Dermatology Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC)

Meeting held on 20 October 2017

(minutes for web publishing)

Dermatology Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2016.*

Note that this document is not necessarily a complete record of the Dermatology Subcommittee meeting; the relevant portions of the minutes relating to Dermatology Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Dermatology Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 8 & 9 February 2018, the record of which will be available in due course.

Record of the Dermatology Subcommittee meeting held at PHARMAC on 20 October 2017

1 Record of previous minutes

1.1 The Subcommittee noted the record of the previous meeting that took place on 30 November 2015 and accepted that they were an accurate record of the meeting.

2 Factors for Consideration

2.1 The Subcommittee noted a presentation by PHARMAC staff outlining PHARMAC's new decision-making criteria, the Factors for Consideration (FFC), which replaced the previous nine Decision Making Criteria on 1 July 2016. Members noted that all recommendations made by the Subcommittee should be now provided in the context of the FFC.

3 Therapeutic Group Review

3.1 The Subcommittee noted the decline in use of isotretinoin 20mg and greater increase in use of the 10mg presentation. Members considered this reflected current best clinical practice to use lower average doses.

3.2 The Subcommittee noted that while prescriptions had declined for fusidic acid cream and mupirocin ointment, there was a significant increase in use of fusidic acid ointment. Members considered that in the interests of antimicrobial stewardship, use of these topical antibiotics should be restricted. The Subcommittee **recommended** that the following endorsement be applied to fusidic acid cream and ointment, and mupirocin ointment:

> Second-line after inadequate response to a minimum 48-hour trial with a non-antibiotic alternative, and the prescription is endorsed accordingly.

3.3 The Subcommittee noted the relatively low usage of podophyllotoxin solution for warts and requested that a salicylic acid product of 30-40% strength in colloidon flex be added to the next Tender.

Other treatments of relevance: biologics for chronic plaque psoriasis

3.4 The Subcommittee noted a request submitted to PHARMAC on behalf of the New Zealand Dermatological Society to consider amending the funding criteria for biologics (adalimumab, etanercept and infliximab) used for plaque psoriasis; in particular to lower the PASI entry criteria and include the Dermatology Life Quality Index (DLQI). Members noted that the rationale for the change is international alignment and to address the unmet health need of a small group of patients who have severe psoriasis but PASI scores in the 10-14 range.

3.5 The Subcommittee noted that the current PASI entry score is greater than 15. Members considered that there is a small group of patients (approximately 40) with severe psoriasis who are currently not eligible for treatment as their PASI scores are below 15 but are not responding well to conventional non-biological psoriasis therapies.

3.6 The Subcommittee noted that current international clinical practice is to commence biologic therapies in psoriasis patients with PASI of over 10 where those patients have tried and not responded to or been intolerant of non-biologic therapies.

3.7 The Subcommittee noted that the DLQI was developed in 1994 and is a frequently used instrument in randomised controlled dermatology trials. Members considered that the DLQI is the best tool currently available, is well-validated and simple to use, the latter being especially important in a clinical setting where time is a finite resource.

3.8 The Subcommittee noted that the DLQI comprises 10 questions, with a maximum possible score of 30. A score of 0-1 represents no disease effect on the patient's quality of life; a score of 6-10 is moderate effect; a score of 11-20 is a very large impact; and a score of 21-30 is extreme impact on quality of life. The Subcommittee noted the minimal important clinical difference was a reduction by 4.

3.9 The Subcommittee considered that while there is reasonable correlation between PASI and DLQI at baseline, there is often a delay of up to 12 months before the DLQI reflects an improvement in PASI due to the time it takes for patients to accept and mentally recalibrate their perception of the change in their disease severity and its reduced impact on their quality of life.

3.10 The Subcommittee considered that the DLQI instrument was appropriate for inclusion in the Special Authority renewal criteria and of clinical value as a measure of adequate response to biologic treatment. Members considered that a DLQI reduction of five or more was a clinically appropriate indicator of response to biologic treatment.

3.11 The Subcommittee **recommended** that the PASI entry score in the Special Authority initial application criteria be lowered from "greater than 15" to "greater than 10" for the funded biologics used in severe chronic plaque psoriasis.

3.12 The Subcommittee **recommended** that a DLQI reduction of five or more be added to the Special Authority renewal criteria for the biologics funded for severe chronic plaque psoriasis, in addition to the current PASI 75 reduction, as an alternative assessment of treatment response.

3.13 The Subcommittee considered that the Special Authority renewal period of six months for biologics funded for psoriasis remained appropriate.

4 Topical pimecrolimus for atopic dermatitis

Application

4.1 The Subcommittee reviewed a funding application from a supplier for pimecrolimus 1% ointment for mild to moderate atopic dermatitis of the face and/or eyelids.

Recommendations

4.2 The Subcommittee recommended that pimecrolimus 1% ointment be listed, without a Special Authority, on the Pharmaceutical Schedule for all patients with atopic dermatitis only if cost-neutral to hydrocortisone acetate 1% cream.

4.3 The Subcommittee recommended that pimecrolimus 1% ointment be listed on the Pharmaceutical Schedule, with a low priority, only for atopic dermatitis on eyelids and subject to the following Special Authority criteria:

> **Special Authority for Subsidy**
> **Initial application** only from a dermatologist, paediatrician or ophthalmologist. Approvals valid for 6 months for applications meeting the following criteria:
> All of the following:
> 1. The condition must be on the eyelid; and

2. The patient must have at least one of the following contraindications to topical corticosteroids: periorificial dermatitis, rosacea, documented epidermal atrophy,documented allergy to topical corticosteroids, cataracts, glaucoma, or raised intraocular pressure; and
3. A maximum of 15 g in 6 months will be subsidised.

Renewal any relevant practitioner. Approvals valid for 6 months where the treatment remains clinically appropriate and the patient is benefiting from treatment. A maximum of 15 g in 6 months will be subsidised.

Note the following restrictions would apply:

a) Only on a prescription
b) Maximum of 15 g per prescription.

Discussion

4.4 The Subcommittee noted that pimecrolimus is a topical immunomodulator and belongs to the immunosuppressant class of calcineurin inhibitors, which has a different mechanism of action to topical corticosteroids (TCS).

4.5 The Subcommittee noted that no topical calcineurin inhibitors are currently funded in New Zealand but a range of varying potency TCS are funded for the management of atopic dermatitis (AD). Members considered that the main clinical comparator for pimecrolimus is a low potency TCS (e.g. 1% hydrocortisone acetate) and topical tacrolimus (the latter is not registered or available in New Zealand).

4.6 The Subcommittee noted the 2007 Cochrane Review (Ashcroft DM et al. CDC005500) of 11 randomised controlled trials (RCTs) using topical pimecrolimus for AD, which found it to be more effective than vehicle but less effective than betamethasone valerate 0.1%. Members noted that while pimecrolimus prevented more acute flares of AD than vehicle (placebo), there is an absence of studies comparing the efficacy of pimecrolimus with less potent topical corticosteroids.

4.7 The Subcommittee considers that the clinical efficacy of topical pimecrolimus is comparable to hydrocortisone acetate 1% cream.

4.8 The Subcommittee noted the 5-year PETITE study (Sigurgeirrson et al. Paed 2015;135:597-606), which primarily investigated (and confirmed) the long term safety of pimecrolimus but also showed similar efficacy between pimecrolimus and 1% hydrocortisone or 0.1% hydrocortisone butyrate.

4.9 Members also noted the Broeders et al (J Am Acad Dermatol 2016; 75:410-19) systematic review of 12 RCTs, published since the 2007 Cochrane Review, that compared topical calcineurin inhibitors (pimecrolimus or tacrolimus) with TCS. Similar rates of improvement in dermatitis and treatment success were seen for all groups. The Subcommittee considered that this review confirmed TCS remain an effective and appropriate first-line treatment for AD.

4.10 The Subcommittee noted the Kempers et al (J Am Acad Dermatol 2004;51: 515-25) study comparing pimecrolimus 1% with tacrolimus 0.03%, which found similar efficacy in paediatric patients with moderate AD.

4.11 The Subcommittee noted that Paller et al (J Am Acad Dermatol 2005;52:810-22) found pimecrolimus to be less effective with a slower onset of action than tacrolimus but similar in adverse events when used in adult and paediatric patients with mild to severe AD.

4.12 The Subcommittee considered that the funding application included a large number of references but many used a topical (inactive) vehicle as the comparator. Members

considered that there remains an absence of clinical trials comparing low-potency topical corticosteroids (a more appropriate comparator) with topical pimecrolimus for mild to moderate AD.

4.13 Members considered that the health need of patients with AD is high, as this is a common disease (up to 20% of children and 5% of adults, with a prevalence of 15% and 16%, respectively, in Māori children and Pacific Island children) that can have a significant impact of quality of life. Conversely, the Subcommittee considered the incidence of TCS adverse effects to be low and that the majority of patients would be adequately managed with TCS. Due to this latter point, the Subcommittee considered that it would be difficult to estimate the potential usage of topical pimecrolimus based on prevalence data.

4.14 The Subcommittee noted that burning was the most common application site reaction occurring with topical pimecrolimus. Luger et al (J Dermatological Treatment 2004:15;169-78) found 25.9% of patients using pimecrolimus experienced skin burning compared to 10.9% of TCS users.

4.15 The Subcommittee noted that potential safety concerns about lymphoma and malignancy, raised in Europe in 2006, have not been substantiated following a decade of monitoring and analysis of various cancer registries. Members noted that topical calcineurin inhibitors have not been found to cause cataracts, glaucoma or skin atrophy. However, members also considered that much of TCS phobia is unfounded as serious side effects arising from appropriate use of TCS are very rare.

4.16 The Subcommittee considered that the overall strength and quality of the evidence appraised suggests topical pimecrolimus has no clear advantage over TCS in AD. There are insufficient studies comparing pimecrolimus directly with TCS or topical tacrolimus. The Subcommittee considered that pimecrolimus would be either used instead of or in combination with TCS.

4.17 Members noted that the funding application was specifically for use of pimecrolimus on the face and/or eyelids. Members considered that there is nowhere on the body (including the face and eye area) where TCS cannot be used, and that potency of TCS and duration of use are the key determinants guiding the appropriate choice of TCS for use on the face and eye area.

4.18 Members expressed concern that while topical pimecrolimus is a niche product for a narrowly defined indication, there is a significant risk of use outside the intended indication. This could possibly be contained by a subsidy restriction maximum of 15 gram per prescription, which would help limit the extent of off-label use for a wider range of skin conditions.

4.19 The Subcommittee identified that there may be an unmet health need in patients with persistent eyelid dermatitis for whom TCS are contraindicated due to glaucoma or the presence of risk factors for glaucoma, or where other TCS contraindications exist.

4.20 The Subcommittee considered that the Special Authority criteria proposed by the supplier was not appropriate because mild to moderate AD not controlled by TCS is unlikely to respond to topical pimecrolimus. Members also considered the maximum quantity proposed by the supplier of 30 grams in six months to be excessive for use on the eyelids.

5 Topical tacrolimus for atopic dermatitis

Application

5.1 The Subcommittee reviewed a funding application from a clinician for tacrolimus ointment (0.03% and 0.1%) for moderate to severe atopic dermatitis, especially on the face/neck.

Recommendations

5.2 The Subcommittee recommended that tacrolimus ointment (0.03% and 0.1%) be listed on the Pharmaceutical Schedule, with a high priority, for facial atopic dermatitis not controlled by appropriate use of a mid-potency topical corticosteroid and prescribed only by, or on the recommendation of, a dermatologist or paediatrician; and subject to the following Special Authority criteria:

Special Authority for Subsidy
Initial application only from a dermatologist or paediatrician, or medical practitioner on the recommendation of a dermatologist or paediatrician. Approvals valid for 6 months where the patient has atopic dermatitis of the face, which is not controlled by appropriate use of a mid-potency topical corticosteroid.

Renewal from a dermatologist or paediatrician, or medical practitioner on the recommendation of a dermatologist or paediatrician. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1. treatment remains clinically appropriate; and
2. the patient is benefiting from treatment; and
3. the patient has trialled a 2-week break from treatment and relapse has occurred; and
4. the patient must not receive more than 30 g per 3 months.

Note the following restrictions would apply:

a) Only on a prescription
b) Maximum of 30 g per prescription.

Discussion

5.3 The Subcommittee noted that topical tacrolimus belongs to the immunosuppressant class of calcineurin inhibitors, and that there is currently no registered product in New Zealand (or Australia). Members noted that one supplier has expressed interest in seeking registration, depending on the outcome of the Subcommittee's consideration of the funding application.

5.4 Members considered that 15-20% of children and 5% of adults have AD, with a higher prevalence of 15% in Māori children and 16% in Pacific Island children. The Subcommittee considered that there is a high health need by patients with moderate to severe AD, which comprises 10% of the affected population.

5.5 The Subcommittee noted a meta-analysis of 25 randomised controlled trials (RCTs) by Ashcroft DM et al (BMJ 2005;330:516) that included 14 trials using tacrolimus 0.1% and found it to be as effective as the mid-potency topical hydrocortisone butyrate 0.1%; and found tacrolimus 0.03% less effective than hydrocortisone butyrate 0.1% but more effective than the low-potency topical hydrocortisone acetate 1%.

5.6 The Subcommittee considered the systematic review by El-Batawy et al (J Dermatol Sci 2009;54:76-87), which included ten RCTs using tacrolimus and nine with pimecrolimus; and a total of 7378 patients of whom 2771 used tacrolimus, 1783 used pimecrolimus, and 2824 were controls. Members noted the findings that for moderate to severe AD,

tacrolimus 0.1% and 0.03% were as effective as moderate potency topical corticosteroids, and more effective than mild topical corticosteroids.

5.7 The Subcommittee considered the 2015 Cochrane Review (Cury Martins et al. CD009864) of 20 studies that found tacrolimus 0.1% was better than low-potency corticosteroids, pimecrolimus 1%, and tacrolimus 0.03%. Tacrolimus 0.03% was superior to mild potency corticosteroids and pimecrolimus 1%. Both tacrolimus 0.03% and 0.1% were comparable to moderate-to-potent corticosteroids.

5.8 The Subcommittee considered the 2004 NICE appraisal (nice.org.uk/guidance/ta82) of ten RCTs using topical tacrolimus for moderate to severe AD, where four of the trials were in children and six in adults. Members noted that in children, a number of measures of treatment effect suggested that tacrolimus 0.03% is more effective than mild topical corticosteroids but that no trials have compared tacrolimus with more potent topical corticosteroids. The Subcommittee noted that in adults, compared with potent topical corticosteroids, tacrolimus 0.1% was statistically significantly more effective in one trial but not statistically significantly different in the other two trials.

5.9 The Subcommittee considered that tacrolimus has a greater therapeutic effect than pimecrolimus and a similar effect to moderately potent TCS. Members considered that topical tacrolimus would be used in place of moderate-strength TCS, and may be of therapeutic value in patients where moderate to severe AD is poorly controlled by moderate-potent TCS.

5.10 The Subcommittee expressed a preference for the higher strength tacrolimus formulation as they considered that the evidence shows greater clinical efficacy and utility for the 0.1% strength than the 0.03% formulation.

5.11 The Subcommittee noted that the 2015 Cochrane Review (Cury Martins et al. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No. CD009864) found burning and itching were more frequent in patients using tacrolimus than topical corticosteroids, but there was no difference in skin infection rates. Tacrolimus showed a longer duration of the local symptoms, between 30 minutes and 12 hours, compared to pimecrolimus users who experienced symptoms for less than 30 minutes. Members noted that burning and itching with tacrolimus was more likely when applied to acutely inflamed skin.

5.12 The Subcommittee noted that, as with the other calcineurin inhibitor pimecrolimus, tacrolimus was thought to be associated with lymphoma and malignancy. Members noted that, in Europe, a decade of clinical experience, epidemiological data, post-marketing surveillance and adverse event database monitoring have failed to demonstrate a causal relationship between topical calcineurin inhibitor use and malignancy.

5.13 The Subcommittee considered that 30 gram would be an appropriate sized pack for use on the face and would help reduce the risk of inappropriate use on other areas of the body or for other indications. Members did not support the listing of larger pack sizes. The Subcommittee identified a fiscal risk with topical tacrolimus in terms of potentially be used for mild AD by prescribers or patients with TCS phobia.

6 Secukinumab for chronic plaque psoriasis

Application

6.1 The Subcommittee considered questions from PTAC about a funding application for secukinumab for severe chronic plaque psoriasis, specifically whether secukinumab should be a first-line or second-line biologic, and if the proposed Special Authority criteria should include the Dermatology Quality of Life Index.

Recommendations

6.2 The Subcommittee recommended that secukinumab, as a second-line biologic following treatment failure with or intolerance to an anti-TNF biologic, for severe chronic plaque psoriasis be funded with a high priority, subject to the following Special Authority criteria:

Special Authority for Subsidy
Initial application — (severe chronic plaque psoriasis – second-line biologic) only from a dermatologist. Approvals valid for 4 months for applications meeting the following criteria:
All of the following:

1. The patient has had an initial Special Authority approval for adalimumab or etanercept or has trialled infliximab for severe chronic plaque psoriasis; and
2. Either:
   - 2.1 The patient has experienced intolerable side effects from adalimumab, etanercept or infliximab; or
   - 2.2 The patient has received insufficient benefit from adalimumab, etanercept or infliximab.

Note: Obtain a baseline Psoriasis Area and Severity Index (PASI) or baseline Dermatology Quality of Life Index (DLQI) for renewal purposes.

Renewal — (severe chronic plaque psoriasis – second-line biologic) only from a dermatologist or medical practitioner on the recommendation of a dermatologist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1. Either
   - 1.1 Patient had "whole body" severe chronic plaque psoriasis at the start of treatment; or
   - 1.2 Patient had severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot at the start of treatment; and
2. Either
   - 2.1 Following each prior secukinumab treatment course, the patient has a PASI score which is reduced by 75% or more (PASI 75) from baseline, or is sustained at this level; or
   - 2.2 Following each prior secukinumab treatment course, the patient has a Dermatology Quality of Life Index improvement of 5 or more, when compared with the pre-treatment baseline value; and
3. Secukinumab to be administered at a maximum dose of 300 mg monthly.

Note: A treatment course is defined as a minimum of 12 weeks of treatment.

6.3 The Subcommittee recommended that secukinumab as a first-line biologic for severe chronic plaque psoriasis be funded with a medium priority, subject to the following Special Authority criteria:

Initial application — (severe chronic plaque psoriasis – first-line biologic) only from a dermatologist. Approvals valid for 4 months for applications meeting the following criteria:
All of the following:

1. Either:
   - 1.1 Patient has "whole body" severe chronic plaque psoriasis with a Psoriasis Area and Severity Index (PASI) score of greater than 10, where lesions have been present for at least 6 months from the time of initial diagnosis; or
   - 1.2 Patient has severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, where the plaque or plaques have been present for at least 6 months from the time of initial diagnosis; and
2. Patient has tried, but had an inadequate response (see Note) to, or has experienced intolerable side effects from, at least three of the following (at maximum tolerated doses unless contraindicated): phototherapy, methotrexate, ciclosporin, or acitretin; and
3. The most recent PASI assessment is no more than 1 month old at the time of application.

Consider obtaining a baseline Dermatology Quality of Life Index (DLQI) for renewal purposes.

Note: "Inadequate response" is defined as: for whole body severe chronic plaque psoriasis, a PASI score of greater than 10, as assessed preferably while still on treatment but no longer than 1 month following cessation of the most recent prior treatment; for severe chronic plaque psoriasis of the face, hand or foot, at least 2 of the 3 PASI symptom sub scores for erythema, thickness and scaling are rated as severe or very severe, and the skin area affected is 30% or more of the face, palm of a hand or sole of a foot, as assessed preferably while still on treatment but no longer than 1 month following cessation of the most recent prior treatment.

Renewal — (severe chronic plaque psoriasis – first-line biologic) only from a dermatologist or medical practitioner on the recommendation of a dermatologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

1. Either
    - 1.1 Patient had "whole body" severe chronic plaque psoriasis at the start of treatment; or
    - 1.2 Patient had severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot at the start of treatment; and
2. Either
    - 2.1 Following each prior secukinumab treatment course, the patient has a PASI score which is reduced by 75% or more (PASI 75) from baseline, or is sustained at this level; or
    - 2.2 Following each prior secukinumab treatment course, the patient has a Dermatology Quality of Life Index improvement of 5 or more, when compared with the pre-treatment baseline value; and
3. Secukinumab to be administered at a maximum dose of 300 mg monthly.

Note: A treatment course is defined as a minimum of 12 weeks of treatment

6.4 The Subcommittee recommended that the Dermatology Quality of Life Index be included in the proposed Special Authority renewal criteria for secukinumab, in addition to a PASI 75 reduction, as an alternative assessment of treatment response.

Discussion

6.5 The Subcommittee noted that PTAC reviewed a funding application from a supplier for secukinumab for severe chronic plaque psoriasis at their August 2017 meeting, and that PTAC recommended secukinumab be funded for the treatment of severe chronic plaque psoriasis, with a medium priority. PTAC additionally requested that advice be sought from the Dermatology Subcommittee as to whether there is a place in having anti-TNF biologics as the first-line biologic, and non-anti-TNF biologics (such as secukinumab) as a second-line biologic. PTAC also requested advice on whether the proposed Special Authority criteria should include the Dermatology Quality of Life Index (DLQI) in addition to the currently used Psoriasis Area Severity Index (PASI) assessment.

6.6 The Subcommittee considered that there is a high health need in patients with severe chronic plaque psoriasis, an incurable chronic skin disease with high rates of treatment failure, high impact on quality of life, high morbidity and up to 30% of patients subsequently develop psoriatic arthritis.

6.7 The Subcommittee considered that there is a clearly identified clinical need for a non-anti-TNF biologic for severe chronic plaque psoriasis, due to the development of anti-TNF antibodies that result in loss of persistence of effect in many patients after approximately four years of treatment.

6.8 The Subcommittee noted that secukinumab is an interleukin (IL) inhibitor selective for IL-17A, and that there are a number of IL-inhibitors coming to the market.

6.9 The Subcommittee noted PHARMAC dispensing data for severe chronic plaque psoriasis showing that in the 2016 calendar year, 510 patients were receiving adalimumab and 206 patients were receiving etanercept. Uptake of both biologics for this indication has approximately doubled since 2012.

6.10 The Subcommittee considered that there is a clinical need to have access to both an anti-TNF and a non-anti-TNF biologics (such as secukinumab). The Subcommittee's advice is that 50-60% of patients with severe chronic plaque psoriasis will respond well to treatment with an anti-TNF agent, therefore, it would be fiscally appropriate to trial an anti-TNF biologic agent first in patients who have had an inadequate response to, or experienced intolerable side effects from, at least three of the following (at maximum tolerated doses unless contraindicated): phototherapy, methotrexate, ciclosporin, or acitretin.

6.11 The Subcommittee considered that there may be a fiscal risk for PHARMAC to fund secukinumab as a first-line biologic. Additionally, of the current patients with psoriasis severe enough to require biologic therapy, very few will be biologic naïve so by default secukinumab would likely be a second-line biologic in this patient group. For these reasons, the Subcommittee gave first-line use of secukinumab a medium priority and second-line use a high priority.

6.12 The Subcommittee discussed whether the development of neutralising antibodies seen with the use of TNF-inhibitors could also occur with secukinumab. Members considered that this may occur but the limited evidence available to date suggests there is low potential for IL-inhibitor antibody development with secukinumab (Karle et al. MAbs 2016;8:536-50).

6.13 The Subcommittee discussed the clinical value of including the Dermatology Quality of Life Index (DLQI) in the proposed Special Authority criteria for secukinumab, which would be in addition to the currently used Psoriasis Area Severity Index (PASI) assessment. The validity and robustness of the DLQI was considered by the Subcommittee in the Therapeutic Group Review section of these minutes.

6.14 The Subcommittee considered that an improvement of five or more in the DLQI score would be an appropriate indicator of adequate treatment response to secukinumab for plaque psoriasis. The Subcommittee notes that this score change represents a minimal clinically important difference and is consistent with therapy guidelines that use DLQI (Basra et al. Derm 2015;230:27-33).

7 Adalimumab for severe hidradenitis suppurativa

Application

7.1 The Subcommittee considered questions from PTAC about a funding application for adalimumab for hidradenitis suppurative; specifically, what Special Authority criteria would be appropriate. PTAC gave the application a low listing priority.

Recommendations

7.2 The Subcommittee recommended that adalimumab for hidradenitis suppurativa be funded subject to the following Special Authority criteria:

Special Authority for Subsidy
Initial application – (hidradenitis suppurativa) only from a dermatologist. Approvals valid for 3 months for applications meeting the following criteria:
All of the following:

1 The patient has had an inadequate response to at least a 90 day trial of systemic antibiotics, unless the patient has demonstrated intolerance to or has contraindications for systemic antibiotics; and
2 The patient has hidradenitis suppurativa Hurley Stage II or Hurley Stage III lesions in distinct anatomic areas; and
3 The patient has 3 or more active lesions (eg. inflammatory nodules, abscesses, draining fistulae); and
4 The patient has a Dermatology Quality of Life Index of 10 or more; and
5 Adalimumab is to be administered at doses no greater than 40mg every 7 days.

Renewal – (hidradenitis suppurativa) only from a dermatologist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1 The patient has a reduction in active lesions (eg. inflammatory nodules, abscesses, draining fistulae) of 25% or more from baseline; and
2 A Dermatology Quality of Life Index improvement of 4 or more from baseline; and
3 Adalimumab is to be administered at doses no greater than 40mg every 7 days. Consideration should be given to fortnightly dosing.

Discussion

7.3 The Subcommittee discussed the proposed Special Authority criteria and made changes to improve the clinical utility of the criteria. Members considered that three months was an appropriate duration for initial adalimumab treatment; and for ongoing use in patients demonstrating adequate response, members considered six months to be appropriate for the renewal criteria period to help reduce patient access barriers to dermatology services.

7.4 The Subcommittee considered that a maximum dose of adalimumab 40 mg weekly was appropriate for hidradenitis suppurativa, but members noted that the PIONEER I and II trials (Kimball et al. N Engl J Med 2016;375:422-34) suggested fortnightly dosing may be adequate for some patients after the first three months of adalimumab treatment.

7.5 The Subcommittee considered that hidradenitis suppurativa is a chronic condition, therefore recommended that no restriction be placed on the length of adalimumab treatment as long as the patient continues to show a positive response.

8 Cubitan – Oral feed supplement to aid in pressure ulcer healing: resubmission of evidence

Application

8.1 The Subcommittee considered a resubmission from Nutricia for the funding of oral feed 1.25 kcal per ml (Cubitan) to aid pressure ulcer healing.

Recommendation

8.2 The Subcommittee recommended that the funding application for Cubitan to aid pressure ulcer healing be declined.

Discussion

8.3 The Subcommittee noted that this application was reviewed by the Special Foods Subcommittee and the Dermatology Subcommittee in December 2013. Both

Subcommittees considered that the evidence for use in pressure ulcers was weak in quality and strength, and a recommendation was deferred until a published study (Cereda et al. Ann Intern Med. 2015;162:167-74) was made available for review.

8.4 The Subcommittee noted that Cubitan is a ready-to-drink nutritional supplement with high levels of arginine, zinc, vitamin C and other components considered to aid in the recovery of pressure ulcers (PU). The Subcommittee considered Cubitan is not nutritionally complete and not intended as a supplement to treat malnutrition.

8.5 The Subcommittee considered that PU can be graded as stage I through IV. Members noted PU patients have a high health need which required a high level of intervention for wound care management and secondary care services. Members considered that many of these patients will be in institutional care and a considerable amount of effort goes into preventing PUs.

8.6 The Subcommittee considered the results of Cereda et al (Ann Intern Med. 2015;162:167-74), a randomised controlled trial in seven centres of Cubitan versus a similar nutritional product with less arginine, zinc and antioxidants in patients with pressure ulcers who were malnourished.

- Members considered that all patients in the trial received optimal PU care and that this is may not be reflective of real world situations. Members also considered that many of the patients in the exclusion group are those seen regularly with pressure ulcers and questioned whether this study would be representative of the PU patient population in New Zealand
- Members considered that the trial results show improvement in PU area at eight weeks, 60.9% (CI, 54.3% to 67.5%) reduction compared with 45.2% (CI, 38.4% to 52.0%) in the control formula group. Members noted however, that it was not clear whether these results were clinically significant as there was no statistical difference in complete healing of PU at eight weeks (OR, 2.16 [CI, 0.88 to 5.39]; p=0.097).
- Members considered that this evidence was of moderate quality and strength. Members considered that it was not clear from the study how this intervention would differ from patients receiving a multivitamin supplement containing arginine.

8.7 The Subcommittee considered the results of an economic evaluation by the same authors of the Cereda et al. 2015 RCT. This study compared cost effectiveness and direct medical costs of local PU care (Cereda et al. Clinical Nutrition. 2017;36:246-52).

- Members considered that the evidence was of low quality and modest benefit. The results provided a cost saving of 3-4 %, however, this result had a large standard deviation and was in a European medical care setting which would be difficult to translate into a New Zealand equivalence.

8.8 The Subcommittee considered a systematic review to assess the effect of arginine-enriched enteral formulas in PU healing (Liu et al. J Wound Care. 2017;26:319-23). This review included seven RCTs and 369 patients, four of which assessed healing by PU area reduction.

- Members considered that sample sizes of the individual studies were small, ranging from 16 to 200 patients.
- Members considered that a number of different outcomes were reported such as PU area, Pressure Ulcer Scale for Healing (PUSH) score and Pressure Sore Status Tool (PSST) score. Outcomes were measured at different follow-up

points (from week 2 to 12 weeks) and quantitative meta-analysis was not possible.

- Members noted that all studies reported arginine-enriched enteral nutrition led to a significant improvement in PU healing, however, these findings need to be supported by large-sample RCTs.

8.9 The Subcommittee considered that the evidence reviewed did not show a significant clinical benefit for an arginine-rich supplement in the treatment of PU above that already available in New Zealand.