for various dermatology and ophthalmology indications. The combined Subcommittees noted that, of those people who receive funded adalimumab, approximately 12% do so for the management of dermatological conditions, and approximately 1% for management of severe or chronic ocular inflammation.

2.4 The combined Subcommittees noted the following evidence relating to biosimilar usage within the relevant therapeutic groups of dermatology and ophthalmology:

2.4.1 Blauvelt et al. Br J Dermatol. 2018;179(3):623-31.

2.4.2 Weinblatt et al. Arthritis Rheumatol. 2018;70(6):832-40.

2.4.3 Cohen et al. Ann Rheum Dis. 2018;77:914-21.

2.4.4 Lukas et al. Journal of Crohns and Colitis. 2020;14(7);915-9.

2.4.5 Jorgensen et al. Lancet. 2017:389;2304-16.

2.4.6 Bellinvia et al. BioDrugs. 2019;33:241-53.

2.4.7 Barbier et al, Clin Pharmacol Ther. 2020;108(4):734-55.

2.4.8 Fabian et al. Front Pharmacol 2019;10:1-6.

2.4.9 Papp et al. Br J Dematol. 2017;177(6):1562-74.

2.4.10 Deaner et al. Am J Ophthalmol, 2020;20:S0002-9394(20)30424-4.

2.4.11 Renton et al. Pediatr Rheumatol. 2019;17(67).

2.4.12 Hemmington et al. Pharmacoepidemiol Drug Saf. 2017;25(5):570-77.

2.5 Members noted adalimumab is considered a first line biologic treatment for many patients in the management of dermatology-based indications, noting etanercept and infliximab are alternative funded tumour necrosis factor (TNF) inhibitor treatments, with secukinumab, an anti IL-17, funded for psoriasis . Members noted adalimumab has been funded for ocular inflammation from September 2019, with biologic management restricted to infliximab treatment prior to this.

2.6 The combined Subcommittees considered that time on treatment typically spanned several years for both dermatology and ophthalmology indications. Members considered it was unusual for dermatology patients to experience primary non-response to adalimumab treatment; however, response to treatment is expected to wane over time, with approximately 40% of patients remaining on adalimumab treatment after four years. Members noted the availability of adjunct treatments, such as methotrexate, that may be used to prolong the duration of effect from adalimumab treatment. Members noted that adalimumab is typically a long term treatment and considered that the prolonged duration on treatment in New Zealand may be due to the limited alternative funded biologic treatment options available for this patient group.

2.7 Members noted that ongoing treatment with adalimumab for dermatological conditions such as plaque psoriasis was dependent on treatment response, measured by disease scores such as the psoriasis area and severity index (PASI). Members considered that a patient's tolerance and acceptance of changes or small increases in their disease severity decreased over time particularly if the patient had experienced a period of time during which disease was well controlled with treatment. Members considered that any changes in disease control are visible in the early stages of a relapse and noted that a raised disease score often triggered a change in treatment management.

2.8 Members noted that dispensing data reflecting duration on adalimumab treatment for patients' treated for ocular inflammation was limited, as funding for this group commenced in September 2019; however, Members considered there would likely be 5-10% patients who experience primary non-response to adalimumab and cease treatment within the first six months. Members considered that chronic inflammation required long term treatment, with approximately 20% of responders remaining on treatment beyond two years.

2.9 Members noted the evidence supporting use of biosimilar adalimumab in dermatology patients indicates equal efficacy and considered there were similar incidence rates of treatment emergent adverse events when compared with reference adalimumab. Members considered that the proportion of dermatology patients with stable disease who cease adalimumab treatment annually secondary to loss of response or intolerance would be low, with this proportion likely to remain unchanged following transition and uptake of a biosimilar adalimumab.

2.10 Members discussed the disease spectrum of ocular inflammation and noted that a proportion of patients are considered to have more aggressive disease, placing them at a greater risk of vision loss, and considered this risk could impact the level of anxiety associated with switching these patients to a biosimilar adalimumab product. Members noted a retrospective observational study (Fabian. et al. Frontiers in Pharmacology 2019;10:1-6.), which indicated no statistically significant difference in the frequency of flares and number of patients experiencing ocular flares in the period prior to biosimilar switch and afterward. Members noted that 18% of patients in the study, without prior history of uveitis flares preceding a biosimilar switch, experienced a disease flare during the 12 months following switch to a biosimilar. Members considered that for some patients, a disease flare could be associated with significant impacts, including long term impacts on vision. Members noted this study included a number of TNF inhibitors and predominantly assessed switching of infliximab, however considered this represented the paucity of evidence regarding adalimumab biosimilar usage and switching in uveitis.

2.11 Members noted that, depending on the outcome, a competitive process for adalimumab could result in the first switch for many patients to a biosimilar; however,

acknowledged that biosimilars were being developed and used in growing frequency internationally.

2.12 Members considered it would be important to establish confidence for prescribers and other groups regarding biosimilar adalimumab in order to support any future implementation, noting the management of any switch would likely be shared between both secondary and primary care including General Practitioners, nurses and pharmacists. The combined Subcommittees recommended clear evidence-based information and guidance for clinicians involved in prescribing and dispensing adalimumab, noting this would help to increase both prescriber and patient confidence in treatment efficacy. Members considered that many clinicians would be comfortable with the evidence supporting biosimilar usage, but support would be needed in managing possible clinician and patient anxiety regarding switching to a new product.

2.13 The combined Subcommittees considered that available evidence favoured switching the majority of patients to a biosimilar; however, acknowledged that this evidence was limited in the switching of patients with uveitis, particularly patients with severe disease including history of vision loss, and that this presented clinical risk in light of the effects of any irreversible loss of vision.

2.14 Members considered that there is 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 whether or not there was a switch to a biosimilar. The combined Subcommittees considered that in the event of a switch to a biosimilar, there would be patients who experience adverse events that they may attribute erroneously to the switch, driven by a perception of the biosimilar being less efficacious. Members considered that clear communication of the evidence to support the use of biosimilars as well as adequate information, education and reassurance for healthcare professionals and patients would be required to help reduce this perception.

2.15 The combined Subcommittees considered there is likely to be a subset of patients with heightened anxiety around any change in brand who would be more likely to experience possible nocebo effect following a change; however, considered that identifying these patients prior to any change would be challenging. Members considered comprehensive clinician support and education was valuable for these patients in managing patient concerns. Members noted that prescribers of patients with uveitis may have concerns regarding a change and considered this was likely based on the limited evidence for switching in this group compared to dermatology and rheumatology indications.

2.16 The combined Subcommittees considered that the majority of dermatology patients would be able to successfully switch to a biosimilar adalimumab. However, the combined Subcommittees considered that a mechanism was needed for PHARMAC to consider patients who were unable to switch or had tried and experienced an adverse event following a switch, noting that based on the available evidence, the number of these patients should be low.

2.17 The combined Subcommittees noted Principal Supply Status was a possible management tool for the majority of indications for which adalimumab was used, which would enable some patients to remain on, or switch back to, their originator adalimumab. The combined Subcommittees noted that widened access, both to new indications and widened access to enable greater flexibility of dosing, as well as longer renewal times, would likely assist in both patient and clinician acceptance of a change.

2.18 The combined Subcommittees considered that the use of biosimilars was likely to increase in the future as more products come off patent, and international evidence, and use, increased.

2.19 The combined Subcommittees noted there is a range of different formulations of adalimumab available, including citrate-free formulations and auto-injector devices. The combined Subcommittees considered that there were patients who experience pain associated with the subcutaneous injection of adalimumab; however, considered it was unclear what the direct cause of this pain was and considered it was likely to be a combination of factors. The combined Subcommittees noted some patients experienced pain upon injection, and that this was a barrier to commencing treatment for some patients, particularly in children, but considered that very few, if any, patients ceased treatment due to injection related pain. The combined Subcommittees considered that overall, the benefit of treatment generally outweighed any short-term injection related pain, and whilst there may be some benefits in assisting patients switching to a product likely to result in less pain such as a citrate free formulation, this should not be at a cost to the Pharmaceutical Budget.

2.20 The combined Subcommittees noted there was a range of device and training considerations relevant to the use and administration of adalimumab treatment. Members noted that the majority of patients self-administered treatment, with the exception of children, who typically had treatment administered by a parent or caregiver. The combined Subcommittees considered that an easy to use adalimumab device was an important consideration, particularly the size of the device and ease of administration, noting the preference for different device types varied by indication.

2.21 The combined Subcommittees noted AbbVie funded the nurse support available for patients when initiating on Humira treatment and considered this was well-accessed by patients. Members considered this support was valued in assisting patients leaning how to self-inject, particularly in remote regions where access to available healthcare professionals is limited. Members noted this service extended to include a mechanism for disposal of syringes and sharps for patients and considered the education resources provided to patients was varied to suit a range of different needs, including the requirement for resources in various languages.

2.22 The combined Subcommittees considered that a seven-month transition period in the event of a brand change was reasonable, and noted that some patients, particularly those with stable dermatological conditions, may be seen by their specialist infrequently and typically receive renewal treatments via their General Practitioners, particularly given the short time frame of renewal applications (six months). The combined Subcommittees considered that to improve practicality and reduce the ongoing administration burden on prescribers, consideration could be given to extending the Special Authority renewal duration from six-months to twelve months.

2.23 The combined Subcommittees considered that, whilst adalimumab treatment is typically initiated at a secondary care level by specialists, ongoing treatment management including applications for Special Authority renewals was often managed within primary care. Members considered any change to the brand of adalimumab could therefore put pressure on already constrained resources both in secondary and primary care, particularly for patients experiencing heightened anxiety regarding a change that required further support from their specialist. Members considered that General Practitioners and Pharmacists would therefore play a significant role, and considered assistance with the switching of patients could be successfully managed within these primary care groups but considered it was important that appropriate

counselling, communication, and practical education support was available to assist in the navigation of any change.

2.24 The combined Subcommittees 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.