Dermatology Subcommittee of PTAC
Meeting held 9 December 2013

(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 2008*.

Note that this document is not necessarily a complete record of the Dermatology Subcommittee meeting; only 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 8 & 9 May 2014, the record of which will be available in July 2014.

Record of the Dermatology Subcommittee of PTAC meeting

held on 9 December 2013

1 Hospital Pharmaceuticals - Advice on Dermatological Products requested for listing by District Health Boards (DHB's) post implementation of the Hospital Medicine List (HML)

Bepanthen Cream for excoriated buttocks

1.1 The Subcommittee noted that following the implementation of the Hospital Medicine List (HML), PHARMAC has received requests from various District Health Boards (DHB's) to list products that were not included in the HML. Members noted these requests were largely from long term units (psychiatric or geriatric) or neo-natal units.

1.2 The Subcommittee noted that PHARMAC has received a request from Southern DHB to list Bepanthen Cream. Members noted that the product is used in the Neonatal Unit for excoriated buttocks.

1.3 The Subcommittee noted that there was some weak evidence for efficacy (Ebner et al Am J Clin Dermatol. 2002; 3:427-33). Members considered that it was unclear whether Bepanthen cream should be compared to barrier creams in terms of its therapeutic actions for excoriated buttock skin.

1.4 The Subcommittee considered there was a lack of strong evidence and **recommended** listing Bepanthen Cream only if cost neutral to zinc and castor oil.

Oralife Peppermint Lip Treatment for the prevention of dry lips and dryness of the mouth in the inpatient setting (for palliative care)

1.5 The Subcommittee noted that PHARMAC has received a request from Canterbury DHB for Oralife Peppermint Lip Treatment for the prevention of dry lips and dryness of the mouth in the inpatient setting (for palliative care).

1.6 Members noted the product contains peppermint oil BP 5.3mg/g, wool fat BP 53mg/g, and chlorhexidine gluconate 1mg/g in a paraffin base.

1.7 The Subcommittee **recommended** listing Oralife Peppermint Lip Treatment in the HML only if cost neutral to White Soft Paraffin. "

2 TNF inhibitor therapy in Behçet's Disease

Application

2.1 The Subcommittee noted that PHARMAC had received an application from the New Zealand Rheumatology Association for the funding of TNF inhibitors for patients with Behçet's disease for patients who are refractory to conventional therapy.

Recommendation

2.2 The Subcommittee **recommended** listing infliximab first line as a high priority with entry and exit restrictions.

2.3 The Subcommittee **recommended** listing adalimumab second line as a medium priority with entry and exit restrictions.

Discussion

2.4 The Subcommittee noted that there are 16 patients in New Zealand with Bechets Disease.

2.5 The Subcommittee noted that PTAC had reviewed TNF inhibitors for patients with Behçet's disease at its meeting in August 2013 and had recommended the following:

2.6 The Committee recommended that a TNF inhibitor should be listed in the Pharmaceutical Schedule for patients with severe Behçet's Disease refractory to conventional therapy, with a medium priority. Members considered that although the evidence for efficacy of the individual TNF inhibitors was variable, it is likely they would all provide similar outcomes; therefore the Committee recommended that the funded TNF inhibitor should be the one associated with the lowest cost.

2.7 The Subcommittee noted that PTAC had further **recommended** the application be referred to the Dermatology and Ophthalmology Subcommittees for advice on specific Special Authority criteria and if they had any preference for the specific TNF(s) to be funded.

2.8 The Subcommittee noted that Behçet's Syndrome is a multisystem, relapsing, chronic vasculitic disorder with prominent mucosal inflammation. Common manifestations include recurrent oral ulcers, ocular inflammation, genital ulcers, inflammatory arthritis and skin lesions. Members noted that the most serious manifestations are blindness, neurologic or GI manifestations, venous thrombosis, and arterial aneurysms which may be life threatening. The Subcommittee discussed the clinical possibility of incomplete forms of Behçet's Disease and the need to include this option in funding requests.

2.9 The Subcommittee noted that the International Study Group (ISG) Initial criteria for diagnosis of Behçet's Disease require the occurrence of at least 3 episodes of oral herpetiform or aphthous ulcerations within a 12-month period observed directly by a physician or reported by the patient. Members noted that the ISG guidelines to confirm the diagnosis required the demonstration of at least 2 of the following:

- Recurrent painful genital ulcers that heal with scarring
- Ophthalmic lesions, including anterior or posterior uveitis, hypopyon, or retinal vasculitis
- Skin lesions, including erythema nodosum–like lesions, pseudofolliculitis, or papulopustular or acneiform lesions
- Positive results from pathergy skin testing, defined as the formation of a sterile erythematous papule 2 mm in diameter or larger that appears 48 hours following a skin prick with a sharp sterile needle (22-24 gauge [a dull needle may be used as a control])

2.10 The Subcommittee noted that first line treatment options for Behçet's include corticosteroids and/or immunosuppressants such as methotrexate, azathioprine, cyclosporin, tacrolimus and thalidomide and oral colchicine.

Members noted that Behçet's Disease has a considerable impact on quality of life . (Bernabé et al Rheumatology (Oxford) 2010;49:2165-71)

2.11 The Subcommittee considered whether there may be differences between infliximab, etanercept or adalimumab.

2.12 The Subcommittee noted a review by Arida et al (Semin Arthritis Rheum. 2011; 41:61-70) which analysed published data on Anti-TNF for their efficacy and safety for patients with unmet medical needs due to severe manifestations of Behçet's Disease including ocular, gastrointestinal, and central nervous system involvement. The data involved 369 patients. Members noted that the reviewers found 88, 12, and 13 primary articles from 20 countries on infliximab, etanercept, and adalimumab, reporting on 325, 37, and 28 patients, respectively. All patients were inadequately controlled with, or intolerant to, other immunosuppressive regimens, including interferon; 20 patients received more than 1 anti-TNF agent. Members noted that in the only randomised placebo-controlled trial, 4-week administration of etanercept was effective in suppressing most of the mucocutaneous manifestations.

2.13 The Subcommittee noted that in 16 open prospective studies evaluating the effect of repetitive infliximab injections (174 patients in total, men:women =3:1, median follow-up = 16.2 months), sustained organ-specific, clinical responses were evident in 90%, 89%, 100%, and 91% of patients with resistant mucocutaneous, ocular, gastrointestinal, and central nervous system involvement, respectively. Members noted that the combination of infliximab with azathioprine and/or cyclosporine-A appeared superior to monotherapy for sustained ocular remission.

2.14 The Subcommittee noted that most of the evidence related to infliximab but there was evidence for the other anti-TNF agents. Members consider that there was some evidence to support switching between anti-TNF agents, (for compliance reasons and/or when the first anti-TNF fails).

2.15 The Subcommittee noted a short-term trial, double blind, placebo controlled study of etanercept in Behçet's Disease (Melikoglu et al J Rheumatol. 2005; 32:98-105. Members noted that the trial included forty male patients with BD, who were randomised (20 patients to each study arm) to receive either etanercept 25 mg twice a week or placebo for 4 weeks. The pathergy and monosodium urate (MSU) responses and the frequencies of mucocutaneous and articular manifestations were compared between the 2 groups. Members noted that there were no decreases in the pathergy and MSU responses in the etanercept group compared to the placebo group at any time. The Subcommittee noted that the mean numbers of oral ulcers, nodular lesions, and papulopustular lesions were less in the etanercept group compared to the placebo group at all weekly evaluations, except for the second week for papulopustular lesions. Members noted that the probability of being free of oral ulcers and nodular lesions was also significantly higher in the entanercept group (log-rank chi-square = 9.83, p = 0.0017; log-rank chi-square = 14.17, p = 0.0002, respectively).

2.16 The Sub-Committee considered that the quality of the evidence was weak to moderate, whilst the strength of the effect of the anti-TNF's in the treatment of Behçet's Disease was moderate to good.

2.17 The Sub-Committee noted infliximab is the preferred treatment option but that a number of patients improve when switched from one TNF to another. The Subcommittee considered that interferon-alpha would be the direct comparator to the TNF inhibitors. Members considered that the anti-TNF agents would be used in addition to second line agents, which reflect how they were used in the clinical studies.

2.18 The Subcommittee noted that there would be other non-direct health sector cost associated with anti-TNF agents, such as chest X rays to screen for the possibility of latent tuberculosis. Members considered such costs would not be significant when compared to drug acquisition costs.

3 Cavilon Durable Barrier Cream for maintaining skin integrity

3.1 The Subcommittee considered an application from 3M New Zealand for the funding of Cavilon Durable Barrier Cream containing moisture barrier properties and durable properties. Members noted that the cream is registered in New Zealand as a moisturising dressing. The application is for product use in hospital only.

3.2 The Subcommittee considered that the evidence provided in support of this application was of poor quality.

3.3 Members noted that the studies primary focus was application of the product for incontinent patients and not its other uses such as application around ostomy sites or the dressing of ulcers and wounds.

3.4 The Subcommittee noted the Beckman et al paper (Joumal of Advanced Nursing January 2009, 1141-5) used a poor methodology, with no standardization of definition, diagnosis and assessment. The numbers in the study were small and there was a short period of follow-up. The study was based on a combination of products.

3.5 The Subcommittee noted the Large J paper (British Joumal of Nursing 2011(Tissue Viability Supplement), 20; S22-S25) was funded by 3M. The baseline incidence of pressure ulcers was unclear and the care was provided in combination with other products. During the 6 month pilot only one patient ulcerated – an incidence of 1.28%.

3.6 The Subcommittee noted the other studies within the supplier application provided evidence of poor quality as the studies were based on a combination of products being used rather than the individual product under application. Members noted there was no impartial data.

3.7 The Subcommittee considered that there was some unmet health need in wound management including leg ulcers in that tape and adhesive dressings does not adhere to other proprietary products. The Subcommittee noted that the supplier recommends the concomitant use of the wash and spray when Cavilon Barrier Cream is used for the management of the effects of incontinence.

3.8 Members **recommended** listing Cavilon Barrier Cream with a medium priority.

The decision criteria particularly relevant to this recommendation are:
(i) The health needs of all eligible people within New Zealand; (iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; (v) The cost – effectiveness of meting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services; vi) The budgetary impact (in terms of the pharmaceutical budget and the Governments overall health budget) of any changes to the Pharmaceutical Schedule; (vii) The direct cost to health service users

4 Cubitan oral feed - request for application review

4.1 The Subcommittee considered a request from the Special Food Subcommittee meeting held on 5 December 2013 to review Cubitan oral feed for the treatment of pressure ulcers. Members noted that the Special Foods Subcommittee may then use this information to address these specific questions:

I. Would the use of Cubitan result in an improvement in the quality of life?

II. What cost savings would be achieved by funding Cubitan?.

4.2 The Subcommittee noted that Cubitan contains arginine whose pharmacological action is to increase the deposition of collagen in wound healing. Members noted the guidelines for the maximum safe dose of arginine supplementation in humans have not been published.

4.3 The Subcommittee noted that there are no products containing arginine currently funded in New Zealand.

4.4 The Subcommittee noted the clinical evidence provided with studies researching the cost associated with pressure ulcer prevalence:

- Banks et al (Clinical Nutrition 2010; 29: 180-186) Statistical modelling study from public hospitals in Queensland using data from 2002/3. Cost of pressure ulcers is AUS$13 (SD 4) million in bed days.
- Bennet et al (Age and Aging 2004; 33 (3): 230-235) cost of pressure ulcers in UK. A bottom-up costing approach was used: £1,064 (Grade 1) to £10,551 (Grade 4). 412,000 individuals will develop a new pressure ulcer annually in the UK. Total cost estimated at £1,769 million per year.
- Elia et al (Nutrition 2005; 21: 1100-1106). A secondary analysis of data collected prospectively by the National Diet and Nutrition Survey of people aged 65 years and older was undertaken to assess geographical prevalence of risk of protein-energy malnutrition (1155 subjects) and nutrient status (881 to 1046 subjects).
- Gethin et al (Journal of Wound Care 2005; 14: 162-165) Irish study of costs of pressure ulcers. 2.5% of in-patients have grade IV pressure ulcers at an average cost of Euro 199,000/each or 205 million/year.
- Shahin et al (Nutrition 2010; 1-4) A cross-sectional study of 2393 patients from 29 German nursing homes and 4067 patients from 22 hospitals participated in the study. There was a significant relationship

between malnutrition parameters including undesired weight loss, BMI < 18.5, and low nutritional intake and PU.

4.5 Subcommittee members noted that overall the other studies submitted in the application regarding the benefit of arginine were weak in quality and strength.

4.6 The Subcommittee considered the question from the Special Foods Subcommittee asking if the use of Cubitan would result in an improvement in quality of life. Members commented that there was insufficient data to critically appraise quality of life, however due to the patient demographics quality of life was probably not greatly improved. Members noted that the improvement would be demonstrated by the healing of the ulcer. Members further noted that full healing of the ulcer was required for the result to be considered clinically significant.

4.7 The Subcommittee considered the second question from the Special Foods Subcommittee asking what cost-savings (if any) would be achieved by funding Cubitan. Members noted this was not possible to calculate and costs would have to be compared to other supplements such as zinc capsules.

4.8 The Subcommittee noted that overall the evidence to support the use of Cubitan was weak. Members considered that there may be a benefit from the addition of arginine improving nutrition leading to an improvement of healing. The Subcommittee considered Cubitan should only be listed if cost neutral to other supplements as at this time there is insufficient evidence to indicate product superiority.